Tetrahedron Vol. 48, No. 15, pp. 3147-3162, 1992
Printed in Great Britain

0040-4020/92 $5.00+.00

Influence of Functional Substitution of Allyl Halides on their $Ni(CO)_4$ Promoted Carbonylative Cycloaddition with Acetylenes

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(*Received in UK* 3 *February* 1992)

Key Words: Allyl halide; π-Allyl nickel; cycloaddition; cyclopentenones; cyclohexenones.

***Abstract**: The effect of functional substitution of allyl halides on the outcome of the title reaction has been studied. Electron withdrawing and olefinic groups had different effects depending on their location. When they were placed at the central position of the allyl moiety carbonylative cycloaddition was found to be the main reaction, in acetone, to yield exclusively cyclohexenone (or aromatic) derivatives. In contrast, the same groups at the terminal site and in extended conjugation with the allylic funtion were shown to favour competing side reactions such as allyl self-coupling. However, only cyclopentenones were obtained from either centrally or terminally substituted silylallyl halides. Substitution at both ends of the allyl moiety led to the formation of 4,5-disubstituted cyclopentenones. Important mechanistic information could be achieved from determination of the relative stereochemistry in these compounds.*

INTRODUCTION

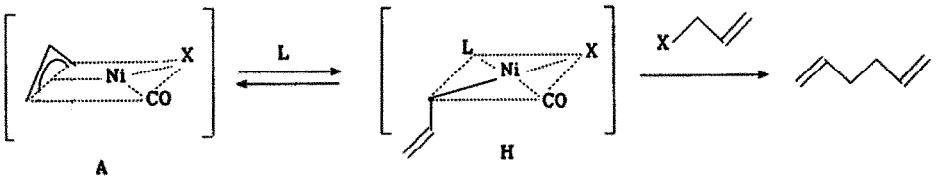
Recently, we restudied the $Ni(CO)_4$ promoted carbonylative cycloaddition of allyl halides and acetylenes, a reaction previously reported by G.P. Chiusoli and coworkers[1], and we showed that it was suitable for obtaining moderate to good yields of cyclopentenone derivatives by appropriate choice of the reaction conditions[2].

In all cases, provided that steric effects were not very severe, the regioselectivity of the reaction was ruled by the acetylene polarization, the allyl moiety being inserted at the negative end of the triple bond dipole. Although, in our hands, this procedure proved to be highly efficient in the synthesis of different cyclopentenone

systems[3,4], we wanted to gain a further insight into the scope of this reaction by studying the influence of allyl substitution on its outcome.

RESULTS AND DISCUSSION

Our preliminary results from the reaction of 1-methoxybut-2-yne with 1- (or 3-) alkyl substituted allyl halides showed that this substitution did not affect the regioselectivity and the yield of the reaction. The acetylene always attacked the less substituted end of the allyl group leading to cyclopentenones with the alkyl substituted carbon atom as the side chain. When the central position of the allyl derivative was substituted, additional attack on the less hindered terminal carbon atom of the allyl group led to the formation of variable amounts of cyclohexenone derivatives (detected as aromatic products after a presumably easy β-elimination process; Scheme I). A striking feature of this reaction is the electrophilic behaviour of the initially formed π-allyl complex in contrast with the generally admitted nucleophilic character of this moiety[5]. We attributed this uncommon reactivity to the putative formation of a carbonyl π-allyl nickel complex (**A**) that has been spectroscopically detected by other authors in related reactions[6]. Different side reactions can compete with this process. Among them, the most important one turns out to be the coupling of π-allyl moieties to give diallyl derivatives[5].This reaction is favoured by the presence of ligands such as phosphines and CO[6] and/or polar solvents which can promote the isomerisation of the π-allyl complex to the monohapto σ-allyl isomer (**H**, Scheme II). The nucleophilic character of this species would allow a fast reaction with the unreacted allyl halide to give the coupling products. Likewise,this monohapto species **H** would be particularly abundant in cases where allyl groups are bearing π-electron withdrawing substituents, and very little stabilization of complex A by backbonding could be expected.



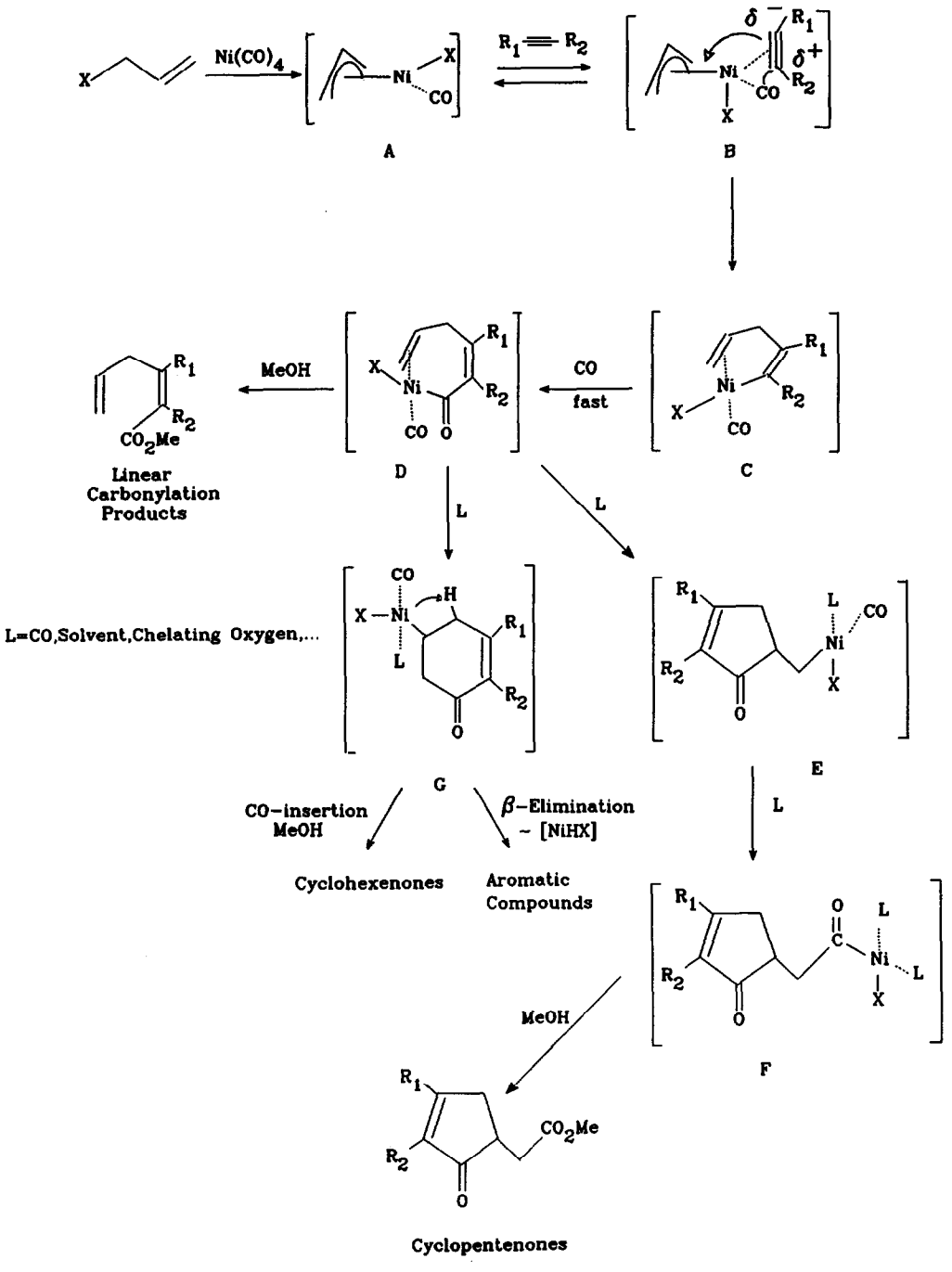
A H

L= Polar Solvent, Ligand, Bridging Halide ...

Scheme II

Alternatively, some recent studies on the coupling of π-allyl nickel complexes with a variety of organic halides, under non carbonylative conditions, proved that they proceeded through a radical mechanism involving the interconversion of Ni(I) and Ni(III) species[7].

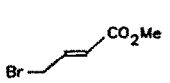
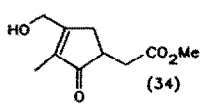
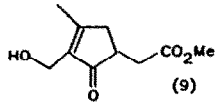
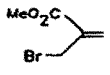
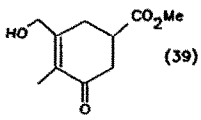
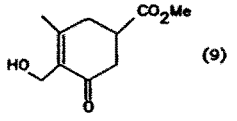
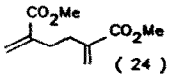
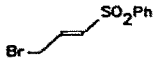
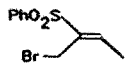
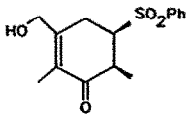
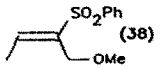
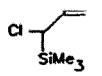
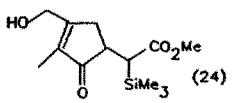
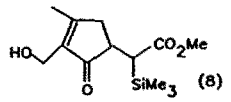
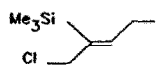
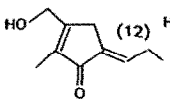
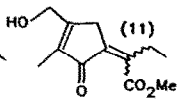
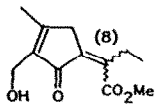
In the light of these considerations we may analyze the results obtained in the carbonylative cycloaddition of 2-butyn-1-ol with different allyl halides. These are shown in Table 1.


Ni(CO)4
A
B
MeOH
CO
fast
D
C
Linear
Carbonylation
Products
L
L
L=CO,Solvent,Chelating Oxygen,...
G
E
CO-insertion
MeOH
β-Elimination
- [NiHX]
L
Cyclohexenones
Aromatic
Compounds
MeOH
F
Cyclopentenones

Scheme I

TABLE I

$Ni(CO)_4$ Promoted Carbonylative Cycloaddition of 2-Butyn-1-ol with Different Allyl Halides

Entry	Allyl Halide	Main Products	(Yield %)[a]	Observations
1	 1	 13	 14	Solvent: acetone[b]
2	 2	 15	 16	Solvent: acetone[c] 
3	 3	 17	(34)	Solvent: acetone 54% of methanolized allyl derivatives
4	 4	 18	(44)	Solvent: acetone[d] 
5	 5	 19	 20	30 % of the original allyl halide recovered
6	 6	 21	 22	 23	14 % of allyl halide recovery Considerable acetylene polyinsertion

a: Yields of isolated cycloadducts referred to reacted acetylene and those from coupling and carbonylation to starting allyl halide

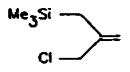
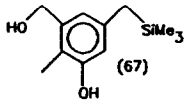
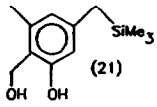
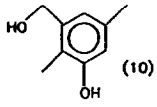
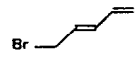
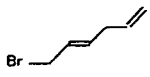
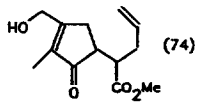
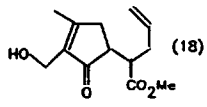
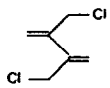
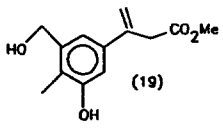
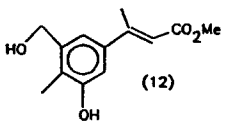
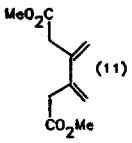
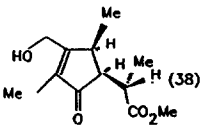
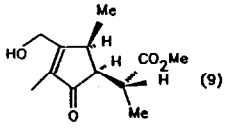
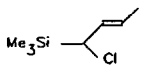
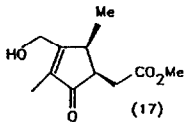
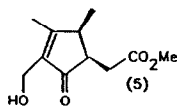
b: In methanol the products were: dimethyl 2,6 -octadienedioate (46%) and dimethyl 2-pentenedioate (20%)

c: In methanol a 13 % of 15 was obtained together with the product from allyl coupling (major product)

d: In methanol only a 35 % of 18 was obtained

TABLE I (Contd·)

$Ni(CO)_4$ Promoted Carbonylative Cycloaddition of 2-Butyn-1-ol with Different Allyl Halides

Entry	Allyl Halide	Main Products	(Yield %)	Observations
7			(67)	
	7	24		
			(21)	
		25		
			(10)	
		26		
8			(40)	Extensive acetylene polyinsertion [e]
	8	27		
9			(74)	
	9	28		
			(18)	
		29		
10			(19)	
	10	30		
			(12)	
		31		
			(11)	
		32		
11			(38)	Important acetylene recovery after sluggish reaction (42 %)
	11	33		
			(9)	
		34		
12			(17)	Important acetylene recovery after sluggish reaction (40 %)
	12	35		
			(5)	
		36		

e: In acetone, no cycloadducts were formed

Electron withdrawing substituents had different effects on the course of the reaction depending on their location in the allyl moiety. When the substituent was present at the terminal position, as in allyl derivatives **1** and **3**, using methanol as solvent, no cycloadducts could be found in the reaction mixture, which consisted almost exclusively of compounds from allyl coupling. However, replacement of most of the methanol by acetone suppressed this coupling reaction for methoxy carbonyl allyl derivative **1** (entry 1) but not in the other case (entry 3).

In contrast, when the substituent was located at the central carbon atom of the allyl group (**2** and **4**), even in methanol, coupling was less important than it was for the extended isomers (**1** and **3**), and in acetone, acetylene insertion took place readily to give the cyclohexenone adducts **15**, **16** and **18** (entries 2 and 4).

Unexpectedly, the outcome of the reaction with the bulky silyl derivatives **5** and **6** was very different; in spite of the fact that these allyl derivatives reacted rather slowly with the $Ni(CO)_4$, possibly, because of their considerable steric hindrance, in both cases cyclopentenone derivatives were isolated as major reaction products (entries 5 and 6). This fact may be rationalized by the carbanionic character conferred by the silicon to the bonded vinylic carbon atom which would facilitate its further attack on the acyl-Ni moiety without prior double bond activation by coordination to the metal. Therefore, in the reaction of **6**, the process can be envisaged as an internal Friedel-Crafts type reaction[8]. The activating role played by the vinylic silicon was evidenced from the reaction of **7**: after removing the silicon substituent by one carbon unit, cyclohexenone adducts were obtained in good yields without any sign of cyclopentenone formation or silyl elimination (entry 7).

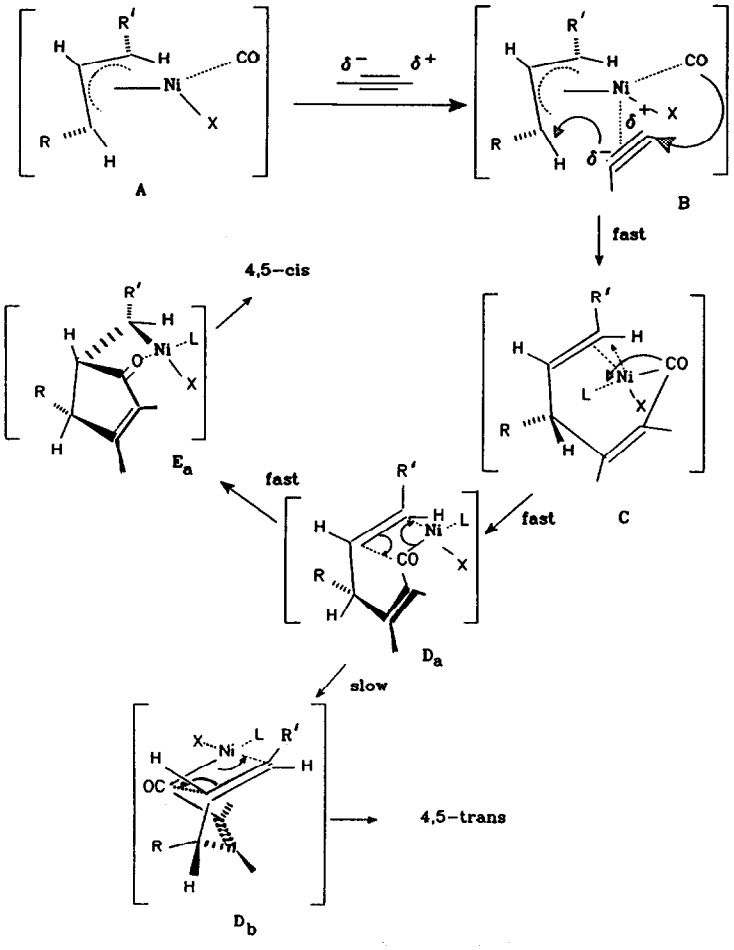
The results from allyl halides containing additional double bonds resembled those obtained in cases 1-4. When the double bond was linearly conjugated with the allyl group, coupling was the main observed process (entry 8). Disruption of this conjugation led to the formation of a very good yield of cyclopentenone derivatives (entry 9). Again, branching the double bond at the central atom of the allyl unit led to moderate production of cyclohexenone adducts with further aromatization and carbonylation (entry 10) (cf. entries 2 and 4). This change in behaviour between extended and branched conjugation towards allyl coupling had also been reported in non-carbonylative conditions[9]. The presence of a second allylic halide has resulted in a further carbonylation without concurrent cycloaddition.

All the results so far obtained show that the π-allyl group inserts the acetylene at its less hindered site. In order to ascertain whether this process was also appropriate for obtaining 4,5-disubstituted cyclopentenones, the reaction with 4-chloro-2-pentene (**11**) was performed, and moderate yields of the corresponding carbonylated cyclopentenones **33** and **34** were obtained. In this case, however, the reaction proceeded at low rate, probably due to a difficult oxidative addition for steric reasons.To further confirm the sensitivity of this reaction to the steric effects of the allyl substituents, an allyl halide, **12**, with two substituents of different size, was selected. In this case, the reaction was slow and consequently yields were low. In spite of this, it was proved that complete steric control may be achieved in this way, since the two regioisomers obtained, **35** and

36, had the alkyl group at the 4-position with the same diastereomeric arrangement (after spontaneous loss of Me_3Si group).

STEREOCHEMICAL INSIGHT

Different stereochemical aspects need to be considered in this reaction. Concerning the regiocontrol found in the acetylene insertion, it appears to be independent of any substitution in the allyl derivative, and it has already been attributed to the electronic effects in the acetylene[2]. Structural assignation of both regioisomers was made on basis of their ^1H NMR spectra[10].



Scheme III

In compounds **33-36**, the relative configurations of the newly created stereogenic centers at C-4 and C-5 are specially relevant to render important mechanistic information. More precisely, the stereochemistry

generated at the C-4 and C-5 positions turned out to be the thermodynamically less favoured *cis*[11] and this evidence should in principle direct us to the most favoured four center intermediate **D**. *A priori*, two coordination modes are foreseen for this intermediate: $\mathbf{D_a}$ and $\mathbf{D_b}$ (Scheme III). Careful inspection of models representing both ligand arrangements gives no clue to any steric difference between them, since they are symmetrical. Therefore, the reason for the resulting diastereoselection must derive from kinetic factors rather than from thermodynamic ones. Thus, if **B** is the only intermediate to be formed and cycloaddition operates in a "quasi-concerted" manner, the 4,5 *cis*-adduct would be the only one formed. That in fact **B** is exclusively formed is easy to explain since it represents the most sterically favourable disposition of ligands around the metal centre[12]. After acetylene coordination, a very fast double insertion would lead to intermediate $\mathbf{D_a}$.

The concertedness of the process is strongly supported by the general absence of products arising from independent allyl or carbonyl insertion. Products may not be cyclic or the second carbonylation be absent, but acetylene carbonylation and allyl insertion seem to be intrinsically associated in this reaction as deduced from the reaction products obtained. This picture also accounts for the formation of product **21**[13]. In fact, for this compound, intermediate **E**, after anti-elimination, would produce the major product reported in entry 6 (Figure 1).

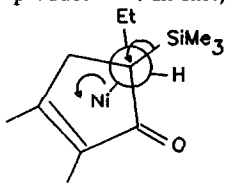


Figure 1

Finally, the formation of **33** as the major product rather than the minor isomer **34** may be due to the effect of a not so strict steric retention at this "free end" in intermediate **D**.

CONCLUSIONS

Substitution of the allyl system at the terminal position by groups able to extend conjugation (either electron withdrawing or alkene) favours allyl coupling versus carbonylative acetylene insertion, in particular in methanol where coupling is usually fast and complete, in agreement with what has been reported for other systems[9]. Another general result is the absence of a second carbonylation at the side branch for substrates with electron withdrawing substituents. However, when extended conjugation is disrupted by placing these groups at the central position (and/or the solvent polarity diminished by replacing most of the methanol with acetone), carbonylative cycloaddition proceeded in the usual way with a clear steric effect in the regioselective formation of 5-substituted cyclohex-2-enones (or aromatics) from branched allyls or 5-cyclopent-2-enone derivatives from extended ones.

All these results can be rationalized by the involvement of a π-allyl nickel species in the mechanism. This ligand, being electronically symmetrical, will sterically arrange itself with its more substituted end far from the coordinated acetylene.This explains that 4-substituted cyclopent-2-enones may also be obtained by this method, if both ends of the allyl halide are substituted.

A particular role seems to be played by the Me_3Si moiety: while no special effects were detected when this group was located at the terminal position, cyclopentenones were also only obtained when it was linked to the central carbon atom of the allyl moiety.

For 1,3-disubstituted allyl derivatives, the exclusive formation of 4,5-*cis*-disubstituted cyclopent-2-enones strongly supports a "quasi concerted" mechanism in which the three reacting moieties (ligands) are arranged around the metal in a stereodefined manner.

EXPERIMENTAL

CAUTION! $Ni(CO)_4$ is an extremely harmful chemical and special precautions have to be taken when using it.

IR spectra were recorded with a Perkin-Elmer 399B Spectrometer. ^1H NMR and ^{13}C NMR were recorded with WP-80-SY Bruker and Unity 300 Varian machines. Chemical shifts are reported in delta (δ) units, parts per million (ppm) downfield from tetramethylsilane, or in ppm relative to the singlet at 7.26 ppm for chloroform-d_1. Splitting patterns are designated as: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; b, broad. Coupling constants are reported in hertz (Hz). ^{13}C NMR are reported in ppm relative to the centre line of a triplet at 77.0 ppm for chloroform-d_1. Routine ^{13}C NMR spectra were fully decoupled by broad-band decoupling. Elemental analyses were performed with a Carlo Erba apparatus (1107 and 1500 Models). Mass spectra were obtained using 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. 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. 2-Butyn-1-ol was furnished by Aldrich. Allyl halides were prepared in our laboratory by conventional procedures (see references for each allyl halide), except for 2-chloromethyl-3-trimethylsilyl-1-propene (**7**) which was supplied by Aldrich.

Reaction with Methyl 4-bromocrotonate[14] (**1**). In a typical procedure a solution of methyl 4-bromocrotonate (2.5 g, 14 mmol) in dry acetone (2 ml) was added dropwise at 30-35 °C into a solution of 2-butyn-1-ol (0.5 g, 7 mmol), nickel(0)tetracarbonyl (1.8 ml, 14 mmol) and dry methanol (0.6 ml, 14 mmol) in acetone (15 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 12 h at 30°C. Then, the temperature was raised to 40°C and after one additional hour a stream of nitrogen passed through the mixture for 2 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, 1.5:1) of the residue afforded cyclopentenones **13** and **14** in 34% and 9% yield, respectively. Also isolated from the crude product was a 18% yield of 2-butyn-1-ol.

13: IR ($CHCl_3$) 3600-3200, 1730, 1690, 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.7 (3H, s, Me), 2.1-3.3 (6H, m, 2xCH_2, CH, OH), 3.7 (3H, s, OMe), 4.5 (2H, bs, CH_2O); ^{13}C NMR ($CDCl_3$) δ 7.6 (q), 33.8 (t), 34.7 (t), 40.7 (d), 51.3 (q), 60.0 (t), 134.1 (s), 170.4 (s), 172.3 (s), 209.8 (s). Anal.Calcd. for $C_{10}H_{14}O_4$: C, 60.60; H, 7.07. Found: C, 60.34; H, 7.28.

14: IR ($CHCl_3$) 3600-3200, 1730, 1690, 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.1 (3H, s, Me), 2.3-3.0 (6H, m, 2xCH_2, CH, OH), 3.7 (3H, s, OMe), 4.3 (2H, bs, 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). Anal.Calcd. for $C_{10}H_{14}O_4$: C, 60.60; H, 7.07. Found: C, 60.44; H, 7.17.

Reaction with Methyl 2-bromomethylacrylate[15] (**2**). To a mixture of 2-butyn-1-ol (0.42 g, 6 mmol), nickel(0)tetracarbonyl (1.6 ml, 12 mmol) and methanol (0.49 ml, 12 mmol) in dry acetone (15 ml) was added methyl 2-bromomethylacrylate (2.2 g, 12 mmol), under the same procedure described above, to give 1.4 g of crude reaction product. Flash chromatography eluting with a 1.5:1 mixture of hexane-ethyl acetate afforded the cyclohexenones **15** and **16** in 39% and 9% yield, respectively.

15: IR ($CHCl_3$) 3500, 2950, 1735, 1670, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.7 (3H, s, Me), 2.2-3.2 (6H, m, 2xCH_2, CH, OH), 3.7 (3H, s, OMe), 4.4 (2H, bs, CH_2O); ^{13}C NMR ($CDCl_3$) δ 9.4 (q), 28.8 (d), 38.6 (t), 38.9 (t), 51.6 (q), 61.7 (t), 129.6 (s), 154.9 (s), 173.4 (s), 197.1 (s). Anal. Calcd. for $C_{10}H_{14}O_4$: C, 60.60; H, 7.07. Found: C, 60.23; H, 7.29.

16: IR ($CHCl_3$) 3500, 2980, 1740, 1670, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.0 (3H, s, Me), 2.5-2.7 (4H, m, CH_2, CH, OH), 3.2-3.4 (2H, m, CH_2), 3.65 (3H, s, OMe), 4.25 (2H, bs, CH_2O); ^{13}C NMR ($CDCl_3$) δ 20.8 (q), 34.6 (d), 38.8 (t), 38.9 (t), 52.1 (q), 56.1 (t), 134.1 (s), 156.9 (s), 173.3 (s), 197.5 (s). Anal. Calcd. for $C_{10}H_{14}O_4$: C, 60.60; H, 7.07. Found: C, 60.40; H, 7.05.

Reaction with 1-Bromo-3-benzensulfonyl-2-propene[16] (**3**). The reaction was carried out as above, replacing methyl 2-bromomethylacrylate by 1-bromo-3-benzensulfonyl-2-propene. Flash chromatography (ethyl acetate-hexane 1:2) afforded 54% yield of methanolized allyl derivatives (phenyl allyl sulfone), 2% of recovered acetylene and 34% yield of 1,6-dibenzensulfonyl-1,5-hexadiene **17**.

17: IR ($CHCl_3$) 3020, 1630, 1325, 1310, 1150, 1090 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.4-2.44 (4H, m, 2xCH_2), 6.3-6.4 (2H, m, HC=), 6.9-7.0 (2H, m, HC=), 7.5-7.7 (6H, m, Ph), 7.8-7.9 (4H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 28.9 (t), 126.9 (d), 127.2 (d), 129.1 (d), 131.6 (d), 133.2 (d), 144.0 (s). Anal. Calcd. for $C_{18}H_{18}S_2O_4$: C, 59.64; H, 5.02; S, 17.69. Found: C, 59.69; H, 4.99; S, 17.68.

Reaction with (E)-1-Bromo-2-phenylsulfonyl-2-butene[17] (4). The reaction was carried out as for 3, replacing 1-bromo-3-benzensulfonyl-2-propene by (E)-1-bromo-2-phenylsulfonyl-2-butene and performing the reaction at 20°C. Flash chromatography of the crude reaction mixture eluting with a 1.5:1 ethyl acetate-hexane mixture afforded **18** in 44% yield. Also isolated from the crude was a 38% of the methanolyzed allyl derivative 1-methoxy-2-phenylsulfonyl-2-butene.

18: IR ($CHCl_3$) 3500-3400, 1705, 1670, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (3H, d, J= 7.2 Hz, Me), 1.6 (3H, bs, Me), 1.7 (1H, bs, OH), 2.85 (1H, dq, J= 1.5, 7.2 Hz, CH), 2.8 (1H, m, CH), 3.0 (1H, m, CH), 3.1 (1H, m, CH), 4.26 (2H, AB sys., J= 3.9, 18.3 Hz, CH_2O), 7.4-7.85 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 10.3 (q), 16.5 (q), 24.1 (t), 40.1 (d), 62.3 (t), 65.2 (d), 127.9 (d), 129.0 (d), 129.4 (s), 134.1 (d), 149.4 (s), 173.5 (s), 197.3 (s). Anal. Calcd. for $C_{15}H_{18}O_4S$: C, 61.21; H, 6.18; S, 10.87. Found: C, 60.96; H, 6.03; S, 10.50.

Reaction with 3-Chloro-3-trimethylsilyl-1-propene[18] (5). To nickel(0)tetracarbonyl (1.4 ml, 11 mmol), 2-butyn-1-ol (0.37 g, 5 mmol) and methanol (0.42 ml, 11 mmol) in dry acetone (12 ml) 3-chloro-3-trimethylsilyl-1-propene (1.6 g, 11 mmol) was dropwise added at 15°C. After 12 h, the reaction was warmed to 40°C and nitrogen flow was started. Flash chromatography of the crude reaction product (1.28 g) eluting with a 1:1.5 mixture of ethyl acetate-hexane afforded cyclopentenones **19** and **20** in 24% and 8% yield respectively. Also isolated from the crude was 30% of the original allyl halide.

19: IR (CCl_4) 3450, 1770, 1710, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.05 (9H, s, $SiMe_3$), 1.6 (3H, s, Me), 2.2-2.8 (5H, m, OH, CH_2, CH, CHCO), 3.6 (3H, s, OMe), 4.4 (2H, s, CH_2O); ^{13}C NMR ($CDCl_3$) δ -1.4 (q), 7.8 (q), 34.2 (t), 38.2 (d), 43.4 (d), 50.9 (q), 60.0 (t), 134.3 (s), 168.5 (s), 174.8 (s), 209.9 (s). Anal. Calcd. for $C_{13}H_{22}O_4Si$: C, 57.75; H, 8.20. Found: C, 58.15; H, 8.08.

20: IR (CCl_4) 3450, 1770, 1710, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.06 (9H, s, $SiMe_3$), 2.05 (3H, s, Me), 2.2-2.8 (5H, m, OH, CH_2, CH, CHCO), 3.5 (3H, s, OMe), 4.15 (2H, bs, CH_2O); ^{13}C NMR ($CDCl_3$) δ -1.6 (q), 28.9 (q), 35.5 (t), 37.9 (d), 43.1 (d), 50.8 (q), 65.5 (t), 134.7 (s), 169.6 (s), 174.2 (s), 211.0 (s). Anal. Calcd. for $C_{13}H_{22}O_4Si$: C, 57.75; H, 8.20. Found: C, 58.14; H, 8.09.

Reaction with 1-Chloro-2-trimethylsilyl-2-pentene[19] (6). To a solution of nickel(0)tetracarbonyl (1.4 ml, 10 mmol) and 2-butyn-1-ol (0.37 g, 5 mmol) in dry methanol (10 ml) 1-chloro-2-trimethylsilyl-2-pentene (0.8 g, 5 mmol) was added at 15°C, following the same procedure described above. Flash chromatography of the crude reaction product (1.5 g, ethyl acetate-hexane 1:1.5) afforded cyclopentenones **21**, **22** and **23** in 12%, 11% and 8% yield, respectively. Also isolated from the crude was a 14 % of recovered allyl, as well as some ill-defined polyinsertion product.

21: IR (CCl_4) 3640, 3450, 1710, 1670, 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15 (3H, t, J= 8 Hz, Me), 1.7-1.8 (3H, m, Me), 2.3 (2H, q, J= 8 Hz, CH_2), 2.4-2.5 (1H, m, OH), 3.0-3.2 (2H, m, CH_2), 4.55 (2H, bs, CH_2O), 6.55 (1H, tt, Ja= 8 Hz, Jb= 2 Hz, HC=); ^{13}C NMR ($CDCl_3$) 8.2 (q), 13.1 (q), 22.6 (t), 30.5 (t), 59.7 (t),

133.7 (s), 136.0 (s), 136.4 (d), 165.1 (s), 198.7 (s); MS (EI) 166 (M^+, 54), 137 (100), 105 (38), 91 (51), 79 (30), 67 (20), 53 (26). Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.24; H, 8.51. Found: C, 71.97; H, 8.57.

22: IR (CCl_4) 3640, 3500, 1740, 1710, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) 0.95 (3H, t, J= 8 Hz, Me), 1.6-1.8 (5H, m, CH_2, Me), 2.5-2.8 (3H, m, OH, CH_2), 3.6 (3H, s, OMe), 4.55 (2H, bs, CH_2O); ^{13}C NMR ($CDCl_3$) δ 7.7 (q), 30.9 (q), 45.4 (t), 46.5 (t), 51.2 (q), 60.2 (t), 134.6 (s), 136.2 (s), 169.9 (s), 170.5 (s), 174.1 (s), 209.9 (s). Anal. Calcd. for $C_{12}H_{16}O_4$: C, 64.26; H, 7.21. Found: C, 64.30; H, 7.11.

23: IR (CCl_4) 3640, 3500, 1740, 1710, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (3H, t, J= 8 Hz, Me), 1.7 (2H, bs, CH_2), 2.0-2.2 (3H, s, Me), 2.5-2.8 (3H, m, CH_2, OH), 3.8 (3H, s, OMe), 4.35 (2H, bs, CH_2O); ^{13}C NMR ($CDCl_3$) 11.8 (q), 22.9 (q), 46.4 (t), 47.4 (t), 51.4 (q), 54.5 (t), 133.6 (s), 134.7 (s), 140.0 (s), 166.5 (s), 175.3 (s), 209.4 (s); MS (EI) 226 (M^+, 13), 194 (28), 166 (79), 151 (36), 137 (41), 126 (100), 109 (38), 97 (56). Anal. Calcd. for $C_{12}H_{16}O_4$: C, 64.26; H, 7.21. Found: C, 64.39; H, 7.10.

Reaction with 2-Chloromethyl-3-trimethylsilyl-1-propene[20] (**7**). To a solution of 2-butyn-1-ol (0.5 g, 7 mmol), nickel(0)tetracarbonyl (1.8 ml, 14 mmol) and dry methanol (0.6 ml, 14 mmol) in acetone (15 ml) at 15°C was added dropwise 2-chloromethyl-3-trimethylsilyl-1-propene (2.3 g, 14 mmol). After 12 h the reaction was warmed to 35°C and nitrogen passed through it. The usual workup afforded 1.7 g of as crude reaction product, showing three major products on TLC analysis. Flash chromatography, eluting with 1.5:1 ethyl acetate-hexane mixture afforded alcohols **24** and **25** in 67% and 21% yield respectively, and 2-hydroxy-4,6-dimethylbenzyl alcohol **26** in 10% yield.

24: IR ($CHCl_3$) 3500-3400, 1580, 1460, 1310, 1250 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.1 (9H, s, $SiMe_3$), 2.1-2.2 (3H, m, OH, CH_2Si), 2.3 (3H, s, Me), 4.75 (2H, bs, CH_2O), 6.45 (1H, s, H-Ar), 6.70 (1H, s, H-Ar), 8.0 (1H, s, Ar-OH); ^{13}C NMR ($CDCl_3$) δ -1.4 (q), 10.35 (q), 20.2 (t), 65.9 (t), 117.7 (d), 120.9 (d), 123.0 (s), 137.5 (s), 138.9 (s), 153.9(s).

25: IR ($CHCl_3$) 3500-3400, 1580, 1460, 1310, 1250 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.1 (9H, s, $SiMe_3$), 2.1 (5H, m, CH_2Si, Me), 2.4 (1H, bs, OH), 4.65 (2H, bs, CH_2O), 6.4 (1H, s, H-Ar), 6.6 (1H, s, H-Ar), 8.0 (1H, s, OH); ^{13}C NMR ($CDCl_3$) -1.9 (q), 11.3 (q), 20.6 (t), 63.8 (t), 114.6 (d), 120.4 (d), 122.1 (s), 137.4 (s), 139.4 (s), 152.5 (s).

26: IR (KBr) 3500-3000, 1620, 1580, 1415 cm^{-1}; ^1H NMR (ac-d_6) δ 2.1 (3H, s, Me), 2.2 (3H, s, Me), 3.6 (1H, s, OH), 4.6 (2H, s, CH_2O), 6.6 (1H, s, H-Ar), 6.8 (1H, s, H-Ar), 8.0 (1H, s, Ar-OH); ^{13}C NMR (ac-d_6) 10.0 (q), 20.6 (q), 62.8 (t), 114.8 (d), 119.9 (s), 120.0 (d), 135.4 (s), 141.4 (s) 155.3 (s); MS (EI) 152 (M^+, 68), 134 (100), 121 (41), 109 (31), 91 (57), 73 (74). Anal. Calcd. for $C_9H_{12}O_2$: C, 71.21; H, 7.96. Found: C, 71.58; H, 8.17.

Reaction with 1-Bromo-2,4-pentadiene[21] (**8**). To a solution of nickel(0)tetracarbonyl (1.4 ml, 10 mmol) and 2-butyn-1-ol (0.37 g, 5 mmol) in dry methanol (10ml) 1-bromo-2,4-pentadiene (1.48 g, 10 mmol) was added at 15°C, following the same procedure described above. Flash chromatography of the crude reaction product

with a 1:2 mixture of ethyl acetate-hexane gave 1,3,7,9-decatetraene **27**[22] in 40% yield and 10% of recovered acetylene. Extensive acetylene polyinsertion also occurred.

Reaction with 1-Bromo-2,5-hexadiene[21] (**9**). The reaction was carried out as usual using 1-bromo-2,5-hexadiene as the allyl derivative and methanol as solvent. Flash chromatography of the crude eluting with a 1:2 mixture of ethyl acetate-hexane afforded a mixture of cyclopentenones **28** and **29** in 74% and 18% yield respectively. Anal. Calcd. for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.20; H, 7.66.

28: IR ($CHCl_3$) 3500-3400, 1740, 1690, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.7 (3H, s, Me), 2.2-2.8 (7H, m, 2xCH_2, CHCO, $CHCO_2$, OH), 3.7 (3H, s, OMe), 4.5 (2H, s, CH_2O), 4.9-5.2 (2H, m, HC=), 5.5-5.9 (1H, m, HC=); ^{13}C NMR ($CDCl_3$) δ 7.6 (q), 30.8 (t), 33.9 (d), 45.0 (d), 45.4 (d), 51.4 (q), 60.1 (t), 116.8 (t), 134.7 (s), 134.8 (d), 170.3 (s), 174.2 (s), 209.1 (s).

29: IR ($CHCl_3$) 3500-3400, 1740, 1690, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.1 (3H, s, Me), 2.2-2.8 (7H, m, 2xCH_2, CHCO, $CHCO_2$, OH), 3.7 (3H, s, OMe), 4.3 (2H, s, CH_2O), 4.9-5.2 (2H, m, HC=), 5.5-5.9 (1H, m, HC=); ^{13}C NMR ($CDCl_3$) δ 16.8 (q), 30.8 (t), 32.9 (t), 44.5 (d), 45.7 (d), 51.3 (q), 60.1 (t), 117.2 (t), 134.7 (s), 134.8 (d), 173.3 (s), 174.4 (s), 209.05 (s); MS (EI) 239 (M^++1, 3), 179 (39), 126 (100), 109 (20), 97 (57), 81 (26), 55 (17).

Reaction with 2,3-Bis(chloromethyl)-1,3-butadiene[23] (**10**). The reaction was carried out as for **9**, replacing 1-bromo-2,5-hexadiene by 2,3-bis(chloromethyl)-1,3-butadiene and performing the reaction at 15°C. Flash chromatography of the crude reaction product eluting with a 1:2 ethyl acetate-hexane mixture afforded **30**, **31** and **32** in 19%, 12% and 11% yield respectively. Also isolated from the crude was 15% of recovered acetylene.

30: IR ($CHCl_3$) 3600-3500, 1730, 1620, 1580, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.1 (2H, m, 2xOH), 2.2 (3H, bs, Me), 3.5 (2H, bs, CH_2CO), 3.7 (3H, s, OMe), 4.7 (2H, bs, CH_2O), 5.2 (1H, bs, HC=), 5.5 (1H, bs, HC=), 6.8 (1H, d, J= 2 Hz, H-Ar), 7.0 (1H, d, J= 2 Hz, H-Ar); ^{13}C NMR ($CDCl_3$) δ 10.7 (q), 30.9 (t), 52.1 (q), 63.4 (t), 112.1 (d), 112.4 (s), 117.2 (t), 122.6 (s), 137.7 (s), 140.1 (s), 140.2 (s), 154.6 (s), 172.7 (s). Anal. Calcd. for $C_{13}H_{16}O_4$: C, 66.07; H, 7.48. Found: C, 66.28; H, 7.41.

31: IR ($CHCl_3$) 3600-3500, 1720, 1625, 1580, 1440, 1060, 865 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.0 (1H, m, OH), 2.2 (3H, s, Me), 2.5 (3H, d, J= 1 Hz, Me), 3.3 (1H, m, OH), 3.8 (3H, s, OMe), 4.7 (2H, bs, CH_2O), 6.1 (1H, q, J= 1 Hz, HC=), 6.8 (1H, d, J= 2 Hz, H-Ar), 7.1 (1H, d, J= 2 Hz, H-Ar); ^{13}C NMR ($CDCl_3$) 10.6 (q), 17.6 (q), 51.0 (q), 63.1 (t), 112.2 (d), 115.4 (s), 117.5 (t), 123.9 (s), 139.8 (s), 139.9 (s), 140.1 (s), 154.4 (s), 167.6 (s); MS (FAB+) 236 (M^+, 89), 218 (100), 203 (35), 187 (41), 175 (70), 159 (27), 147 (20), 131 (29), 115 (29). Anal. Calcd. for $C_{13}H_{16}O_4$: C, 66.07; H, 7.48. Found: C, 66.17; H, 7.30.

32: IR (CCl_4) 3095, 1740, 1600, 1435 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.3 (4H, s, CH_2), 3.7 (6H, s, OMe), 5.2 (2H, bs, HC=), 5.3 (2H, bs, HC=); ^{13}C NMR ($CDCl_3$) δ 40.2 (t), 51.9 (q), 117.2 (t), 139.3 (s), 171.7 (s); MS (EI) 198 (M^+, 27), 177 (25), 159 (28), 145 (100), 139 (61), 135 (48), 131 (35), 105 (43).

Reaction with 4-Chloro-2-pentene[19] (**11**). To a solution of nickel(0)tetracarbonyl (1.2 ml, 10 mmol) and 2-butyn-1-ol (0.39 g, 5 mmol) in dry methanol (12 ml) 4-chloro-2-pentene (1.1 g, 10 mmol) was added dropwise at 30°C. After 12 h the reaction was warmed to 35°C and nitrogen flushing was started. Flash chromatography of the crude reaction product (0.4 g) afforded (eluting with a 1.5:1 ethyl acetate-hexane mixture) both cyclopentenones **33** and **34**. Subsequent flash chromatography through an Omnifit column (medium pressure chromatography) eluting with a 1:1 ethyl acetate-hexane mixture afforded **33** and **34** separately in 38% and 9% yield respectively. Also isolated from the crude reaction was a 42% of recovered acetylene.

33: IR (CCl_4) 3500-3400, 1740, 1705, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (3H, d, J= 8 Hz, Me), 1.15 (3H, d, J= 8 Hz, Me), 1.7 (3H, bs, Me), 1.8 (1H, m, OH), 2.3 (1H, dd, Ja= 2.3 Hz, Jb= 5.7 Hz, CH), 2.75 (1H, m, CH), 2.9 (1H, dq, Ja= 2.3 Hz, Jb= 8 Hz, $CHCO_2$), 3.65 (3H, s, OMe), 4.5 (2H, AB sys., J= 8 Hz, CH_2O); ^{13}C NMR ($CDCl_3$) δ 7.8 (q), 12.1 (q), 18.5 (q), 39.1 (d), 40.0 (d), 51.6 (d), 54.8 (q), 58.4 (t), 135.3 (s), 173.4 (s), 175.6 (s), 209.1 (s). Anal. Calcd. for $C_{12}H_{18}O_4$: C, 63.90; H, 8.03. Found: C, 64.29; H, 8.15.

34: IR (CCl_4) 3500-3400, 1740, 1705, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.2 (3H, d, J= 8 Hz, Me), 1.3 (3H, d, J= 8 Hz, Me), 1.7 (3H, bs, Me), 1.85 (1H, m, OH), 2.05 (1H, dd, Ja= 2.3 Hz, Jb= 5.7 Hz, CH), 2.8 (1H, m, CH), 3.0 (1H, dq, Ja= 2.3 Hz, Jb= 8 Hz, $CHCO_2$), 3.55 (3H, s, OMe), 4.5 (2H, AB sys., J= 8 Hz, CH_2O); ^{13}C NMR ($CDCl_3$) δ 8.1 (q), 14.9 (q), 19.2 (q), 38.3 (d), 39.9 (d), 51.7 (d), 55.8 (q), 58.7 (t), 135.5 (s), 173.1 (s), 174.8 (s), 208.6 (s); MS (EI) 226 (M^+, 28), 195 (64), 167 (71), 149 (71), 138 (70), 121 (34), 113 (61), 91 (52), 69 (100), 53 (65). Anal. Calcd. for $C_{12}H_{18}O_4$: C, 63.90; H, 8.03. Found: C, 64.30; H, 8.18.

Reaction with 1-Chloro-1-trimethylsilyl-2-butene[18] (**12**). To a solution of nickel(0)tetracarbonyl (0.65 ml, 5 mmol), 2-butyn-1-ol (0.2 g, 3 mmol) and methanol (0.21 ml, 5 mmol) in acetone (10 ml) 1-chloro-1-trimethylsilyl-2-butene (0.8 g, 5 mmol) was dropwise added at 30°C. After 12 h the reaction was warmed to 40°C under a nitrogen flow. Flash chromatography of the crude oil (0.25 g) eluting with a 1:1 ethyl acetate-hexane mixture afforded cyclopentenones **35** and **36** in 17% and 5% yield respectively. Also isolated from the crude reaction mixture was 40% of recovered acetylene.

35: IR (CCl_4) 3500, 1740, 1705, 1655, 1430 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0 (3H, d, J= 6.9 Hz, Me), 1.7 (3H, bs, Me), 2.45 (2H, AB sys., J= 19.1 Hz, CH_2CO_2), 2.7 (1H, m, OH), 2.8 (1H, m, CH), 3.0 (1H, dq, Ja= 5.1 Hz, Jb= 6.9 Hz, CH), 3.7 (3H, s, OMe), 4.6 (2H, bs, CH_2O); ^{13}C NMR ($CDCl_3$) δ 8.0 (q), 11.9 (q), 30.2 (t), 39.3 (d), 46.5 (d), 51.9 (q), 60.7 (t), 135.8 (s), 169.7 (s), 175.7 (s), 209.5 (s). Anal. Calcd. for $C_{11}H_{16}O_4$: C, 62.23; H, 7.61. Found: C, 62.31; H, 7.64.

36: IR (CCl_4) 3500, 1740, 1705, 1655, 1430 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0 (3H, d, J= 7 Hz, Me), 2.1 (3H, bs, Me), 2.45 (2H, AB sys., J= 19.1 Hz, CH_2CO_2), 2.7 (1H, dd, Ja= 6.8 Hz, Jb= 19.1 Hz, CH), 2.9 (1H, m, OH), 3.0 (1H, dq, Ja= 6.8 Hz, Jb= 7.0 Hz, CH), 3.7 (3H, s, OMe), 4.3 (2H, bs, CH_2O); ^{13}C NMR

($CDCl_3$) δ 11.8 (q), 17.0 (q), 35.2 (t), 38.9 (d), 46.8 (d), 51.9 (q), 55.4 (t), 138.6 (s), 172.2 (s), 175.5 (s), 209.7 (s). Anal. Calcd. for $C_{11}H_{16}O_4$: C, 62.23; H, 7.61. Found: C, 62.17; H, 7.62.

ACKNOWLEDGMENT. Financial support by DGICYT (Project n° PB87-0201-C-0303) is gratefully acknowledged. One of us (Ll. P.) thanks the Spanish M.E.C. for a fellowship.

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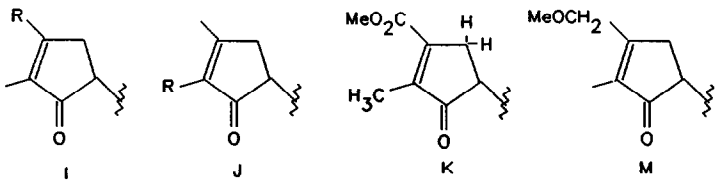

11. C-4/C-5 *cis* relative stereochemistry was established after the coupling constant value for respective protons: $J_{H4,H5}$= 5.7 Hz for **33**, 5.7 Hz for **34**, 5.1 Hz for **35** and 6.8 Hz for **36**. For the relative stereochemistry of the side chain, the coupling constant of the α-carboxylic proton with the α-carbonyl one, and the chemical shifts for the nearby CO_2Me and Me substituents support the depicted relative stereochemistry.
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