# Nickel-Catalyzed Double Carbonylation of Halo Dienes: A Possible New Mechanism for the Double Carbonylation Reaction

Kawkab Younis and Ibrahim Amer*

*Department of Chemistry, Ben-Gurion University of the Negev, Beer-Sheva 84105, Israel*

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The conversion of halo dienes to α-keto acids or α-keto γ-lactones under phase-transfer conditions and 1 atm of CO in the presence of a catalytic amount of nickel cyanide is described. A detailed examination of the factors controlling the selectivity for the double carbonylation product revealed the following characteristics of the reaction: (1) Temperatures above 80 °C and a base concentration above 5 N NaOH were required to produce the double carbonylation product with high selectivity. (2) Substrates having the 2-halo 1,3-diene moiety in which the diene moiety is free to rotate gave the double carbonylation product with high selectivity. (3) The use of phase-transfer agents (especially those having one long chain alkyl group) increases the carbonylation reaction yields. On the basis of the experimental results a mechanism involving the formation of a nickel metallacycle that subsequently gives the double carbonylation product is proposed.

Carbonylation reactions of organic compounds catalyzed by transition-metal complexes are widely utilized in organic synthesis to produce carbonyl compounds, such as aldehydes, ketones, carboxylic acids, esters, and amides.[1] These reactions are generally monocarbonylation processes in which a single CO molecule is introduced into an organic compound in one step. For example, alkoxycarbonylation[2] and amidation[3] of organic halides are catalyzed by transition metal compounds to give esters and amides, respectively (eq 1).

$$RX + CO + HY \xrightarrow{[M]} RCOY + HX \quad (1)$$

RX = organic halide; HY = alcohol or amine; [M] = transition metal complex

In contrast to monocarbonylation reactions, only very few reports of double carbonylation reactions (eq 2) have appeared in the literature.[4] These reactions, in which

$$RX + CO + HY \xrightarrow{[M]} RCOCOY + HX \quad (2)$$

RX = organic halide; HY = alcohol or amine; [M] = Pd or Co complex

two molecules of carbon monoxide are incorporated into an organic molecule (e.g., organic halides, olefins, amines, or alcohols), gave products with adjacent carbonyl groups. Such compounds containing two reactive carbonyl groups in adjacent positions can be used as convenient starting materials in organic syntheses, e.g., for α-amino acids, α-hydroxy acids, heterocyclic compounds,[5] and α-keto lactones.[6]

With the exception of reactions producing oxalic acid derivatives,[4b,c] the double carbonylation of benzyl halides[7] by means of a phase-transfer technique with a cobalt carbonyl anion constituted the sole example of this type of reaction until only recently (eq 3). This

$$RX + CO \xrightarrow[C_6H_6,\ R_4N^+X^-,\ 1\ atm]{Co_2(CO)_8,\ Ca(OH)_2} RCOOH + RCOCOOH \quad (3)$$

process, for which consecutive CO insertion into the benzyl–cobalt bond was postulated, appears to involve the participation of an enolized form of the benzylic protons for driving the second CO insertion.[8–10]

Recently, Yamamoto[11] and Tanaka[12] independently found that palladium complexes can catalyze the carbonylation of aryl halides to α-keto amides in the presence of secondary amines (eq 4). The selectivities of these reactions are dependent on the conditions of the carbonylation reaction, the type of amine, and the

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(2) (a) Schoenberg, A.; Bartoletti, I.; Heck, R. F. *J. Org. Chem.* **1974,** *39,* 3318. (b) Stille, J. K.; Wong, P. K. *J. Org. Chem.* **1975,** *40,* 532. (c) Hidai, M.; Hikita, T.; Wada, Y.; Fujikura, Y.; Uchida, Y. *Bull. Chem. Soc. Jpn.* **1975,** *48,* 2075.

(3) Schoenberg, A.; Heck, R. F. *J. Org. Chem.* **1974,** *39,* 3327.

(4) (a) Collin, J. *Bull. Soc. Chim. Fr.* **1988,** *6,* 976 and references therein. (b) Tsuji, J.; Iwamoto, N. *J. Chem. Soc., Chem. Commun.* **1966,** 380. (c) Fenton, D.; Steinwand, P. *J. Org. Chem.* **1974,** *39,* 701. (d) Monflier, E.; Mortreux, A.; Petit, F. *Appl. Catal. A* **1993,** *102,* 53.

(5) (a) Yamamoto, A.; Yamamoto, T.; Ozawa, F. *Pure Appl. Chem.* **1985,** *57,* 1799. (b) Valentine, D., Jr.; Scott, J. W. *Synthesis* **1978,** 329. (c) Cooper, A. J. L.; Ginos, J. Z.; Meister, A. *Chem. Rev.* **1983,** *83,* 321. (d) Yamamoto, A.; Yanagihara, H.; Ozawa, F. *J. Org. Chem.* **1986,** *51,* 415.

(6) Murray, F. T.; Samsel, G. E.; Varma, V.; Norton, J. R. *J. Am. Chem. Soc.* **1981,** *103,* 7520.

(7) The first example of a double carbonylation reaction of benzyl halides was found by Perron in 1975: Perron, R. C. Fr. Pat. 2297200, 1975; DOS 2600352, 1976.

(8) (a) Alper, H. *ACS Symp. Ser.* **1987,** *326,* 8. (b) Alper, H. *J. Organomet. Chem.* **1986,** *300,* 1. (c) Petrignani, J. F. In *The Chemistry of the Metal-Carbon Bond*; Hartley, F. R., Ed.; Wiley: New York, 1989; Vol. 5, pp 63–106.

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(10) Kashimura, T.; Kudo, K.; Mori, S.; Sugita, N. *Chem. Lett.* **1986,** 483.

(11) (a) Yamamoto, A.; Ozawa, F.; Yanagihara, H.; Son, T. *Bull. Chem. Soc. Jpn.* **1988,** *61,* 1251 and references cited therein. (b) Yamamoto, A.; Ozawa, F.; Osakada, K.; Huany, L.; Son, T. *Pure Appl. Chem.* **1991,** *63,* 687.

(12) Tanaka, M.; Hayashi, T.; Kobayashi, T.; Yamashita, H.; Sakakura, T. *J. Org. Chem.* **1987,** *52,* 5733 and references cited therein.

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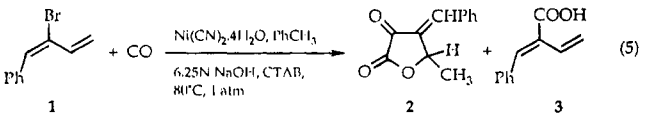
$$ArX + 2CO + 2R_2NH \xrightarrow{[Pd]} RCOCONR_2 + R_2NH_2X \qquad (4)$$

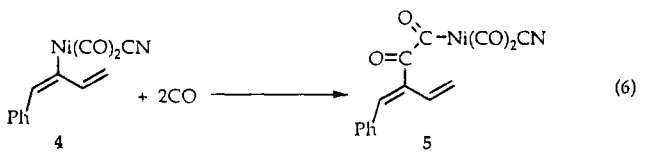
phosphine ligands complexed to the palladium. In most of the catalytic double carbonylation reactions described so far, the catalysts were cobalt carbonyls[13] or palladium complexes.[12] Lanthanide and actinide complexes react in these systems only in a stoichometric fashion.[14]

Following a report of carbonylation of vinyl halides[15a] to α,β-unsaturated acids using catalytic quantities of nickel cyanide under phase-transfer conditions, Alper and Vasapollo[15b] reported the double carbonylation of 2-bromo-1-phenyl-1,3-butadiene (**1**) to 4-benzylidene-5-methyl-2,3,5-trihydrofuran-2,3-dione (**2**) (eq 5). They




1 2 3 (5)

suggested a mechanism in which a nickel—alkenyl intermediate **4** inserts two molecules of carbon monoxide in a concerted pathway forming an α-keto acyl—nickel intermediate **5** (eq 6).

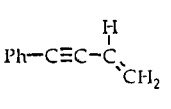



4 5 (6)

We were not convinced that this mechanism is correct, since other vinyl halides[15a] do not give any double carbonylation products under the same conditions and since such intermediates undergo rapid decarbonylation.[16] We wish to report here the double carbonylation reaction of halodienes catalyzed by nickel cyanide under phase-transfer conditions.[17] We have attempted to elucidate the double carbonylation mechanism and have examined the factors that could improve the selectivity of the double carbonylation reaction.

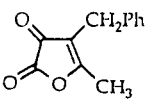
## Results and Discussion

Treatment of 2-bromo-1-phenyl-1,3-butadiene (**1**) with catalytic amounts of nickel cyanide (in a ratio of 10:1) and a quaternary ammonium salt at 1 atm of carbon monoxide gave 2-benzylidene-3-butenoic acid (**3**), 4-benzylidene-5-methyl-2,3,5-trihydrofuran-2,3-dione (**2**), and 1-phenyl-3-buten-1-yne (**6**) (the last as the elimination




6

product in the organic phase) in 7, 33, and 5% yields, respectively, with 45% conversion of the starting material. Compound **2** isomerized to 4-benzyl-5-methyl-2,3-dihydrofuran-2,3-dione (**7**) if a strong acid was used for

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the acidification of the aqueous phase at the end of the reaction or if the crude reaction products were passed over silica gel. Yields of the single and double carbonylation products were influenced by various factors including the type of phase-transfer agent, the temperature, the basicity of the aqueous phase, and the nature of the substrate, as follows.

**Table 1. Nickel Cyanide and Phase-Transfer-Catalyzed Carbonylation of 1**[a]

| phase-transfer agent | conversion (%) | yield (%) 2 | 3 | 6 |
|---|---|---|---|---|
| | 13 | 4 | 2 | 7 |
| $(C_4H_9)_4N^+Br^-$ | 66 | 11 | 2 | 44 |
| $(C_{10}H_{21})_4N^+Br^-$ | 76 | 0.3 | 0.7 | 75 |
| $(C_8H_{17})_3NCH_3^+Cl^-$ [b] | 80 | 3 | 3 | 70 |
| $(C_{10}H_{21})_2N(CH_3)_2^+Br^-$ | 58 | 16 | 0 | 30 |
| $(C_{14}H_{29})N(CH_3)_3^+Br^-$ | 76 | 40 | 0 | 20 |

[a] Reaction conditions: $Ni(CN)_2 \cdot 4H_2O$ (1 mmol), **1** (10 mmol), phase-transfer agent (0.2 mmol), 6.25 N NaOH (20 mL), toluene (25 mL), CO (1 atm), 100 °C, 5 h. [b] As Aliquate-336.

**(i) Phase Transfer Agent.** Only 6% of **2** plus **3** (ratio 2:1) was obtained when the reaction was carried out in the absence of a phase-transfer agent. Of the various phase-transfer agents employed for the carbonylation of 2-bromo-1-phenyl-1,3-butadiene (**1**) it seems that the quaternary ammonium salt containing one long chain alkyl group ($C_{14}H_{29}N(CH_3)_3^+Br^-$) favored the formation of carbonylation products (Table 1). This may indicate that such catalytic systems function in a surfactant-like manner.[18] Symmetrical tetraalkylammonium salts and ammonium salts having two or more long chain alkyl groups enhance the elimination process and reduce the carbonylation reaction. The initial consumption rates of the starting material were found to be 1.3, 1.6, 1.7, 2.9, and 3.5 mmol/h for $(C_{10}H_{21})_2N(CH_3)_2^+Br^-$, $(C_4H_9)_4N^+Br^-$, $C_{14}H_{29}N(CH_3)_3^+Br^-$, $(C_8H_{17})_3NCH_3^+Cl^-$, and $(C_{10}H_{21})_4N^+Br^-$, respectively. This behavior was also observed in the catalytic carboxylation of benzyl halides by $Ni(CN)_2 \cdot 4H_2O/LaCl_3 \cdot 7H_2O$ under phase-transfer conditions.

**(ii) Effect of Temperature.** The temperature has a crucial influence on the ratio of single to double carbonylation, the higher the temperature, the greater the ratio of double/single carbonylation products (Table 2). While temperatures higher than 95 °C (in the presence of 6.25 N NaOH) resulted mainly in the production of double carbonylation products, temperatures below 60 °C gave largely the single carbonylation products. This behavior is in contrast with that reported for the palladium-catalyzed double carbonylation of aryl or vinyl halides.[19]

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(14) Frans, J. W.; Drummond, D. K.; Chamberlain, L. R.; Doedens, R. J.; Bott; G. S. Zhang, H.; Atwood, J. L. *J. Am. Chem. Soc.* **1988**, *110*, 4983 and references therein.
(15) (a) Amer, I.; Alper, H.; Vasapollo, G. *Tetrahedron Lett.* **1989**, *30*, 2615. (b) Alper, H.; Vasapollo, G. *Tetrahedron Lett.* **1989**, *30*, 2617.
(16) Casey, C. P.; Bunnell, C. A.; Calabrese, J. T. *J. Am. Chem. Soc.* **1976**, *98*, 1166 and references therein.
(17) Part of this work was reported at the VIIIth International Symposium on Homogeneous Catalysis, Amsterdam, Netherlands, 1992 (p P5) and at the XVth International Conference on Organometallic Chemistry, Warsaw, Poland (p O20).
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(19) Ozawa, F.; Soyama, H.; Yanagihara, H.; Aoyama, I.; Takino, H.; Izawa, K.; Yamamoto, T.; Yamamoto, A. *J. Am. Chem. Soc.* **1985**, *107*, 3235.

**Table 2. Effect of Temperature on the Nickel-Catalyzed Carbonylation of 1 under Phase-Transfer Conditions[a]**

| temp (°C) | base (N) | time (h) | conversion (%) | yield (%) 2 | yield (%) 3 |
|---|---|---|---|---|---|
| 60 | 3 | 18 | 31 | 0 | 30 |
| 80 | 4 | 18 | 52 | 27 | 13 |
| 110 | 4 | 18 | 63 | 29 | 1 |
| 95 | 5 | 18 | 80 | 52 | 13 |
| 70 | 6.25 | 14 | 60 | 10 | 15 |
| 80 | 6.25 | 14 | 80 | 33 | 7 |
| 95 | 6.25 | 12 | 90 | 64 | 1 |
| 110 | 6.25 | 6 | 100 | 75[b] | 3 |
| 95 | 7.5 | 9 | 100 | 14 | 3 |

[a] Reaction conditions: **1** (10 mmol), $Ni(CN)_2{\cdot}4H_2O$ (1 mmol), $(C_{14}H_{29})N(CH_3)_3{}^+Br^-$ (0.2 mmol), base (20 mL), toluene (25 mL), CO (1 atm). [b] 3–5% of hydrogenated products were detected.

**(iii) Effect of the Base.** The influence of the concentration of the base on the ratio of single to double carbonylation products is shown in Table 2. A base concentration above 6.25 N NaOH gave mainly the double carbonylation product (at 95 °C); lower base concentrations increased the single carbonylation. A concentration higher than 6.25 N NaOH (i.e., 7.25 N NaOH) lowered the total yield of carbonylation products and stimulated the elimination process that led to the formation of **6**.

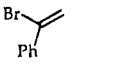
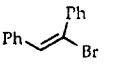
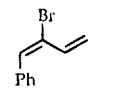
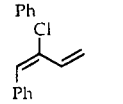
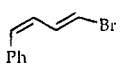
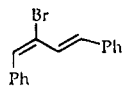
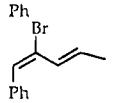
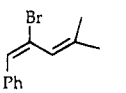
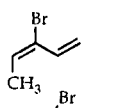
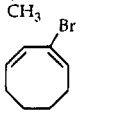
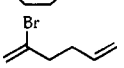
**(iv) Nature of the Organic Halide.** Table 3 presents a comparison of the carbonylation of various organic halides. Halides derived from monoenes gave only monocarbonylation products, independently of the concentration of the base or the temperature (experiments 1 and 2 in Table 3).[15a] Chloro dienes were less reactive than the bromine analogs. The position of the bromine atom significantly affected the double carbonylation reaction: when the bromo atom was transferred from position 2 to position 4 in the 1,3-diene system, only the monocarbonylation product was formed (experiment 5). Introduction of substituents (i.e., $CH_3$, Ph, $2(CH_3)$), into position 4 of 2-bromo-1-phenyl-1,3-butadiene decreased both the yield and the extent of the double carbonylation (experiments 6–8). In the case of 2-bromo-1-phenyl-4-methyl-1,3-pentadiene, the only carbonylation product was the monocarbonylation compound (2-benzylidene-4-methyl-3-pentenoic acid). Replacing the phenyl group in **1** by a methyl group (e.g., 3-bromo-1,3-pentadiene) had little effect on the double carbonylation.

Apart from the location of the substituent on the diene system, the *s-cis/s-trans* conformational orientation also proved to influence the reaction. When the 1,3-butadiene moiety was fixed in the *s-cis* form (i.e., 2-bromo-1,3-cyclooctadiene), no double carbonylation products were formed, 1,3-cyclooctadiene-2-carboxylic acid being the only carbonylation product (experiment 10). The distance between the two double bonds also had a significant effect on the double carbonylation process. Carboxylation of 2-bromo-1,5-hexadiene resulted only in monocarbonylation (i.e., 2-methylene-5-hexenoic acid was the sole product). In the case in which the double bond was conjugated to an aromatic ring (e.g., α-bromostyrene or α-bromo-β-phenylstyrene), the only product was the monocarbonylation compound.

The effect of the structural features on the double: single carbonylation ratio is explained below in the discussion of the mechanism of the reaction.

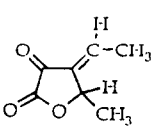
**Identification of the Products.** The double and

**Table 3. Carbonylation of Haloolefins Catalyzed by Nickel Cyanide[a]**

| exp no. | substrate | temp (°C) | time (h) | conversion (%) | yield of carbonylation products (%) double | yield of carbonylation products (%) single |
|---|---|---|---|---|---|---|
| 1 |  | 95 | 16 | 70 | | 70 |
| 2 |  | 95 | 6 | 95 | | 65 |
| 3 |  | 95 | 22 | 100 | 66[b] | |
| 4 |  | 90 | 68 | 71 | 27[b] | 13 |
| 5 |  | 85 | 6 | 65 | 0 | 50 |
| 6 |  | 105 | 30 | 40 | 16 | 4 |
| 7 |  | 110 | 30 | 50 | 27 | 3 |
| 8 |  | 85<br>110 | 146<br>22 | 62<br>70 | | 57<br>40 |
| 9 |  | 100 | 20 | 100 | 70[c] | |
| 10 |  | 90<br>110 | 8<br>5 | 98<br>90 | | 54<br>50 |
| 11 |  | 95 | 3 | 100 | | 48 |

[a] Reaction conditions: substrate (10 mmol), $Ni(CN)_2{\cdot}4H_2O$ (1 mmol), $C_{14}H_{29}N(CH_3)_3{}^+Br^-$ (0.2 mmol), 6.25 N NaOH (20 mL), toluene (25 mL), CO (1 atm). [b] Isolated as lactone **2**. [c] Isolated as lactone **8**.

single carbonylation products were identified by elemental and/or spectroscopic analysis ($^1H$ and $^{13}C$ NMR, IR, MS). It is noteworthy that for 2-bromo-1-phenyl-1,3-butadiene (**1**), 2-chloro-1-phenyl-1,3-butadiene, and 3-bromo-1,3-pentadiene the double carbonylation products were associated with ring closure (i.e., formation of β-alkylidene-α-keto-γ-lactones). The double carbonylation product derived from 3-bromo-1,3-pentadiene [i.e., 4-ethylidene-5-methyl-2,3,5-trihydrofuran-2,3-dione (**8**)]



**8**

was identified as follows: The NMR assignments were corroborated by NOE, COSY, and HETCOR techniques. $^1H$ NMR of **8**: δ-6.26 (q, $J$ = 7.3 Hz, =CH), 3.50 (q, $J$ = 7.1 Hz, −CH−O) 2.09 (d, $J$ = 7.3 Hz, $H_3C$−CH=), 1.37 (d, $J$ = 7.1 Hz, $CH_3$−CHO). $^{13}C$ NMR: δ-175.52 (α-carbonyl), 168.11 (lactonic carbonyl), 136.53 (C=$CHCH_3$), 132.38 (C=$CHCH_3$), 42.67 ($OCHCH_3$), 15.86 ($CH_3CH$=), 15.08 ($CH_3CHO$). IR: ν(CO) 1702, 1670, (C=C) 1635

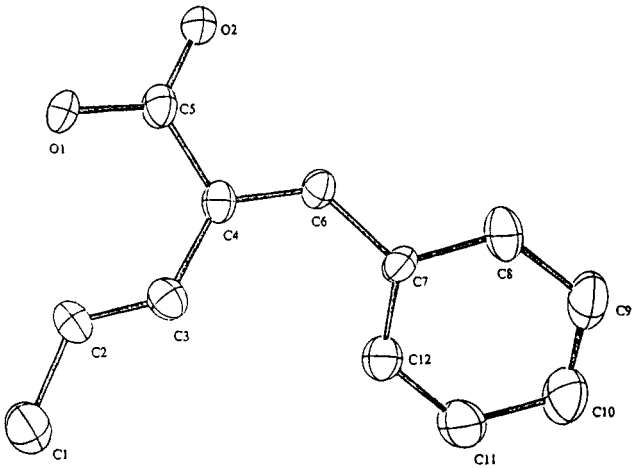
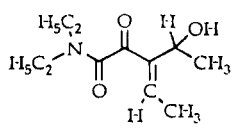



**Figure 1.** ORTEP diagram of (*E*)-2-benzylidene-3-pentenoic acid. Selected interatomic distances (Å) and angles (deg) are as follows: O1—C5 1.311(7), O2—C5 1.239(8), C1—C2 1.488(10), C2—C3 1.316(9), C3—C4 1.466(9), C4—C5 1.496(9), C4—C6 1.358(8), C7—C8 1.398(9), C8—C9 1.387(10), C1—C2—C3 124.1(6), C2—C3—C4 129.3(6), C3—C4—C5 120.9(5), C3—C4—C6 125.5(6), C5—C4—C6 113.5(5), O1—C5—O2 121.9(6), O1—C5—C4 116.4(5), O2—C5—C4 121.7(5), C4—C6—C7 129.2(6), C6—C7—C8 116.6(6), C6—C7—C12 124.2(5), C8—C7—C12 119.0(6), C7—C8—C9 121.0(7), C8—C9—C10 119.4(7), C1—C2—C3—C4 −179.6(7), C2—C3—C4—C5 29.8(4), C3—C4—C5—O1 8.1(3), C6—C4—C5—O1 −168.6(7), C5—C4—C6—C7 179.9(7), C4—C6—C7—C8 −155.8(7), C2—C3—C4—C6 −156.9(7), C6—C4—C5—O2 12.4)3), C4—C6—C7—C12 29.3(4).

$cm^{-1}$. The geometric structure around the double bond was determined by NOE and in analogy with the X-ray structure of the monocarbonylation product in the case of the carbonylation of 2-bromo-1-phenyl-1,3-pentadiene [i.e., 2-benzylidene-3-pentenoic acid (Figure 1)].

Reaction of 4-ethylidene-5-methyl-2,3,5-trihydrofuran-2,3-dione (**8**) with diethylamine in ethanol gave, as expected, *N,N*-diethyl-3-ethylidene-4-hydroxy-2-oxopentanamide (**9**). The structure was deduced from the



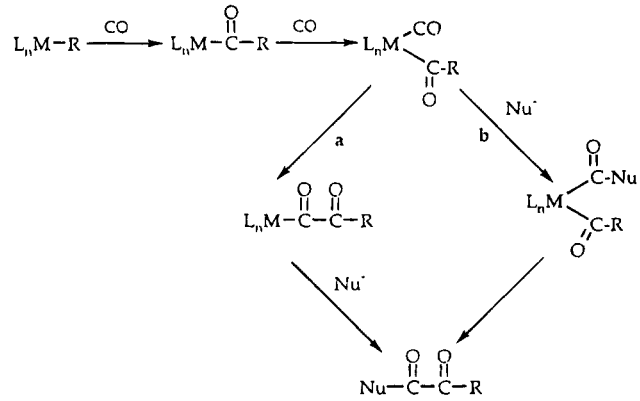
9

NMR and IR assignments [$^1$H NMR: δ-5.84 (q, $J$ = 7.8 Hz, =CHCH$_3$), 3.23 (q, $J$ = 7.4 Hz, CHOH), 3.04 (q, $J$ = 7.2 Hz, 2 CH$_2$N), 2.99 (b, OH), 1.89 (d, $J$ = 7.8 Hz, =CHCH$_3$), 1.34 (d, $J$ = 7.4 Hz, OCHCH$_3$), 1.33 (t, $J$ = 7.2 Hz, 2 CH$_2$CH$_3$). $^{13}$C NMR: δ-180.00, 173.74, 135.96, 131.45, 47.33, 42.14, 16.39, 15.13, 11.28. IR: ν(CO) 1710, 1640, (C=C) 1550 $cm^{-1}$].

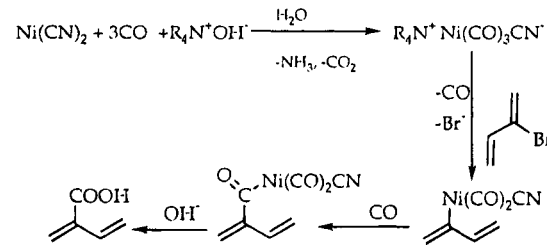
**Mechanistic Considerations.** Of special interest is the elucidation of the reaction mechanism of the double carbonylation process. Insertion of carbon monoxide in a metal—carbon bond will lead to a metal—acyl species. There are two possible mechanistic pathways from the metal—acyl species to the double carbonylation product (Scheme 1).

The mechanism for the double carbonylation of aryl halides and benzyl halides with cobalt carbonyl has been partially studied. Alper[20] and Cassar[21] proposed a

**Scheme 1**




**Scheme 2**




11 10

mechanism for the double carbonylation of benzylic halides, which involved an equilibrium between the acyl intermediate and its enolic form. The latter is then carbonylated, producing an α-keto acid. Recently,[22] however, it was suggested that the mechanism of double carbonylation by the cobalt tetracarbonyl anion involves an acyl(alkoxycarbonyl)cobalt complex.

The mechanism of the palladium-catalyzed double carbonylation reaction of haloaromatic compounds to α-keto amides and α-keto esters has been studied at length by a number of groups.[23–25] They suggested that nucleophilic attack on a CO ligand coordinated to the metal will lead to the formation of a carboalkoxy or carbamoyl species, which will then form α-keto amides or α-keto esters by reductive elimination.

In our case, the carbonylation of halo dienes with nickel cyanide starts by conversion of Ni(CN)$_2$·4H$_2$O to Ni(CO)$_3$CN$^-$,[26] followed by nucleophilic substitution of the halo diene. CO insertion then produces a nickel—acyl intermediate **11**. Nucleophilic attack on **11** by the hydroxide anion gives the monocarbonylation product (Scheme 2). The transformation of the nickel—acyl intermediate **11** to the double carbonylation product can proceed via three pathways, as follows (Scheme 3).

(I) Insertion of a second carbon monoxide molecule into the nickel—acyl bond will give an α-keto acyl—nickel intermediate **12**. Attack by a base will then yield the double carbonylation product.

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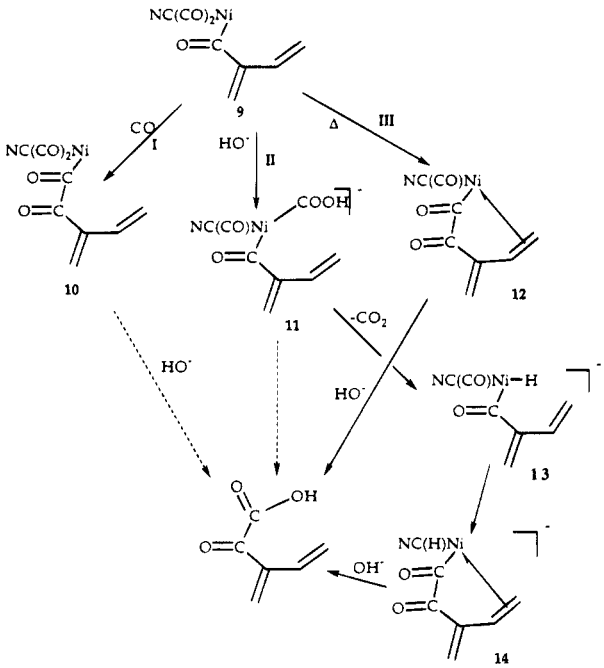
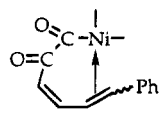
(26) Joo, F.; Alper, H. *Organometallics* **1985**, *4*, 1775.

**Scheme 3**



(II) Attack by a hydroxide anion on a coordinated carbon monoxide will give the acyl(hydroxycarbonyl)-nickel intermediate **13**, which then furnishes the double carbonylation products by reductive elimination.

(III) A concerted pathway, in which the free double bond attacks the nickel center and CO is inserted into the nickel—acyl bond, may yield a stable metallacycle **14**. Attack of a hydroxide ion on **14** then produces the double carbonylation product. Metallacycles may also be formed through the acyl(hydroxycarbonyl)nickel intermediate **13**. Decarbonylation of **13** would afford **15**, which can undergo insertion of a second carbon monoxide and formation of the five-membered metallacycle **16**.



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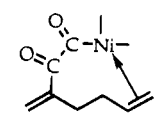
Pathways I and II are unlikely to represent the mechanism of the double carbonylation reaction in our case, because halo monoenes, such as α- and β-bromostyrene and α-bromo-β-phenylstyrene, do not themselves undergo double carbonylation (even at high temperatures and high base concentrations). It is clear that the second double bond must have an important role in the mechanism leading to the double carbonylation product. The following explanations support mechanism III (Scheme 3), in which the double carbonylation results from the formation of the five-membered metallacycle **14**.

(1) There is no electronic substituent effect on the 1-position of the 1,3-diene moiety. Replacing the phenyl group in **1** by a methyl group had no influence on the formation of the double carbonylation product. This indicates that there are no resonance or inductive effects on the metal—acyl bond. This finding is in contrast to the palladium-catalyzed double carbonylation of haloolefins.[11]

(2) Substituents on the 4-position of the 2-bromo-1,3-diene moiety have a remarkable influence on the double carbonylation pathway. The presence of methyl, phenyl, or dimethyl groups on the 4-position of compound **1** (2-bromo-1-phenyl-1,3-pentadiene, 2-bromo-1,4-diphenyl-1,3-butadiene, or 2-bromo-4-methyl-1-phenyl-1,3-pentadiene) leads to a reduction in the yields of the double carbonylation products. In the case of dimethyl, the monocarbonylation compound was the only product in the aqueous phase. This indicates that the steric effect on the free double bond is important, and steric hindrance will prevent the coordination of this double bond to the nickel center and subsequent formation of a metallacycle.

(3) The 2-halo 1,3-diene moiety is important for the double carbonylation reaction: *trans*-1-halo 1,3-dienes (e.g., *trans*-4-bromo-1-phenyl-1,3-butadiene) gave only the monocarbonylation product, while for *cis*-1-bromo 1,3-dienes, 5% of the double carbonylation product was formed. The *trans* isomer is not able to form a nickel metallacycle, while the *cis* isomer forms a six-membered metallacycle **17**, which is expected to be less stable than the five-membered metallacycle **14**. For the same reasons 2-halo 1,5-dienes do not give any double carbonylation products, and these compounds will be able to form the unstable seven-membered metallacycle **18**.[27]



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(4) Not only is the 2-halo 1,3-diene moiety itself essential for double carbonylation, but the double bonds must be free of rotation around the single C—C bond between them. Fixation of the diene moiety in the *s-cis* form (2-bromo-1,3-cyclooctadiene) gave no double carbonylation products, since in this case the nickel atom was not able to reach the π moiety of the double bond and thus could not form a metallacycle.

(5) The temperature effect on the double carbonylation also supports the metallacycle pathway, since the main step in the formation of the metallacycle intermediate **14** was the attack of the double bond (like ligand exchange) on the nickel(II) center with an insertion step. This step requires a high activation energy to form the more stable metallacycle intermediate.[28]

(6) The effect of high base concentrations may be explained by the attack of the base on the nickel—acyl complex leading to a (hydroxycarbonyl)nickel **13** intermediate. Decarboxylation of **13** will lead to the hydrido(acyl)nickel intermediate **15**, which will form the metallacycle **16**.[29]

It should be added that there is another mechanistic explanation for the formation of the double carbonylation products, which involves a second carbonylation of the monocarbonylation products (i.e., the carbonylation of the acids). Such a possibility was examined by introducing the acid into the carbonylation system under different conditions. When **3** was used as the

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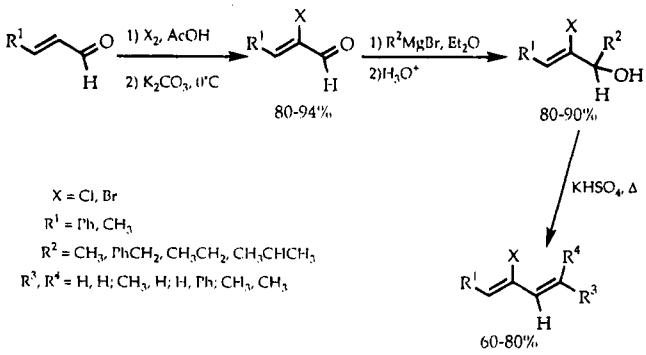
(29) Under drastic conditions (>6.25 N NaOH and >90 °C) some hydrogenated double carbonylation products were isolated.

**Scheme 4**




substrate, such an acid could be carbonylated to the double carbonylation product **2** under more drastic conditions than those used for the carbonylation of **1**.[30] The mechanism of the double carbonylation of **3** in this system is initiated by the decarboxylation of the acid, leading to the alkenyl—nickel intermediate which is the same intermediate as that for the double carbonylation of halo dienes (i.e., **10** in Scheme 2).

In summary, the combination of nickel cyanide and a phase-transfer agent constitutes an efficient double carbonylation catalyst for the conversion of 2-halo 1,3-dienes into α-keto-β-alkylidene acids or α-keto-β-alkylidene lactones. The proposed double carbonylation mechanism for such a reaction is the first reported example in which two molecules of carbon monoxide are introduced into a metal—carbon bond in a concerted mechanism via the formation of a stable metallacycle.[31]

## Experimental Section

Solvents were purified according to standard procedures. Proton and carbon NMR were performed on a Varian XL-200 spectrometer. Infrared spectra were recorded on a Nicolet 5ZDX FT-IR spectrometer. Mass spectra were obtained on a GC—MS spectrometer, with a mass selective detector HP 5971A and on a VG5050 micromass spectrometer.

$Ni(CN)_2{\cdot}4H_2O$ was purchased from Strem Chemical Co. 2-Bromo-1,5-hexadiene,[32] 2-bromo-1,3-cyclooctadiene,[33] and 1-bromo-4-phenyl-1,3-butadiene[34] were prepared according to literature procedures. The yields given in this work are based on the isolated products.

**General Synthesis of the Compounds Having the 2-Halo 1,3-Diene Moiety.** The compounds 2-bromo-1-phenyl-1,3-butadiene, 2-chloro-1-phenyl-1,3-butadiene, 2-bromo-1,4-diphenyl-1,3-butadiene, 2-bromo-1-phenyl-1,3-pentadiene, 2-bromo-4-methyl-1-phenyl-1,3-pentadiene, and 3-bromo-1,3-pentadiene were prepared by the reaction sequence given in Scheme 4.[35]

**General Procedure for the Carbonylation of Halo Dienes in the Presence of $Ni(CN)_2{\cdot}4H_2O$ under Phase-Transfer Conditions.** A 100-mL triple-necked flask equipped with a Neoprene seal and a small magnetic stirrer was charged with a mixture of 1 mmol of $Ni(CN)_2{\cdot}4H_2O$, 20 mL of aqueous NaOH solution, 20 mL of toluene, and 0.22 mmol of tetradecyltrimethylammonium bromide. The mixture was stirred at 90 °C under carbon monoxide. After 1 h, 10 mmol of substrate in 5–10 mL of toluene was added in small portions (*p*-xylene, decane, or naphthalene were added as the internal standard). After a period of time (see Tables 1 and 2 for reaction temperatures), the reaction mixture was cooled to room temperature and the phases were separated. The aqueous phase was neutralized with cooled 10% hydrochloric acid. The products were isolated by extraction with methylene chloride (3 × 50 mL) and dried on magnesium sulfate, and the solvent was removed under reduced pressure. The single and the double carbonylation products were separated by column chromatography or by crystallization (ether/hexane).

**5-Phenyl-2,4-pentadienoic acid**: $^1$H NMR (200 MHz, $CDCl_3$) δ 7.52–6.92 (m, 6H), 6.85–6.81 (m, 2H), 5.91 (d, $J$ = 15.3 Hz, 1H); $^{13}$C NMR 171.47, 146.93, 141.63, 135.88, 129.30, 128.86, 127.36, 126.00, 120.25; IR (Nujol) ν(CO) 1682 cm$^{-1}$; MS *m/z* (relative intensity), 175 (3), 174 (25), 130 (12), 129 (100), 128 (57).

**2-Methylene-5-hexenoic acid**: $^1$H NMR (200 MHz, $CDCl_3$) δ 6.33 (s, 1H), 5.82–5.74 (m, 1H) 5.67 (s, 1H), 5.08–4.96 (m, 2H), 2.42 (t, $J$ = 7.9 Hz, 2H), 2.27 (m, 2H); IR (Nujol) ν(CO) 1689 cm$^{-1}$; MS *m/z* (relative intensity) (silylated) 198 (1), 183 (68), 167 (12), 126 (2), 125 (4), 111 (100).

**1,3-Cyclooctadiene-2-carboxylic acid**: $^1$H NMR (200 MHz, $CDCl_3$) δ 7.10 (t, $J$ = 8.0 Hz, 1H), 6.33 (d, $J$ = 11.5 Hz, 1H), 5.88 (td, $J_1$ = 11.5 Hz, $J_2$ = 6.8 Hz, 1H), 2.33 (m, 2H) 2.14 (m, 2H), 1.52 (m, 4H); $^{13}$C NMR 172.89, 145.03, 133.85, 129.53, 122.54, 28.49, 28.22, 22.63, 22.07; IR (Nujol) ν(CO) 1680 cm$^{-1}$; MS *m/z* (relative intensity) 255 (4), 224 (22), 209 (52), 179 (17), 134 (34).

**2-Benzylidene-4-methyl-3-pentenoic acid**: $^1$H NMR (200 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.57 (dd, $J_1$ = 7.9 Hz, $J_2$ = 2.4 Hz, 2H), 7.37–7.20 (m, 3H), 5.95 (bs, 1H), 1.87 (d, $J$ = 1.2 Hz, 3H), 1.45 (s, 3H); $^{13}$C NMR 171.85, 140.03, 138.45, 135.32, 129.82, 128.64, 128.10, 127.68, 118.36, 25.07, 17.48; IR (Nujol) ν(CO) 1683 cm$^{-1}$; MS *m/z* (relative intensity) 202 (2), 186 (4), 158 (5), 157 (9), 143 (26).

**3-Benzylidene-2-oxo-4-hexenoic acid**: $^1$H NMR (200 MHz, $CDCl_3$) δ 7.60 (s, 1H), 7.49–7.20 (m, 5H), 6.37 (m, 2H), 1.85 (d, $J$ = 5.0 Hz, 3H); $^{13}$C NMR 180.00, 173.29, 141.83, 139.16, 135.26, 130.86, 129.99, 128.88, 128.61, 123.42, 19.01; IR (Nujol) ν(CO) 1723, 1675 cm$^{-1}$; MS *m/z* (relative intensity) 216 (21), 201 (12), 188 (20), 173 (15), 144 (17), 143 (100).

**2-Benzylidene-3-pentenoic acid**: $^1$H NMR (200 MHz, $CDCl_3$) δ 6.27 (m, 2H), 7.64–7.20 (m, 6H), 1.84 (d, 3H, $J$ = 4.68 Hz, 3H); $^{13}$C NMR 172.81, 139.96, 135.79, 133.41, 130.22, 129.07, 128.69, 128.30, 123.95, 19.21; IR (Nujol) ν(CO) 1670 cm$^{-1}$; MS *m/z* (relative intensity) 188 (33), 173 (7), 144 (24), 143 (100), 129 (66), 128 (88), 127 (24).

**3-Benzylidene-5-phenyl-2-oxo-4-pentenoic acid**: $^1$H NMR (200 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.48–7.24 (m, 10H), 6.85 (m, 2H); $^{13}$C NMR 17.00, 170.07, 140.49, 137.00, 131.54, 129.75, 128.23, 127.82, 127.53, 127.59, 126.18, 121.12; IR (Nujol) ν(CO) 1757, 1715 cm$^{-1}$; MS *m/z* (relative intensity 278 (45), 260 (7), 234 (30), 205 (30), 156 (34), 91 (100).

**2-Benzylidene-4-phenyl-3-butenoic acid**: $^1$H NMR (200 MHz, $CDCl_3$) δ 7.47–7.26 (m, 11H), 6.87–6.81 (m, 2H); $^{13}$C NMR 169.37, 139.49, 136.423, 134.61, 130.67, 128.23, 127.99, 127.65, 127.12, 125.76, 121.12; IR (Nujol) ν(CO) 1715 cm$^{-1}$; MS *m/z* (relative intensity) 250 (24), 205 (100), 190 (12), 128 (12).

**2-Benzylidene-3-butenoic acid (3)**: $^1$H NMR (200 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.49–7.36 (m, 5H), 6.65 (dd, $J_1$ = 18.6 Hz, $J_2$ = 11.6 Hz, 1H), 5.89 (dd, $J_1$ = 18.6 Hz, $J_2$ = 1.5 Hz, 1H), 5.51 (dd, $J_1$ = 11.6 Hz, $J_2$ = 1.5 Hz, 1H); $^{13}$C NMR ($CDCl_3$) 173.134, 141.689, 134.917, 130.270, 129.176, 128.921, 128.378, 121.590; IR (Nujol) ν(CO) 1702 cm$^{-1}$.

**1-Phenyl-3-buten-1-yne (6)**: $^1$H NMR (200 MHz, $CDCl_3$) δ 7.69 (d, $J$ = 7.6 Hz, 1H), 7.42–7.15 (m, 3H), 6.02 (dd, $J$ =

(30) Amer, I.; Alper, H. *J. Mol. Catal.* **1993**, *85*, 117.
(31) The reported stoichiometric insertion of CO into a metal—acyl bond is the only case in which such a mechanism has been proved: Sheridan, B. J.; Han, S.-H.; Geoffroy, L. G. *J. Am. Chem. Soc.* **1987**, *109*, 8097.
(32) Peterson, P. E.; Nelson, D. J.; Risener, R. *J. Org. Chem.* **1986**, *51*, 2381.
(33) Grunewald, G. L.; Grindel, J. M. *J. Med. Chem.* **1976**, *19*, 10.
(34) Matsumoto, M.; Kuroda, K. *Tetrahedron Lett.* **1980**, *21*, 4021.
(35) (a) Allen, C. F. H.; Edens, C. O. *Organic Syntheses*; Wiley: New York, 1955; Collect. Vol. III, p 731. (b) Grummit, O.; Becker, E. I. *Organic Syntheses*; Wiley: New York, 1963; Collect. Vol. IV, p 771. (c) Overberger, C. G.; Saunders, J. H. *Organic Syntheses*; Wiley: New York, 1955; Collect. Vol. III, p 204.

16.6 Hz, $J_2$ = 11.0 Hz, 1H), 5.73 (d, $J$ = 16.6 Hz, 1H), 5.54 (d, $J$ = 11.0 Hz, 1H); MS *m/z* (relative intensity) 128 (100), 102 (23).

**4-Ethylidene-5-methyl-2,3,5-trihydrofuran-2,3-dione (8)**: $^1$H NMR (200 MHz, $CDCl_3$/DMSO) $\delta$ 6.26 (q, $J$ = 7.3 Hz, 1H), 3.50 (q, $J$ = 7.1 Hz, 1H), 2.09 (d, $J$ = 7.2 Hz, 3H), 1.37 (d, $J$ = 7.1 Hz, 3H); $^{13}$C NMR ($CDCl_3$) 175.516, 168.109, 136.533, 132.383, 42.670, 15.857, 15.082; MS *m/z* (relative intensity) 140 (5), 112 (40), 96 (35), 67 (100); IR (Nujol) $\nu$(CO) 1702.3, 1670, 1635 cm$^{-1}$; mp 146–147 °C.

**Acknowledgment.** We thank Professor H. Alper for his helpful discussions. This work was supported by the Israeli Ministry of Science and Technology through Grant No. 3294190 and by Grant No. 471/92 from the Basic Research Foundation of the Israel Academy of Sciences and Humanities.

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