Nickel-Catalyzed Electrochemical Couplings of Vinyl Halides: Synthetic and Stereochemical Aspects

C. Cannes, S. Condon,* M. Durandetti,* J. Périchon, and J.-Y. Nédélec

Laboratoire d'Electrochimie, Catalyse et Synthèse Organique, UMR 7582 CNRS-Université Paris 12, 2, rue Henry-Dunant, 94320 Thiais, France

e-mail: condon@glvt-cnrs.fr or durandetti@glvt-cnrs.fr

Received February 9, 2000

Homo- and cross-coupling involving alkenyl halides have been performed efficiently using an electroassisted nickel-complex catalysis. Valuable product such as conjugated dienes, β,γ- or γ,δ-unsaturated esters, ketones, or nitriles, as well as alkenylated aryl compounds are thus prepared with high yields and high stereoselectivity. Partial isomerization is only observed in a few cases, when the alkenyl halide is involved in a late step of the catalytic cycle. This is the case in the preparation of (*Z*,*Z*)-1,3-diene.

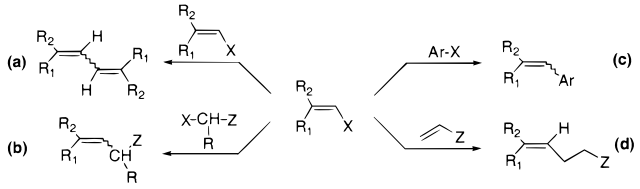
Introduction

Dehalogenative reductive coupling of organic halides is one of the most straightforward methods of C−C bond formation. However, the preparation of conjugated biaryls from aromatic halides or 1,3-dienes from alkenyl halides is difficult to conduct by the classical Ullmann procedure,[1] which requires rather drastic reaction conditions. The activation of aryl or alkenyl halides is best carried out today by use of low-valent transition metal catalysts such as nickel or palladium, which can be generated in situ, chemically or electrochemically from Ni(II) or Pd(II)[2] precursors. Apart from occurring in mild reaction conditions, this approach also tolerates sensitive functional groups on the organic halides. Valuable products are thus obtained, via catalytic processes, such as symmetrical and unsymmetrical biaryls,[3,4] polymers from aryl dihalides, and also cross-coupling products from mixtures of aryl and alkyl halides.[5]

The reductive activation of alkenyl halides is less common, notably because of the limited availability of isomerically pure compounds. We present in this paper the investigation of various nickel-catalyzed electroreductive homo- and cross-coupling reactions from alkenyl halides, as well as the alkenylation of activated olefins (Scheme 1), leading respectively to conjugated dienes, β,γ- or γ,δ-unsaturated compounds, and alkenylated aryl compounds.

We intend to show that the electrochemical methods, well developed in the chemistry of aryl halides,[6−8] can be suitably used for the activation of alkenyl halides. The chemistry of alkenyl halides also includes the additional stereochemical aspect, which will be discussed in connection with the reaction mechanisms.

Scheme 1



Results and Discussion

The general reaction conditions are derived from those used for the electrochemical coupling of aryl halides, previously developed in this laboratory. All of the reactions are performed at constant current density, in a one-compartment cell fitted with nickel foam as the cathode and, as the anode, a sacrificial aluminum rod for the homo- and cross-coupling reactions, or an iron rod for the alkenylation of activated olefins. All reactions are carried out in DMF as solvent. $NiBr_2$bpy (bpy = bipyridine) is the catalyst precursor for the homo- and cross-coupling reactions (Scheme 1, reactions a−c), whereas for the alkenylation of activated olefins (Scheme 1, reaction d), acetonitrile is added as cosolvent and the catalyst precursor is $NiBr_2 \cdot 3H_2O$. Also, for the homocoupling or the alkenylation of the activated olefins, the reagents are introduced at the very beginning of the electrosynthesis, whereas for the cross-coupling reactions one reagent (i.e., the most reactive with Ni(0)) is added constantly during the electrolysis. In the reactions reported below the alkenyl halides mostly used are (*E*)- and (*Z*)-β-halostyrene, and 1-halohept-1-ene.

Homocoupling Reactions. Many papers have dealt with the homocoupling of alkenyl halides mediated by nickel complexes. Those reactions are conducted either stoichiometrically with nickel complexes such as $K_2[Ni_2(CN)_6]$,[9,10] $Ni(COD)_2$,[11] NiCRA(bpy),[12] $Ni(PPh_3)_nCl_2$/Zn-

(1) (a) Cohen, T.; Poeth, T. *J. Am. Chem. Soc.* **1972**, *94*, 4363. (b) Fanta, P. E. *Synthesis* **1974**, 9. (c) See also Zhang, S.; Zhang, D.; Liebeskind L. S. *J. Org. Chem.* **1997**, *62*, 2312.

(2) Nédélec, J. Y.; Périchon, J.; Troupel, M. *Topics in Current Chemistry*, 185; Springer-Verlag: Berlin Heidelberg, 1997.

(3) Meyer, G.; Troupel, M.; Périchon, J. *J. Organomet. Chem.* **1990**, *393*, 137.

(4) Iyoda, M.; Otsuka, H.; Sato, K.; Nisato, N.; Oda, M. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 80.

(5) Durandetti, M.; Périchon, J.; Nédélec, J.-Y. *J. Org. Chem.* **1997**, *62*, 7914.

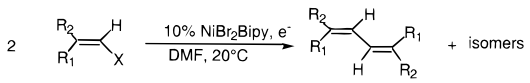
(6) Condon Gueugnot, S.; Leonel, E.; Nédélec, J. Y.; Périchon, J. *J. Org. Chem.* **1995**, *60*, 7684.

(7) Rollin, Y.; Troupel, M.; Tuck, D. G.; Périchon, J. *J. Organomet Chem.* **1986**, *303*, 131.

(8) (a) Durandetti, M.; Sibille, S.; Nédélec, J. Y.; Périchon, J. *Synth. Commun.* **1994**, *24*, 145. (b) Durandetti, M.; Nédélec, J. Y.; Périchon, J. *J. Org. Chem.* **1996**, *61*, 1748. (c) Durandetti, M.; Sibille, S.; Nédélec, J. Y.; Périchon, J. In *Novel Trends in Electroorganic Synthesis*; Torii, S., Ed.; Kodansha: Tokyo, 1995; p 209.

10.1021/jo000182f CCC: $19.00
Published on Web 07/06/2000

Table 1. Ni(0)-Catalyzed Homocoupling of Alkenyl Halides



entry	R_1	R_2	X	composition (%) *E*/*Z*	(%) Isomers[a] (*E*,*E*)	(*E*,*Z*)	(*Z*,*Z*)	yield (%)[b]
1	H	C_6H_5	Cl[c]	87/ 13	73.5	22.5	3	61
2	H	C_6H_5	Br	85.5/14.5	71.5	27	1.5	69
3	H	C_6H_5	Br	100/0[d]	100	0	0	69
4	H	C_5H_{11}	Br	100/0[d]	100	0	0	74
5	H	C_5H_{11}	I	100/0	98	2	0	76.5
6	C_6H_5	H	Cl[c]	2/98	3	29	68	50
7	C_6H_5	H	Br	2/98	3	31	66	59
8	C_5H_{11}	H	Br	2/98	9	43.5	47.5	70
9	C_5H_{11}	H	I	1/99	8	42	50	73

[a] Compositions of isomers were determinated by GC from the crude product. [b] Isolated yields of mixture after purification. [c] At 50 °C. [d] See ref 31.

(0),[13] or catalytically with Ni(II) salts[14] or complexes reduced by zinc powder.[4,14−16]

We already reported, a few years ago, that the homocoupling[7] of alkenyl bromides can be achieved electrochemically in the presence of catalytic amounts of $NiBr_2$bpy + 2 bpy, in the reaction conditions similar to those used for aryl halides, i.e., at 20 °C, in NMP, in an undivided cell fitted with a gold grid as the cathode and a magnesium rod as the anode. More recently, we reported a study on the mechanism of the nickel-catalyzed dimerization of alkenyl halides,[17] which is referred to below when necessary.

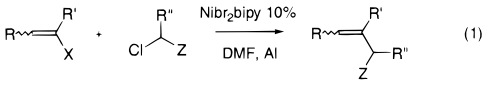
We now report the application at a preparative scale of the $NiBr_2$bpy-promoted homocoupling reaction of geometrically pure (*Z*)- or (*E*)-alkenyl halides prepared by known methods. Results are reported in Table 1.

All of the alkenyl halides tested couple to give the corresponding 1,3-dienes. (*Z*)- or (*E*)-Alkenyl bromides or iodides react efficiently at 20 °C, whereas heating at above 50 °C is necessary with alkenyl chlorides (Table 1, entries 1 and 6). For the same series of alkenyl halides, the geometry of the double bond affects the reactivity. Indeed, the reaction proceeds faster and is slightly more efficient with the (*E*)-isomer than with the (*Z*)-isomer. This was already found in the mechanistic study.[17] In addition, coupling of (*E*)-alkenyl halides (Table 1, entries 1−5) produces symmetrical 1,3-diene with retention of the stereochemistry of the starting compound, whereas a mixture of isomeric 1,3-dienes is obtained from (*Z*)-alkenyl halides (Table 1, entries 6−9). However the geometry of the double bond is maintained in the main stereoisomer formed. Comparison of the two model compounds studied reveals some influence of the substituent ($R_1 = C_5H_{11}$ or C_6H_5), bonded to the β-position of the (*Z*)-alkenyl halide, on the isomer distribution. Indeed, the extent of isomerization is less with $R = C_6H_5$ than with $R = C_5H_{11}$ (Table 1, entries 6 and 7 vs 8 and 9). The nature of the halogen seems not to be determinant.

The synthesis of symmetrical conjugated (*E*,*E*)-dienes can thus be performed readily by this method from (*E*)-alkenyl halides. However, despite its simplicity and the good yields obtained, the synthetic utility of the procedure is limited due to the lack of stereoselectivity observed for the preparation of symmetrical conjugated (*Z*,*Z*)-dienes. Examinations of samplings during the course of the reaction have not revealed isomerization of the starting (*Z*)-vinyl halide. No clear-cut evidence for the origin of the isomerization can be obtained from these results, since we cannot discriminate the fragments in the final symmetrical product.

Cross-Coupling Reaction between Vinyl Halides and Alkyl Halides. Functionnalized alkenyl compounds such as β,γ-unsaturated ketones, esters, or nitriles are of high interest as precursors of natural products[18] and pharmaceuticals.[19] Many synthetic strategies have been described,[20−29] but the most straightforward approach to these products would be the direct attachment of the vinyl group onto the substrate. Thus, β,γ-unsaturated esters can be prepared by coupling between 1-alkenylboranes with ethyl diazoacetate.[25] Alternatively, carbonyl compounds can be obtained by the transition-metal-catalyzed carbonylation of allylic compounds.[20−24] Some other methods have been reported such as Wittig reactions and related processes[27,28] or the addition of esters to a zirconium-isoprene complex at 50 °C leading to the (*Z*)-β,γ-unsaturated ketones.[29]

We have found that the cross-coupling between vinyl halides and activated alkyl halides can be performed efficiently by nickel (equation 1) using the general procedure described previously for the coupling between activated alkyl chlorides and aryl halides.[8,30]

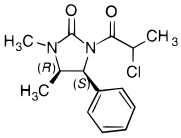


Z = COR, CO_2R, CN

The reactions were thus conducted in DMF containing, at the beginning, $NiBr_2$bpy (1 mmol), the alkenyl halide

(9) Hashimoto, I.; Ryang, M.; Tsutsumi, S. *Tetrahedron Lett*. **1970**, 4567.
(10) Hashimoto, I.; Tsuruta, N.; Ryang, M.; Tsutsumi, S. *J. Org. Chem*. **1970**, *35*, 3748.
(11) (a) Semmelhack, M. F.; Helquist, P. M.; Gorzynski J. D. *J. Am. Chem. Soc*. **1972**, *94*, 9234. (b) Semmelhack, M. F.; Helquist, P.; Jones, L. D.; Keller, L.; Mendelson, L.; Speltz Ryono L.; Gorzynski Smith, J.; Stauffer, R. D. *J. Am. Chem. Soc*. **1981**, *103*, 6460.
(12) Vanderesse, R.; Brunet, J. J.; Caubere, P. *J. Organomet Chem*. **1984**, *264*, 263.
(13) Kende, A. S.; Liebeskind, L. S.; Braitsch, D. M. *Tetrahedron Lett*. **1975**, *39*, 3375.
(14) (a) Takagi, K.; Hayama, N.; Inokawa, S. *Chem. Lett*. **1979**, 917. (b) Takagi, K.; Mimura, H.; Inokawa, S. *Bull. Chem. Soc. Jpn*. **1984**, *57*, 3517.
(15) Zembayashi, M.; Tamao, K.; Yoshida, J. I.; Kumada, M. *Tetrahedron Lett*. **1977**, *47*, 4089.
(16) Sasaki, S.; Nakao, K.; Kobayashi, Y.; Sakai, M.; Uchino, N.; Sakakibara, Y.; Takagi, K. *Bull. Chem. Soc. Jpn*. **1993**, *66*, 2446.
(17) Cannes, C.; Labbé, E.; Durandetti, M.; Devaud, M.; Nédélec, J. Y. *J. Electroanal. Chem*. **1996**, *412*, 85.
(18) (a) Alkaloids: Tufariello, J. J.; Mulkan, G. B.; Tegeler, J. J.; Trybulski, E. J.; Wong, S. C.; Ali, S. A. *J. Am. Chem. Soc*. **1979**, *101*, 2435. (b) Cyclodepsipeptides: Grieco, P. A.; Hon, Y. S.; Perez-Medrano A. *J. Am. Chem. Soc*. **1988**, *110*, 1630. (c) Pheromone: Battiste, M. A.; Rocra, J. R.; Wydra, R. L.; Tumlinson, J. H.; Chuman, T. *Tetrahedron Lett*. **1988**, *29*, 6565. (d) Terpenoid: Gnonlonfoun, N.; Zamarlik, H. *Tetrahedron Lett*. **1987**, *28*, 4053.
(19) β-Lactams: (a) Bilosky, A. J.; Wood, R. D.; Ganem, B. *J. Am. Chem. Soc*. **1982**, *104*, 3233. (b) Miller, M. J. *Acc. Chem. Res*. **1986**, *19*, 49. (c) Knapp, S.; Levorse, A. T. *J. Org. Chem*. **1988**, *53*, 4006.
(20) Kiji, J.; Gleano, T.; Konishi, H.; Nishiumi, W. *Chem. Lett*. **1989**, 1873.
(21) Neibecker, D.; Poirier, J.; Tkatchenko, I. *J. Org. Chem*. **1989**, *54*, 2459.
(22) Murahashi, S.-I.; Imada, Y.; Taniguchi, Y.; Higashiura, S. *J. Org. Chem*. **1993**, *58*, 1538.
(23) Tsuji, J.; Sato, K.; Gkumoto, H. *J. Org. Chem*. **1984**, *49*, 1341.
(24) Murahashi, S.-I.; Imada, Y.; Nishimura, K. *Tetrahedron* **1994**, *50*, 453.
(25) Brown, H. C.; Salunkhe, A. M. *Synlett* **1991**, 684.
(26) Tran, L.; Deshmukh, A. R.; Biehl, E. *Synth. Commun*. **1996**, *26*, 963.

Table 2. Nickel-Catalyzed Electroreductive Coupling between (*E*)-*β*-Bromostyrene and Activated Alkyl Halides

Entry	*E* / *Z* ratio for ß-bromostyrene (10 mmol)	Cl-CH(R")Z (mmol)	Isolated yields[a] (%) of coupling product	*E* / *Z* ratio for coupling product
1	*E* / *Z* = 87 / 13	$ClCH_2CO_2CH_3$ (13)	53	*E* / *Z* = 89 / 11
2	*E* / *Z* = 87 / 13	$ClCH(CH_3)CO_2CH_3$ (10)	70	*E* / *Z* = 83 / 17
3	*E* / *Z* > 99 / 1[b]	$ClCH(CH_3)CO_2CH_3$ (10)	72	*E* / *Z* = 99 / 1
4	*E* / *Z* = 87 / 13	$ClCH(CH_3)COCH_3$ (12)	57	*E* / *Z* = 85 / 15
5	*E* / *Z* = 87 / 13	$ClCH_2COCH_3$ (15)	65	*E* / *Z* = 87 / 13
6	*E* / *Z* = 87 / 13	$ClCH(CH_3)CN$ (18)	62	*E* / *Z* = 80 / 20
7	*E* / *Z* > 99 / 1[b]	 (7)	55[c]	*E* / *Z* > 99 / 1

[a] Based on initial alkenyl halide. All products gave satisfactory NMR and mass spectra. [b] C_6H_5−CH=CHBr *E*/*Z* = 87/13 refluxed in 2-propanol in the presence of NaOH (0.8 equiv) affords C_6H_5−CH=CHBr *E*/*Z* > 99/1.[31] [c] 78% based on initial RX; the diastereoisomeric excess was determined by GC; de = 90% ((*S*) major configuration).

(10 mmol), and a portion of the activated alkyl halide RX (ca. 0.3 mmol). RX was then added constantly to the solution, via a syringe pump, at a rate of 5 mmol/h. The electrolyses were run at 60 °C (or at room temperature for alkenyl iodide), under a current intensity of 0.25 A.

Results are given in Table 2 for the reactions involving (*E*)-*β*-bromostyrene.

Yields of the coupling products are good. As already observed with aryl halides, the coupling with chloropropionate is more efficient than with chloroacetate. The reaction is also highly stereoselective. Thus, starting from commercial (*E*)-*β*-bromostyrene which contained 13% of the (*Z*)-isomer, the *E*/*Z* isomer ratio in the coupling product is between 89/11 and 80/20 (Table 2, entries 1−2 and 4−6). From isomerically pure (*E*)-*β*-bromostyrene, prepared by purification of the commercial sample with *i*-PrONa,[31] the coupling with methyl 2-chloropropanoate led to 72% of methyl 2-methyl-4-phenyl-3-butenoate, with a *E*/*Z* ratio of 99/1, thus indicating that the reaction is stereospecific. We also prepared methyl 2-methyl-4-phenyl-3-butenoate in the chiral form. This is an intermediate in the synthesis of the natural product cryptophycin.[32] We used the method already described for the asymmetric electroreductive cross-coupling of α-chloropropionic acid derivatives with aryl halides.[5] Thus coupling of chiral α-chloroimide with the (*E*)-*β*-bromostyrene (Table 2, entry 7) gives the product in good yield (78% based on the α-chloroimide), high *E*/*Z* stereoselectivity (> 99/1), and high diastereoselectivity (de = 90%). On the basis on our previous studies in the aryl series, we can expect an (*S*)-configuration.

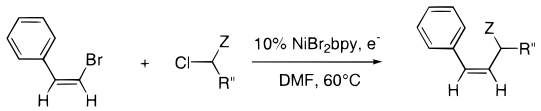
(*Z*)-*β*-Bromostyrene was also studied to look more carefully at the stereoselectivity. Results are given in Table 3.

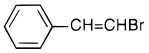
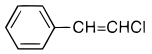
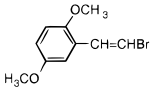
(*Z*)-*β*-Bromostyrene gave the same good yield and high stereoselectivity as (*E*)-*β*-bromostyrene. Indeed, if the starting material has a *Z*/*E* ratio of 99.5/0.5 the coupling product is obtained with a *Z*/*E* ratio of 92/8 to 98/2. The method can also be applied to alkenyl chlorides. Thus, the direct coupling between (*Z*)-*β*-chlorostyrene and methyl 2-chloropropanoate proceeds in high yield and high stereoselectivity (Table 3, entry 6). Actually, the chemical yield is even higher than with the bromo compound, because (*Z*)-*β*-bromostyrene dimerizes more rapidly than the (*Z*)-*β*-chlorostyrene, and all reactions with *β*-bromostyrene give significant amount of dimer. Some natural products have hydroxy or methoxy functionalities on the aromatic ring. We then prepared a (*Z*)-*β*-bromostyrene bearing two methoxy on the aromatic ring to study the effect of electron-releasing groups on the efficiency of the reaction. We obtained 71 and 63% of the coupling product with methyl 2-chloropropanoate and methyl 2-chloro-3-phenylpropanoate, respectively. The stereochemistry of the double bond was retained (*Z*/*E* = 95/5 and 94/6, respectively). The difference between the ratio for the *β*-bromostyrene and the coupling product can be explained by the fact that the (*E*)-*β*-bromostyrene dimerizes more rapidly than the (*Z*)-*β*-bromostyrene and so, during the electrolysis, a part of the (*E*)-*β*-bromostyrene was converted into the homocoupling product. So, electron-releasing groups on the aromatic ring do not affect the reactivity of the *β*-halostyrene.

We finally studied other (*E*)- or (*Z*)-alkenyl halides. Results are given in Table 4.

(27) Earnshaw, C.; Torr, R. S.; Warren, S *J. Chem. Soc., Perkin Trans. 1*, **1983**, 2893.
(28) Cristau, H. J.; Torreilles, E.; Barois-Gacherieu, C. *Synth. Commun.* **1988**, *18*, 185.
(29) Akita, M.; Yasuda, H.; Nakamura, A. *Chem. Lett.* **1983**, 217.
(30) Durandetti, M.; Devaud, M.; Périchon, J. *New J. Chem.* **1996**, *20*, 659.
(31) (a) Karpaty, M.; Davidson, M.; Hellin, M.; Coussemant, F. *Bull. Soc. Chim. Fr.* **1971**, *5*, 1731. (b) Lloyd-Jones, G. C.; Butts, C. P. *Tetrahedron* **1998**, *54*, 901.
(32) Salamonczyk, G. M.; Han, K.; Guo, Z.-W.; Sih, C. J. *J. Org. Chem.* **1996**, *61*, 6893.

Table 3. Nickel-Catalyzed Electroreductive Coupling between (*Z*)-*β*-Halostyrene and Activated Alkyl Halides



Entry	*Z* / *E* ratio for ß-halostyrene (10 mmol)	Cl-CH(R")Z (mmol)	Isolated yields[a] (%) of coupling product	*Z* / *E* ratio for coupling product
1		$ClCH_2CO_2CH_3$ (14)	68	*Z* / *E* = 94 / 6
2		$ClCH(CH_3)CO_2CH_3$ (10)	68	*Z* / *E* = 98 / 2
3	*Z* / *E* = 99.5 / 0.5	$ClCH(CH_3)COCH_3$ (12)	64	*Z* / *E* = 94 / 6
4		$ClCH_2COCH_3$ (13)	53	*Z* / *E* = 92 / 8
5		$ClCH(CH_3)CN$ (20)	58	*Z* / *E* = 97 / 3
6	 *Z* / *E* > 99 / 1	$ClCH(CH_3)CO_2CH_3$ (16)	88	*Z* / *E* = 98 / 2
7		$ClCH(CH_3)CO_2CH_3$ (8)	57 (71/RX)	*Z* / *E* = 95 / 5
8	*Z* / *E* = 89 / 11	$ClCH(CH_2\text{-}C_6H_5)CO_2CH_3$ (9)	57 (63/RX)	*Z* / *E* = 94 / 6

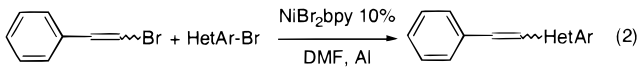
[a] Based on initial alkenyl halide. All products gave satisfactory NMR and mass spectra.

With this third series of reagents, chemical yields are also moderate to good, depending on the reactivity of the alkenyl halide. With respect to the stereoselectivity, if the starting material has the (*E*)-geometry, the coupling product has this geometry (Table 4, entries 6 and 8). But if the starting material has a (*Z*)-geometry, a *Z*/*E* ratio in the coupling product of 90/10 to 80/20 is observed due to the partial isomerization of the (*Z*)-reagent (Table 4, entries 3, 5, 7, 9, and 10). Alkenyl iodides are very reactive and they dimerize quite rapidly. Experimental conditions were then modified to increase the chemical yield. The reactions were thus conducted with addition of the alkenyl iodide to a solution of activated organic halide via a syringe pump (Table 4, entries 6 and 7). In this case, a higher chemical yield is obtained from the (*Z*)- than the (*E*)-isomer probably because the dimerization of the alkenyl halide occurs to a lesser extent with the (*Z*)-isomer than with the (*E*)-isomer. At last, the same stereoselectivity is obtained with alkenyl chloride or alkenyl bromide (Table 4, entries 9 and 10).

In summary, chemical yields of cross-coupling products between alkenyl halides and activated alkyl chlorides are moderate to good, and the stereoselectivity of the reaction is generally high: (*E*)-alkenyl halides lead to the (*E*)-coupling product, and (*Z*)-alkenyl halides lead to 74 to 98% of (*Z*)-isomer.

Cross-Coupling Reaction between Alkenyl Halides and Heteroaromatic Bromides. 2- or 3-Styrylthiophenes as well as 2-, 3- or 4-styrylpyridines have been widely investigated in the past decade because of their photochemical and photophysical properties[33] (fluorescence, luminescence, etc.). They are also precursors of potentially active optical materials. These compounds are usually prepared from aldehydes by a Wittig-type coupling.

These products can also be obtained by electroreductive cross-coupling between alkenyl halides and heteroaryl halides. This is illustrated below in the case of bromostyrene (vinylBr) and bromopyridine or bromothiophene (HetAr-Br) (eq 2).



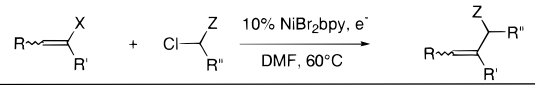
(2)

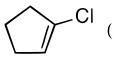
The reactions were carried out with HetAr−Br (10 mmol) in the solution, while vinylBr was added constantly to the solution via a syringe pump at a rate of 3.9 mmol/h. The electrolyses were run at constant current intensity of 0.2 A at room temperature for bromothiophene, 30 °C for 2-bromopyridine, and 60 °C for 3-bromopyridine. Chemical yields of cross-coupling are in the range of 40−59% and the couplings are stereoselective: (*E*)-*β*-bromostyrene gives the (*E*)-product and (*Z*)-*β*-bromostyrene gives 85% to 95% of the (*Z*)-product. Results are given in Table 5.

Higher yields are obtained with 2- than with 3-heteroaromatic bromide. We have already mentioned that (*E*)-*β*-bromostyrene tends to dimerize more rapidly than (*Z*)-*β*-bromostyrene. This does not have any influence when we use a very reactive compounds such as 2-bromothiophene (Table 5, entries 2 and 4). But with the less reactive 3-bromothiophene, the homocoupling reaction is more important with (*E*)-*β*-bromostyrene than with (*Z*)-*β*-bromostyrene. Thus a larger excess of (*E*)-*β*-bromostyrene was used, and a lower chemical yield was obtained (Table 5, entries 1 and 3). With 2- and 3-bromothiophene,

(33) (a) Iseki, Y.; Watanabe, E.; Mori, A.; Inoue, S. *J. Am. Chem. Soc.* **1993**, *115*, 7313. (b) Angeloni, L.; Castellucci, E.; Bartocci, G.; Mazzucato, U.; Spalletti, A.; Marconi, G. *Gazz. Chim. Ital.* **1996**, *126*, 609. (c) Chen, C.-C.; Pan, K.; Wang, S.-L.; Ho, T.-I. *J. Lumin.* **1997**, *71*, 321.

Table 4. Nickel-Catalyzed Electroreductive Coupling between Alkenyl Halides and Activated Alkyl Halides



Entry	alkenyl halide (mmol)	*Z* / *E* ratio	Cl-CH(R")Z (mmol)	Isolated yields[a] (%) of coupling product	*Z* / *E* ratio for coupling product
1	 (10)		$ClCH(CH_3)CO_2CH_3$ (15)	51	
2	CH_3-CH=CHBr (10)	*Z* / *E* = 50 / 50	$ClCH_2COCH_3$ (18)	70[b]	*Z* / *E* = 50 / 50
3	CH_3-CH=C(CH_3)Br (10)	*Z* / *E* > 99 / 1	$ClCH_2COCH_3$ (22)	65[b]	*Z* / *E* = 74 / 26
4	CH_3-CH=C(CH_3)Br (10)	*Z* / *E* = 25 / 75	$ClCH_2COCH_3$ (18)	65[b]	*Z* / *E* = 12 / 88
5	CH_3-CH=C(CH_3)Br (10)	*Z* / *E* > 99 / 1	$ClCH_2COC_6H_5$ (18)	51	*Z* / *E* = 80 / 20
6	C_5H_{11}-CH=CHI[c] (4,3)	*Z* / *E* < 1 / 99	$ClCH(CH_3)CO_2CH_3$ (4,4)	44	*Z* / *E* < 1 / 99
7	C_5H_{11}-CH=CHI[c] (5)	*Z* / *E* > 99 / 1	$ClCH(CH_3)CO_2CH_3$ (5)	70	*Z* / *E* = 89 / 11
8	C_5H_{11}-CH=CHBr (5)	*Z* / *E* < 1 / 99	$ClCH(CH_3)CO_2CH_3$ (9)	58	*Z* / *E* < 1 / 99
9	C_5H_{11}-CH=CHBr (5)	*Z* / *E* = 99 / 1	$ClCH(CH_3)CO_2CH_3$ (7)	63	*Z* / *E* = 74 / 26
10	C_5H_{11}-CH=CHCl (5)	*Z* / *E* > 99 / 1	$ClCH(CH_3)CO_2CH_3$ (6)	44	*Z* / *E* = 74 / 26

[a] Based on initial alkenyl halide. All products gave satisfactory NMR and mass spectra. [b] GC yields, based on internal standard. [c] At room temperature. To minimize the dimerization of the alkenyl halide, Cl−CH(R″)Z was introduced in solution, and alkenyl halide was added constantly to the solution via a syringe pump.

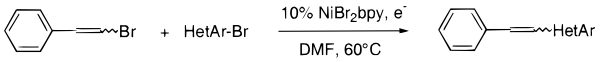
the stereochemistry of the alkenyl halide is retained. (*E*)-*β*-Bromostyrene gives (*E*)-styrylthiophene, (*Z*)-*β*-bromostyrene gives (*Z*)-styrylthiophene with *Z*/*E* ratio = 96/4. With bromopyridine, the reaction is not as stereoselective as with bromothiophene. Indeed, with (*Z*)-*β*-bromostyrene, the *Z*/*E* ratio of the coupling product is 85/15 (Table 5, entries 7 and 8) instead of 96/4 with bromothiophene (Table 5, entries 3 and 4).

Stereoselective Alkenylation of Activated Olefins. Many papers refer to the alkenylation of electron deficient olefins. In a number of methods the alkenyl moiety can be introduced by using organomanganese,[34] -zirconium,[35] -boron,[36] -alane,[37] or -copper[38] reagents, but the most often used method involves organocopper reagents. It is worth noting that they are multistep procedures, though in most cases the reported yields refer to the final addition step. In addition, problems of functional compatibility restrict the scope of the method. A few reactions of the alkenylation of activated olefins[39] from alkenyl halides have already been reported in the presence of nickel catalyst, the catalyst being generated in situ by Zn reduction.

The reaction conditions used for performing the nickel-catalyzed electrochemical conjugate addition of alkenyl halides on activated olefins are based on those reported for the arylation reactions.[6] However, we have now found that they can be optimized by a pre-electrolysis involving the oxidation of the iron anode along with the reduction of 1,2-dibromoethane in the absence of the other reagents and catalyst precursor. A short electrolysis is first run at constant current density (0.3 Adm^{-2}) in the presence of a solution of 1,2-dibromoethane and in DMF/acetonitrile 1/1 mixture in order to generate iron ions. The electrosynthesis is then conducted at constant current density (ca. 0.3 Adm^{-2}) at 70 °C. Weak donor ligands are necessary to prevent the loss of the catalyst; acetonitrile can play this role, along with the activated olefin. Results are reported in Table 6.

(34) (a) Cahiez, G.; Alami, M. *Tetrahedron Lett.* **1989**, *30*, 3541. (b) Cahiez, G.; Alami, M. *Tetrahedron Lett.* 1989, *45*, 4163.
(35) Schwartz, J.; Loots, J. M.; Kosugi, H. *J. Am. Chem. Soc.* **1980**, *102*, 1333.
(36) (a) Jacob, P.; Brown, H. C. *J. Am. Chem. Soc.* **1976**, *98*, 7832. (b) Hara, S.; Ishimura, S.; Suzuki, A. *Synlett* **1996**, 993. (c) Yanagi, T.; Sasaki, H.; Susuki, A.; Miyaura, N. *Synth. Commun.* **1996**, *26*, 2503.
(37) Hooz, J.; Layton, R. B. *Can. J. Chem.* **1973**, *51*, 2098.
(38) Perlmutter, P. *Conjugate Addition Reactions in Organic Synthesis*; Pergamon: Oxford, 1992.
(39) Sustmann, R.; Hopp, P.; Holl, P. *Tetrahedron Lett.* **1989**, *30*, 689.

Table 5. Nickel-Catalyzed Electroreductive Coupling between Bromostyrene and Heteroaromatic Bromides



Entry	HetArBr (10 mmol)	ß-bromostyrene (mmol)	*Z* / *E* ratio	Isolated yields[a] (%) of coupling product	*Z* / *E* ratio for coupling product
1		24	*Z* / *E* = 13 / 87	40	*Z* / *E* = 14 / 86
2		15	*Z* / *E* = 13 / 87	51	*Z* / *E* = 19 /81
3		20	*Z* / *E* = 99.5 / 0.5	50	*Z* / *E* = 96 / 4
4		15	*Z* / *E* = 99.5 / 0.5	51	*Z* / *E* = 96 / 4
5		14	*Z* / *E* = 13 / 87	48	*Z* / *E* = 10 / 90
6		14	*Z* / *E* = 13 / 87	69	*Z* / *E* = 12 /88
7		17	*Z* / *E* = 99.5 / 0.5	49	*Z* / *E* = 88 / 12
8		20	*Z* / *E* = 99.5 / 0.5	61	*Z* / *E* = 82 / 18

[a] Based on initial HetArBr. All products gave satisfactory NMR and mass spectra.

All of the (*Z*)- or (*E*)-alkenyl bromides and iodides used gave the desired product in good yields whereas a moderate yield was obtained from alkenyl chlorides. In this reaction (*Z*)- and (*E*)-alkenyl halides showed the same reactivity. A single isomer was formed with the same double bond geometry as that of the reagent. A slight loss of stereoselectivity, as determinated by GC, was observed only in the case of (*Z*)-*β*-bromostyrene (Table 6, entries 7−9). The result seen in entry 10 of Table 6 requires a comment. Actually, the yield of the reaction is likely higher. Indeed, we observed a very low stability of the starting material, even at −20 °C. This accounts for the moderate yield, but stereoselectivity is quite remarkable.

Alkenylation reactions mediated by low-valent nickel-(0) complex are characterized by their simplicity: the two reagents are introduced in the reaction mixture before starting the electrosynthesis, and the active nickel catalyst is formed in situ. The reaction proceeds in mild conditions and is highly regioselective (no 1,2-addition product) and stereoselective.

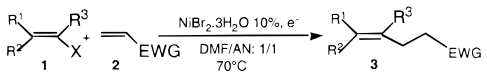
Mechanistic and Stereochemical Aspects. We have reported above the results for four reactions involving alkenyl halides in homo- and cross-coupling processes catalyzed by electrogenerated nickel complexes. They give good chemical yields, and they present advantages over the usual chemical routes. They are stereospecific in a number of cases, i.e., in the cross-coupling between bromostyrene and activated alkyl halides (Tables 2 and 3), as well as in the alkenylation of activated olefins (Table 6). They also show a high stereoselectivity in the case of other cross-couplings, partial isomerization being observed from the (*Z*)-isomer. This isomerization is also observed in the dimerization of the (*Z*)-alkenyl halides. In all reactions described above, we found that no isomerization of the starting alkenyl halide occurs during the course of the reaction as examinated by GC analyses.

The isomerization has already been observed in nickel-promoted cross-coupling and homocoupling reactions of alkenyl halides. However, there are discrepancies in the understanding of the origin of the loss of double bond configuration. It may occur during the first oxidative step[11] or during a further methathesis step.[14b]

All of these reactions occur through a catalytic cycle. It is then necessary to focus first on the reaction mechanisms to try to point out the critical step for the isomerization.

We have already studied the electrochemical and chemical steps involved in the nickel-catalyzed electrosynthesis of conjugated dienes.[17] We have notably described two catalytic cycles according to the potential applied to the cathode. These two have the same first step which is the oxidative addition of the vinyl halide on the electrogenerated zero-valent nickel leading to RNiX (Scheme 2, eq 2). RNiX can be further reduced (Scheme 2, eq 3), would the cathode potential be negative

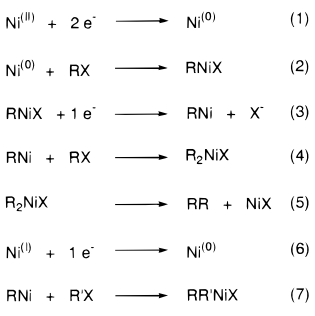
Table 6. Stereoselective Alkenylation of Electron-Deficient Olefins



Entry	Alkenyl halide	X	EWG	Isomeric purity % *Z/E* of crude product	Yield[a] (%)
1	C_5H_{11}	Cl	$COCH_3$	0/100	49
2		Br	-	0/100	77
3		I	-	0/100	80
4	C_5H_{11}	Br	$COCH_3$	100/0	77
5[b,c]		I	-	100/0	81
6[d]	C_6H_5	Br	$COCH_3$	7/93	73
7	C_6H_5	Br	$COCH_3$	97/3	84
8			CN	98/2	68
9			CO_2Et	95/5	76
10		I	$COCH_3$	94/6	50
11		I	$COCH_3$	0/100	71

[a] Isolated yield of pure isomer. [b] Yield 52%, when performed at 30 °C. [c] Yield 52%, in the presence of a stainless steel rod as nickel ions supplier. [d] *β*-Bromostyrene is a commercial product of *Z*/*E* isomers in ratio 10/90.

Scheme 2



enough, and the coupling reaction proceeds via a catalytic sequence similar to the one described by Amatore[41] for the dimerization of aryl halides (Scheme 2, eqs 4 and 5).

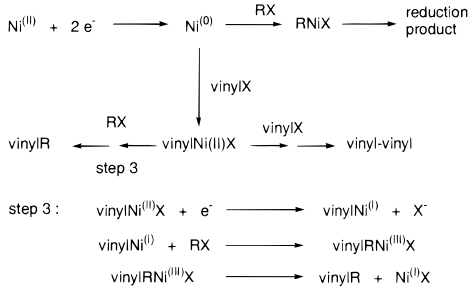
This mechanism is likely the most appropriate for reactions conducted under constant current density. When it is not reduced, RNiX can undergo the coupling via a methathesis process.

From this study it was also found that the stereochemistry of the alkenyl halide does not have a strong influence on the rate of the first oxidative addition (Scheme 2, eq 2), whereas the nature of the isomer is much more pronounced in the second oxidative reaction (Scheme 2, eq 4). The (*Z*)-isomer was also found to react slower than the (*E*)-isomer.

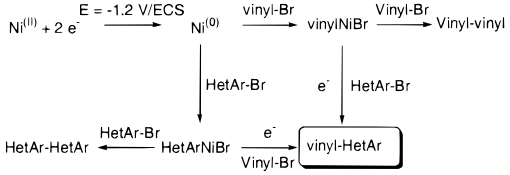
In the case of cross-coupling reactions, the key step is now reaction 7 (Scheme 2, eq 7).

It is also obvious that in the cross-couplings, a metathesis process should be ruled out. The involvement of

Scheme 3



Scheme 4



the alkenyl halide can occur either in the first oxidative addition step (Scheme 2, eq 2) or in the second oxidative addition (Scheme 2, eq 7).

We can get an idea of the sequence of the steps in the cross-coupling reaction of vinyl halide with alkyl halides. In this case, the mechanism is very likely the same as the one we have described previously for the coupling of alkyl chlorides with aryl halides[8,30] as shown in Scheme 3.

These reactions require that the more reactive organic halide, which is the activated alkyl halide (RX = α-chloroester, or α-chloroketone), be added slowly to the electrolytic medium containing the full amount of the alkenyl halide. In this case, the electrolysis of a 1/1 mixture is less efficient, and a reverse order of the introduction of the organic halides, i.e., the addition of vinyl-X to RX, gives no cross-coupling product; the products are only RH and RR. This clearly indicates that the cross-coupling can only occur if it goes through the formation of a *σ*-vinylnickel intermediate which corresponds to the eq 2 (Scheme 2). Therefore the stereospecificity which is observed in reactions involving bromostyrene (Tables 2 and 3) means that in the oxidative addition between Ni(0) and the vinyl halide the geometry of the double bond is kept unchanged. This is less true with other alkenyl halides such as 1-halohept-1-ene, though in this case the partial isomerization in the cross-coupling products does not exceed 25% (see Table 4).

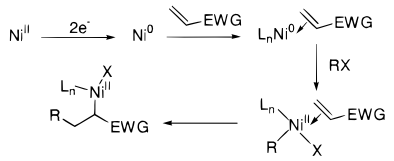
In the case of cross-coupling between alkenylbromides and heteroaromatic bromides there are two possible competitive pathways, i.e., the formation of vinylNiBr and the formation of HetArNiBr, and which can, at first, lead to the cross-coupling product (Scheme 4).

We can then favor one of these two pathways by adjusting the relative instant concentrations and, therefore, correlate the stereoselectivity and the mechanism. Indeed, when the reaction involving 2-bromopyridine and *β*-bromostyrene was conducted with a slower addition than usual (i.e., 2 mmol/h instead of 3.9 mmol/h), we obtained only the (*E*)-isomer from the commercial *β*-bromostyrene (*E*/*Z* = 87/13) and with the (*Z*)-*β*-bromostyrene the cross-coupling product has a *Z*/*E* ratio of 60/40. In addition the yields in the cross-coupling were lower, and the major product was bipyridine. It comes out that in this coupling high yield and high stereoselectivity can

(40) Condon Gueugnot, S.; Dupré, D.; Nédélec, J. Y.; Périchon, J. *Synthesis* **1997**, 1457.

(41) (a) Amatore, C.; Jutand, A. *Organometallics* **1988**, *7*, 2203. (b) Amatore, C.; Jutand, A.; Mottier, L.. *J. Electroanal. Chem*. **1991**, *306*, 125. (c) Amatore, C.; Jutand, A. *J. Electroanal. Chem*. **1991**, *306*, 141.

Scheme 5



only be obtained if the first step is the activation of the alkenyl halide.

In the alkenylation reaction, although the mechanism remains to be elucidated, a possible reaction pathway would involve the coordination of the activated olefin to the electrochemically formed Ni(0) species followed by the oxidative addition of the vinyl halide to the catalyst and the insertion reaction (Scheme 5).

This hypothetical mechanism shows that alkenyl halide is likely involved in the oxidative addition to Ni(0), and this leads to a highly stereoselective reaction.

To summarize this analysis we can say that little or no isomerization occur in the oxidative addition of the alkenyl halide to a Ni(0) complex, whatever the geometry of the double bond or the nature of the halogen. It comes out that the isomerization which is observed in the dimerization reaction mostly occurs in the following steps, i.e., either in the second oxidative addition to RNi (Scheme 2, eq 4), in the reductive elimination, when to alkenyl groups are attached to the Ni complex, or during a methathesis step which may occur competitively.

Conclusion

We have reported in this paper a straightforward method of activation of alkenyl halides enabling the preparation of valuable target molecules such as conjugated dienes, β,γ- or γ,δ- unsaturated esters, ketones, or nitriles, as well as alkenylated aryl compounds. The mechanistic aspects suggest that in these stereoselective reactions, the first step should concern the oxidative addition of the alkenyl halide. We also showed that it is possible to activate alkenyl iodides, bromides, or chlorides. However, with alkenyl chlorides, the reaction should be conducted at 50 °C or higher. In cross-coupling reactions, the use of alkenyl iodides is not advantageous because of the dimerization; this is also observed with bromostyrene.

Experimental Section

GC analysis was carried out using a 25-m DB-1 capillary column. Mass spectra were recorded with an ITD spectrometer coupled to a gas chromatograph (DB1, 30 m). Elemental analysis were performed by the Service Central de Microanalyses (C.N.R.S., Lyon). Column chromatography was performed on silica gel 60, 70−230 mesh. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 200 MHz with TMS as an internal standard.

The electrochemical cell has been described previously.[42]

Unless indicated, all solvents and reagents were purchased and used without further purification. DMF and acetonitrile were stored under argon.

Nickel bromide and 2−2′-bipyridine were used as obtained commercially. NBu_4BF_4 was dried by heating overnight at 70 °C in a vacuum.

Preparation of Ni(II) Complexes. $NiBr_2$bpy[43] was prepared according to literature methods.

Preparation of Alkenyl Halide. (*E*)-1-Bromo and (*E*)-1-iodo-1-heptene and (*E*)-2-(1-cyclohexenyl)-1-iodoethene were prepared from the commercially available corresponding alkynes via hydroalumination reaction.[44] (*E*)-1-Chloro-1-heptene was obtained by reaction of (*E*)-1-iodo-1-heptene with copper(I) chloride.[45] (*Z*)-1-Iodo-1-heptene and (*Z*)-2-(1-cyclohexenyl)-1-iodoethene were prepared from the corresponding 1-iodo-1-alkyne[46] followed by hydroboration reaction[47] and acidic workup. (*Z*)-β-Bromostyrene and (*Z*)-1-bromo-1-heptene were prepared respectively by bromination of cinnamic acid and (*E*)-oct-2-enoic acid followed by decarboxylative elimination in alkaline conditions.[31] The commercial β-bromostyrene was a mixture of *Z*/*E* isomers where (*E*)-β-bromostyrene was the main compound. Isomerically pure (*E*)-β-bromostyrene was obtained by treatment of the commercial product in alkaline conditions.[31] All alkenyl halides prepared were isomerically pure unless indicated in the tables.

General Procedure for the Ni(0)-Catalyzed Homocoupling Reaction (Table 1). In an undivided cell equipped with a nickel grid (area 30 cm^2) as the cathode and an aluminum rod as the anode, under argon tetrabutylammonium bromide (0.34 mmol) and tetrabutylammonium iodide (0.21 mmol) were dissolved as supporting electrolytes in a mixture of DMF (34 mL). Then $NiBr_2$bpy (0.80 mmol) was added. After solubilization of the catalytic precursor, alkenyl halide (16 mmol) was introduced and electrosynthesis was run at 20 °C at constant current density (0.3 Adm^{-2}). The reaction was monitored by GC and stopped after alkenyl halide was consumed. The mixture was then poured in hydrochloric acid solution (1 N). The aqueous layer was extracted with diethyl ether. The combined organic layers were washed with water, dried over $MgSO_4$, and concentrated. The conjugated dienes were purified by column chromatography on silica gel (70−230 mesh; eluent pentane/diethyl ether 9.5/0.5).

General Procedure for the Electrosynthesis with Activated Alkyl Halide. The electrolysis was fitted with a nickel-sponge cathode (20 cm^2) and an aluminum rod (1 cm diameter) anode. To a DMF solution (40 mL) containing 0.6 mmol of NBu_4BF_4 and 1 mmol of $NiBr_2$bpy were added the vinyl halide (10 mmol) and the α-chloroester or the α-chloroketone (ca. 0.3 mmol). Reactions were performed at room temperature (vinyl iodide) or at 60 °C (vinyl bromide) under argon. The electrolysis (i = 250 mA) was monitored by GC and was run until the vinyl halide was totally consumed (2−5 h). The reactions were then quenched with 1 N HCl and extracted with diethyl ether. The combined extracts were washed with water to ensure complete removal of DMF. The extracts were dried over $MgSO_4$, and solvent was removed under reduced pressure. The product was isolated by silica gel column chromatography eluted with 95:5 or 90:10 pentane/diethyl ether.

General Procedure for the Alkenylation of Electron-Deficient Olefins (Table 6). In an undivided cell equipped with a nickel grid (area 30 cm^2) as the cathode and an iron rod as the anode, under argon tetrabutylammonium bromide (0.34 mmol) and tetrabutylammonium iodide (0.21 mmol) were dissolved as supporting electrolytes in a mixture of DMF (14 mL) and acetonitrile (14 mL). 1,2-Dibromoethane (0.90 mmol) was introduced. A short electrolysis was run at constant current density (0.3 Adm^{-2}) and at room temperature within 30 min to generate a small amount of iron ions. Then the current was turned off. $NiBr_2 \cdot 3H_2O$ (0.80 mmol) and activated olefin (20 mmol) were added; the mixture was heated at 70 °C, and alkenyl halide (8 mmol) was added. The electrosyn-

(42) (a) Chausard, J.; Troupel, M.; Jacob, G.; Juhasz, J. P. *J. Appl. Electrochem.* **1989**, *19*, 345. (b) Chaussard, J.; Folest, J. C.; Nédélec, J. Y.; Périchon, J.; Sibille, S.; Troupel, M. *Synthesis* **1990**, *1*, 369.

(43) Uchino, M.; Asagi, K.; Yamamoto, A.; Ikeda, S. *J. Organomet. Chem.* **1975**, *84*, 93.

(44) Zweifel, G.; Whitney, C. C. *J. Am. Chem. Soc.* **1967**, *89*, 2753.

(45) Commerçon, A.; Normant, J.; Villieras, J. *J. Organomet. Chem.* **1975**, *93*, 415.

(46) Gardette, M.; Alexakis, A.; Normant, J. F. *J. Chem. Ecol.* **1983**, *9*, 219.

(47) Ratovelomanana, V.; Linstrumelle, G. *Bull. Soc. Chim. Fr.* **1987**, *1*, 174.

thesis was run at constant current density (0.3 Adm^{-2}). The reaction was monitored by GC and stopped after alkenyl halide was consumed (ca. 4.5 h). A charge of 2 F $mole^{-1}$ was used in most reactions described in this paper. The mixture was then hydrolyzed with hydrochloric acid (1 N) and diluted with diethyl ether. The aqueous layer was extracted with diethyl ether, the combined organic layers were washed with water and saturated NaCl solution, dried over $MgSO_4$ and the solvent was evaporated. The oil thus obtained was purified by column chromatography to give desired compounds.[40]

Characterization of the Products. (1*E*,3*E*)-1,4-Diphenylbuta-1,3-diene. Characterization was done unequivocally by comparison with the commercial sample.

(1*Z*,3*Z*)-1,4-Diphenylbuta-1,3-diene. Identification and characterization were achieved from a pure fraction of column chromatography on silica gel: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.44 (m, 10H), 6.75 (m, 4H); ^{13}C NMR ($CDCl_3$, 50.321 MHz) δ 126.8, 127.9, 128.6, 129.4, 132.3, 137.5; MS 206 (base), 129, 91, 77.

(6*E*,8*E*)-Tetradeca-6,8-diene: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 5.83−5.94 (m, 2H), 5.36−5.53 (m, 2H), 1.96 (q, J = 7.0 Hz, 4H), 1.21−1.37 (m, 12H), 0.80 (t, J = 6.5 Hz, 6H); ^{13}C NMR (50.321 MHz, $CDCl_3$) δ 13.8, 22.3, 28.9, 31.2, 32.7, 130.2 (lit.[48] 130.3), 132.0 (lit.[48] 132.6); MS 194, 67 (base); IR 3020, 1470, 990, 970 cm^{-1}.

(6*Z*,8*Z*)-Tetradeca-6,8-diene:[49] ^{1}H NMR ($CDCl_3$, 200 MHz) δ 6.18 (m, 2H), 5.35 (m, 2H), 1.91−2.13 (m, 4H), 1.19−1.39 (m, 12H), 0.80 (t, J = 6.5 Hz, 6H); ^{13}C NMR (50.321 MHz, $CDCl_3$) δ 13.8, 22.4, 27.3, 29.3, 31.4, 123.5, 131.7; MS 194, 67 (base).

(6*Z*,8*E*)-Tetradeca-6,8-diene. Assigment was determinated from a mixture of (*E*,*E*), (*Z*,*Z*), (*E*,*Z*) stereoisomers and compared to literature data:[48] ^{13}C NMR (50.321 MHz, $CDCl_3$) δ 125.5, 128.5, 129.8, 134.3 (lit.[48] δ: 126.0, 129.0, 130.8, 134.8); MS, 194, 67 (base).

(*Z*)-3-Methyl-5-phenyl-4-pentene-2-one: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.23 (3H, d J = 6.85 Hz), 2.09 (3H, s), 3.72 (1H, dq J = 10.5 Hz J = 6.85 Hz), 5.59 (1H, dd J = 11.5 Hz J = 10.5 Hz), 6.6 (1H, d J = 11.5 Hz), 7.21−7.39 (5H, m); ^{13}C NMR ($CDCl_3$, 50.3 MHz) 17 (1C, CH_3), 28 (1C, CH_3), 46.6 (1C, CH), 127.2 (1C, sp^2), 128.4 (4C, sp^2), 131.1 (1C, sp^2), 131.2 (1C, sp^2), 136.7 (1C, sp^2), 209.5 (1C, CO); MS 174 (M), 131 (M − 43 base), 116; IR 3030, 1740, 1610, 700 cm^{-1}. Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.09. Found: C, 82.74; H, 7.88.

(*Z*)-2-Methyl-4-phenyl-3-butenenitrile: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.37 (3H, d J = 6.9 Hz), 3.7 (1H, dq J = 9.9 Hz J = 6.9 Hz), 5.56 (1H, dd J = 11 Hz J = 9.9 Hz), 6.63 (1H, d J = 11 Hz), 7.20−7.40 (5H, m); ^{13}C NMR ($CDCl_3$, 50.3 MHz) 19.2 (1C, CH_3), 24.2 (1C, CH), 121.4 (1C), 126.8 (1C), 127.8 (1C), 128.4 (2C, sp^2), 128.6 (2C, sp^2), 132.7 (1C), 135.4 (1C); MS 157 (M base), 131 (M − CN), 114; IR 3015, 2245, 1610, 700 cm^{-1}. Anal. Calcd for $C_{11}H_{11}N$: C, 84.04; H, 7.05; N, 8.91. Found: C, 83.80; H, 7.02; N, 8.73.

(*Z*)-4-(2,5-Dimethoxyphenyl)-2-methyl-3-butenoic acid, methyl ester: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.27 (3H, d J = 6.8 Hz), 3.3 (1H, m), 3.67 (3H, s), 3.71 (3H, s), 3.74 (3H, s), 5.71 (1H, dd J = 11.4 Hz J = 10.3 Hz), 6.6 (1H, d J = 11.4 Hz), 6.76−7.13 (3H, m); ^{13}C NMR ($CDCl_3$, 50.3 MHz) 18.0 (1C, CH_3), 38.9 (1C, CH), 51.5 (1C, CH_3), 55.2 (1C, CH_3), 55.6 (1C, CH_3), 111.2 (1C, sp^2), 113.1 (1C, sp^2), 115.4 (1C, sp^2), 125.86 (1C, sp^2), 125.93 (1C, sp^2), 130.6 (1C, sp^2), 151.1 (1C, sp^2), 152.9 (1C, sp^2), 174.9 (1C, CO_2); MS 250 (M base), 191 (M − CO_2Me).

(*Z*)-4-(2,5-Dimethoxyphenyl)-2-benzyl-3-butenoic acid, methyl ester: ^{1}H NMR ($CDCl_3$, 200 MHz): δ 2.87 (1H, dd J = 13.7 Hz J = 7.0 Hz), 3.09 (1H, dd J = 13.7 Hz J = 7.8 Hz), 3.63 (3H, s), 3.70 (3H, s), 3.74 (3H, s), 3.75−3.89 (1H, m), 5.75 (1H, dd J = 11.4 Hz J = 10.4 Hz), 6.62 (1H, d J = 11.4 Hz), 6.69−7.25 (8H, m); ^{13}C NMR ($CDCl_3$, 50.3 MHz) 39.1 (1C, CH), 46.8 (1C, CH_2), 51.7 (1C, CH_3), 55.5 (1C, CH_3), 55.9 (1C, CH_3), 111.7 (1C, sp^2), 113.6 (1C, sp^2), 115.4 (1C, sp^2), 126.1 (1C, sp^2), 126.4 (1C, sp^2), 127.8 (1C, sp^2), 128.3 (2C, sp^2), 128.9 (2C, sp^2),129.1 (1C, sp^2), 138.4 (1C, sp^2), 151.4 (1C, sp^2), 153.2 (1C, sp^2), 173.8 (1C, CO_2); MS 326 (M base), 295 (M − OMe), 267 (M − CO_2Me), 235 (M − 91).

Methyl 2-(1-cyclopentenyl)propanoate: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.29 (3H, d J = 7.0 Hz), 1.87 (2H, quint J = 7.2 Hz), 2.30 (4H, m), 3.27 (1H, q J = 7.0 Hz), 3.67 (3H, s), 5.51 (1H, m); ^{13}C NMR ($CDCl_3$, 50.3 MHz) 15.6 (1C, CH_3), 23 (1C, CH_2), 32 (1C, CH_2), 33 (1C, CH_2), 41.2 (1C, CH), 51.3 (1C, CH_3), 125.7 (1C, sp^2), 142.3 (1C, sp^2), 174.5 (1C, CO_2); MS 154 (M), 95 (M − CO_2Me base).

(*E*)-4-Methyl 4-hexen-2-one:[50] ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.62 (3H, s), 1.64 (3H, d J = 5.4 Hz), 2.13 (3H, s), 3.06 (2H, s), 5.36 (1H, q J = 5.4 Hz); ^{13}C NMR ($CDCl_3$, 50.3 MHz) 13.3 (1C, CH_3), 15.6 (1C, CH_3), 28.6 (1C, CH_3), 54.4 (1C, CH_2), 123.6 (1C, sp^2), 129.3 (1C, sp^2), 208 (1C, CO); MS 112 (M), 97 (M − 15 base), 69 (M − 43).

(*E*)-2-Methyl-3-nonenoic acid, methyl ester: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.88 (3H, t J = 6.8 Hz), 1.22 (3H, d J = 7.0 Hz), 1.30−1.40 (6H, m), 2.0 (2H, td J = 6.8 Hz J = 6.5 Hz), 3.1 (1H, dq J = 8.5 Hz J = 7.0 Hz), 3.66 (3H, s), 5.41−5.54 (2H, m); ^{13}C NMR ($CDCl_3$, 50.3 MHz) 13.4 (1C), 16.9 (1C), 21.9 (1C), 28.4 (1C), 31 (1C), 31.9 (1C), 42.3 (1C), 51.1 (1C), 128.4 (1C, sp^2), 131.7 (1C, sp^2), 174.9 (1C, CO_2); MS 185 (M base), 153, 88; IR 3060, 1750, 980 cm^{-1}. Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.7; H, 10.94. Found: C, 71.84; H, 10.89.

(*Z*)-2-Methyl-3-nonenoic acid methyl ester: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.88 (3H, t J = 6.8 Hz), 1.21 (3H, d J = 7.0 Hz), 1.30−1.40 (6H, m), 2.08 (2H, td J = 6.9 Hz J = 6.7 Hz), 3.43 (1H, dq J = 8.5 Hz J = 7.0 Hz), 3.65 (3H, s), 5.32−5.44 (2H, m); ^{13}C NMR ($CDCl_3$, 50.3 MHz) 13.4 (1C), 17.5 (1C), 22.0 (1C), 26.7 (1C), 28.7 (1C), 31.0 (1C), 37.5 (1C), 51.0 (1C), 128.2 (1C, sp^2), 131.3 (1C, sp^2), 174.7 (1C, CO_2); MS 185 (M base), 153, 110; IR 3040, 1750, 730 cm^{-1}.

The following compounds were identified by comparison of their physical and spectral data with those given in the cited references: (*E*)-3-butenoic acid, 4-phenyl methyl ester;[51a] (*Z*)-3-butenoic acid, 4-phenyl methyl ester;[51b] (*E*)-3-butenoic acid, 2-methyl 4-phenyl methyl ester;[26] (*Z*)-3-butenoic acid, 2-methyl 4-phenyl methyl ester;[52] (*E*)-4-pentene-2-one, 3-methyl-5-phenyl;[53] (*E*)-4-pentene-2-one, 5-phenyl;[28] (*Z*)-4-pentene-2-one, 5-phenyl;[28] (*E*)-3-butene nitrile, 2-methyl-4-phenyl;[54] (*E*)-4-hexen-2-one;[55] (*Z*)-4-hexen-2-one;[55] (*Z*)-4-methyl 4-hexen-2-one;[56] (*E*)-3-penten-1-one, 3-methyl-1-phenyl;[57] (*Z*)-3-penten-1-one, 3-methyl-1-phenyl;[57] (*E*)-3-(2-phenylethenyl)thiophene;[33c] (*Z*)-3-(2-phenylethenyl)thiophene;[58] (*E*)-2-(2-phenylethenyl)thiophene;[59] (*Z*)-2-(2-phenylethenyl)thiophene;[60] (*E*)-3-(2-phenylethenyl)pyridine;[61] (*Z*)-3-(2-phenylethenyl)pyridine;[33a] (*E*)-2-(2-phenylethenyl)pyridine;[62] (*Z*)-2-(2-phenylethenyl)pyridine.[62]

JO000182F

(48) Normant, J. F.; Commerçon, A.; Gendreau, Y.; Bourgain, M.; Villieras, J. *Bull. Soc. Chim. Fr.* **1979**, *2*, 309.

(49) Näf, F.; Degen, P. *Helv. Chim. Acta* **1971**, *54*, 1939.

(50) The *Z* and *E* assignments were confirmed by NOE effect.

(51) (a) Linstead, R. P.; Williams, L. T. D. *J. Chem. Soc.* **1926**, 2735. (b) Baumgartner, H.; O'Sullivan, A. C.; Schneider, J. *Heterocycles* **1997**, *45*, 1537.

(52) Yasuyuki, K.; Osamu, T.; Fumis, I.; Hitoshi, Y.; Takashi, M.; Yasumitsu, T. *Chem. Pharm. Bull.* **1987**, *35*, 562.

(53) Chang, S.; Yoon, J.; Brookhart, M. *J. Am. Chem. Soc.* **1994**, *116*, 1869.

(54) Bhandal, H.; Howell, A. R.; Patel, V. F.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2709.

(55) Leigh, W. J.; Srinivasan, R. *J. Am. Chem. Soc.* **1982**, *104*, 4424.

(56) Akita, M.; Yasuda, H.; Nakamura, A. *Chem. Lett.* **1983**, 217.

(57) Cantrell, T. S.; Allen, A. C. *J. Org. Chem.* **1989**, *54*, 135.

(58) De Luca, G.; Martelli, G.; Spagnolo, P.; Tieco, M. *J. Chem. Soc.* **1970**, 2504.

(59) Seus, E. J.; Wilson, C. V. *J. Org. Chem.* **1961**, *26*, 5243.

(60) Karminski-Zamola, G.; Bajic, M. *Heterocycles* **1985**, 1497.

(61) Kikukawa, K.; Maemura, K.; Kiseki, Y.; Wada, F.; Matsuda, T. *J. Org. Chem.* **1981**, *46*, 4885.

(62) Oae, S.; Takeda, T.; Wakabayashi, S. *Tetrahedron Lett.* **1988**, *29*, 4445.