Electrochemical Arylation of Activated Olefins Using a Nickel Salt as Catalyst

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Received July 3, 1995

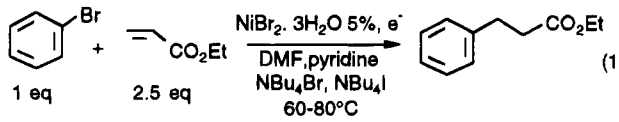
Conjugate addition reactions are among the most useful processes in organic synthesis.[1] They often require, as a first step, the preparation of air- and/or moisture-sensitive organometallic reagents at low temperature. Alternative one-step procedures are thus being developed.

Electrochemistry could be one of these alternatives, as illustrated in the electroreductive coupling between organic halides and activated olefins.[2] This approach is, however, limited to easily reducible olefins, which means that they proceed according to an anti-Michael type reaction mechanism. Homogeneous catalysis involving a transition metal has already been proposed as an interesting one-step route. Indeed, the catalyst can be reduced *in situ* either by zinc,[3] used in large excess, or electrochemically.[4] However, when catalyzed by a transition metal, the electrochemical reactions described so far involve expensive ligands associated with Ni[5] or Co[6] and are not very efficient (low turn over, medium yields), whereas the chemical routes involving zinc are conducted in the presence of an inexpensive ligand such as pyridine[3b,c] or triphenylphosphine.[3a,b]

Our aim is to demonstrate that conjugate additions can be carried out with a simple mild electrosynthesis conducted in an undivided cell using the sacrificial anode procedure[2e] with $NiBr_2 \cdot xH_2O$ as catalyst in *N,N*-dimethylformamide (DMF) with pyridine or acetonitrile as cosolvent. This procedure gives access in one step to addition products with high functional compatibility.

Results and Discussion

The model reaction first studied was the addition reaction from bromobenzene and ethyl acrylate (eq 1).



(1)

In the absence of $NiBr_2 \cdot xH_2O$, no reaction took place. In the presence of $NiBr_2 \cdot xH_2O$ (0.05 equiv), only traces (<5%) of the conjugate addition product were detected when the reaction was carried out in the absence of pyridine, but the yield was 63% when pyridine was used as cosolvent. At least 10% (v/v) of pyridine in DMF was found to be necessary to minimize the formation of the byproducts, benzene and biphenyl.

When $NiBr_2 \cdot xH_2O$ and pyridine were replaced by nickel 2,2′-bipyridine complex, a trace of the desired product was detected and biphenyl was the main product. Activated olefins are known to form coordination compounds with nickel,[7] and some of them have already been isolated. For example, Sustman *et al.*[8] prepared and characterized the bis(methylacrylate)(pyridine)nickel(0) and evidenced that this complex can promote conjugate addition reactions. The reaction most likely takes place in the sphere of coordination of the metal. Thus, bipyridine, which is strongly coordinated to nickel, as compared to pyridine, may prevent the efficient chelation of the olefin.

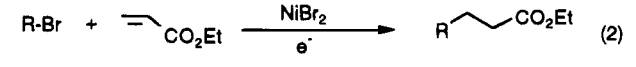
Reactions were best conducted at ca. 70 °C, under argon, at constant current intensity. More than 2 faradays per mol of aryl halide were usually required, in keeping with an overall two-electron reduction process.

The nature of the metal rod used as the anode is also of importance since the anodic oxidation continuously generates ions which probably interfere with the reaction: with magnesium or zinc poor yields were obtained (0 and 12% respectively), while yields reached 42% with aluminum and 63% with iron. The reaction was found to be less efficient when conducted in a divided cell in the absence of metallic ions.

In Table 1 are reported preliminary results obtained in the reaction of aryl bromides with several electron-deficient olefins using the standard experimental conditions (see Experimental Section). Each reaction has not been thoroughly studied so far. Monosubstituted terminal olefins (entries 1–5) reacted with aryl bromides to give the desired adducts in satisfying yield. Lower yields were obtained with 1,1′-disubstituted olefins (entries 6 and 7). With 1,2-disubstituted olefins such as dimethyl maleate or dimethyl fumarate (entry 9), good yields were obtained with no difference in reactivity between the *Z* and *E* isomer.

Interestingly, the yield of the reaction does not depend much on the nature of the aryl bromide. Also, the reaction can be performed without needing to protect sensitive groups such as cyano or ketone (entries 3 and 13) that may be substituted into the aryl bromide. Thus, a wide variety of aryl succinates (entries 9–13) can be prepared, in one step, using indiscriminately dimethyl maleate or fumarate and aryl bromide as starting materials. This simple and efficient synthesis of aryl succinate is a good alternative for the preparation of building blocks involved in the synthesis of potential anti-inflamatory agents.[9]

Recently, we have found that the method can be applied to the alkyl as well as vinyl bromides (eq 2).



(2)

R = C_6H_{11}, sec C_8H_{17}, CH_3-CH=CH, Ph-CH=CH

(1) Perlmutter, P. *Conjugate Addition Reactions in Organic Synthesis*; Pergamon Press: Oxford, 1992

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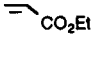
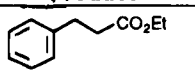
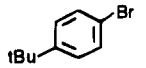
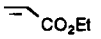
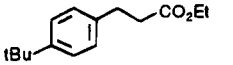
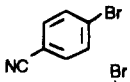
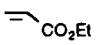
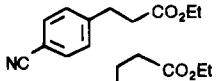
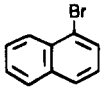
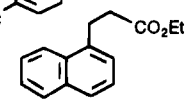
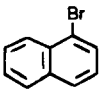
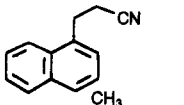
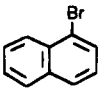
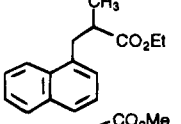
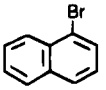
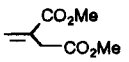
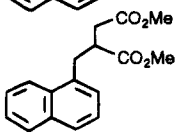
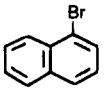
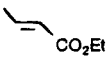
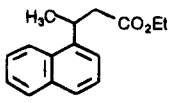
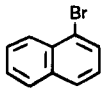
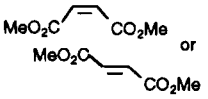
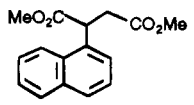
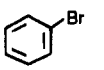
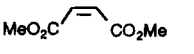
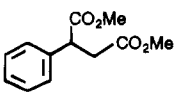
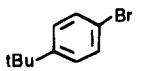
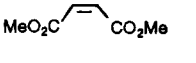
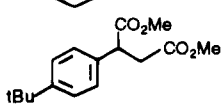
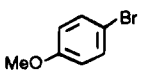
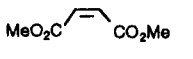
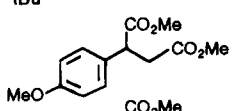
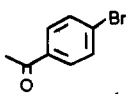
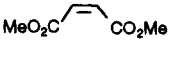
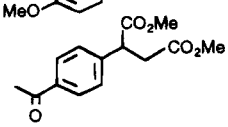
(6) (a) Scheffold, R.; Dike, M.; Dike, S.; Herold, T.; Walder, L. *J. Am. Chem. Soc.* **1980**, *102*, 3642. (b) Orlinski, R.; Stankiewicz, T. *Tetrahedron Lett.* **1988**, *29*, 1601.

0022-3263/95/1960-7684$09.00/0

Table 1. Arylation of Electron-Deficient Olefins[a]

Entry	Aryl halide	Olefin	Product	Isolated yield[(b)]
1				63%
2				47%
3				50%
4				50%
5				61%
6				27%
7				26%
8				20%
9				59%
10				60%
11				59%
12				46%
13				31%

(a) reactions were performed by using arylbromide (15 mmol), 2-2.5 equiv of activated olefins, 0.05 equiv of $NiBr_2$, 6 equiv of pyridine in DMF at 70°C at constant current density 0.3A / dm^2.
(b) all new compounds were characterized by satisfactory analytical and spectral data

We are now investigating the mechanism as well as the scope and limitation of this method.

Experimental Section

General. All solvents and reagents were purchased from commercial sources and used as received. DMF was stored under an argon atmosphere. The electrochemical cell has been described previously.[2e] NMR samples were recorded in $CDCl_3$. MS data were obtained by EI. GC analysis was carried out using a 25-m DB-1 capillary column. Elemental analyses were made by the Service Central de Microanalyses (CNRS, Lyon). Melting points are uncorrected.

General Procedure. Dimethyl α-(1-Naphthyl)succinate. Tetrabutylammonium bromide (0.62 mmol, 0.20 g), tetrabutylammonium iodide (0.40 mmol, 0.15 g), and nickel bromide hydrate (0.75 mmol, 0.18 g) were disolved in DMF (40 mL) in an undivided cell equipped with a nickel grid (area 30 cm^2) as the cathode and iron rod as the anode, under argon atmosphere. Then, dimethyl maleate (30 mmol, 4.30 g) and pyridine (90 mmol, 7 mL) were introduced. The reaction mixture was heated at 60−80 °C, and 1-bromonaphthalene (15 mmol, 3.10 g) was added. The electrolysis was run at constant current density (0.3 A/dm^2). The reaction was monitored by GC and stopped after the aryl bromide was consumed. The reaction mixture was then hydrolyzed with hydrochloric acid (1 N, 30 mL). The aqueous layer was extracted with diethyl ether (2 × 30 mL). The combined organic layers were washed with water, dried over $MgSO_4$, and concentrated. Purification by column chromatog-

(7) (a) Yamamoto, T.; Yamamoto, A.; Ikeda, S. *J. Am. Chem. Soc.* **1971**, *93*, 3350. (b) Guerrieri, F.; Salerno, G. *J. Organomet. Chem.* **1976**, *114*, 339.
(8) Sustmann, R.; Hopp, P. *J. Organomet. Chem.* **1989**, *375*, 259.
(9) Juby, P. F.; Goodwin, W. R.; Hudyma, T. W.; Partyka, R. A. *J. Med. Chem.* **1972**, *15*, 1297.

raphy (silica gel 70−230 mesh; eluent pentane/ether 8/2) afforded 2.41 g (59%) of product: mp 60 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.86 (dd, J = 17.6 Hz, J = 4.4 Hz, 1H), 3.47 (dd, J = 17.6 Hz, J = 10,2 Hz, 1H), 3.90 (s, 6H), 5.05 (dd, J = 10,2 Hz, J = 4.4 Hz, 1H), 7.40−8.37 (m, 7H); ^{13}C NMR (50.321 MHz, $CDCl_3$) δ 37.3, 42.8, 51.8, 52.3, 122.8, 125.0, 125.4, 125.8, 126.5, 128.2, 128.9, 130.9, 134.0, 172.1, 173.8; MS, 272, 240, 212, 171, 153 (base); IR 1740 cm^{-1}. Anal. Calcd for $C_{16}H_{16}O_4$: C,70.57; H, 5.92. Found: C, 70.62; H, 5.94.

Ethyl 3-(*p*-*tert*-Butylphenyl)propanoate: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.16 (t, J = 7.1 Hz, 3H), 1.22 (s, 9H), 2.53 (t, J = 7.8 Hz, 2H), 2.85 (t, J = 7.8 Hz, 2H), 4.05 (q, J = 7.1 Hz, 2H), 7.06 (d, J = 8.2 Hz, 2H), 8.33 (d, J = 8.2 Hz, 2H); ^{13}C NMR (50.321 MHz, $CDCl_3$) δ 14.0, 30.2, 31.2 (3C), 34.1, 35.7, 60.1, 125.1 (2C), 127.8 (2C), 137.3, 148.6, 172.5; MS, 234, 219 (base); IR 1740 cm^{-1}. Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.75; H, 9.41.

Ethyl 3-(*p*-cyanophenyl)propanoate: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.43 (t, J = 7.1 Hz, 3H), 2.84 (t, J = 7.5 Hz, 2H), 3.21 (t, J = 7.5 Hz, 2H), 4.32 (q, J = 7.1 Hz, 2H), 7.52 (d, J = 8.2 Hz, 2H), 7.78 (d, J = 8.2 Hz, 2H); ^{13}C NMR (50.321 MHz, $CDCl_3$) δ 14.0, 30.8, 34.9, 60.4, 110.0, 116.7, 129.1 (2C), 132.1 (2C), 146.1, 172.0; MS, 204, 203, 158, 130, 129 (base), 116, 103, 77; IR 2980, 2940, 2200, 1750, 1600, 1500, 1370, 1160, 850, 830, 760 cm^{-1}. Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45; N, 6.89. Found: C, 71.22; H, 6.64; N, 6.95.

Dimethyl α-(1-naphthylmethyl)succinate: mp 95.7 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.36 (m, 1H), 2.68 (m, 1H), 3.04 (m, 1H), 3.24 (m, 1H), 3.51 (m, 4H), 3.59 (s, 3H), 7.16−8.02 (m, 7H); ^{13}C NMR (50.321 MHz, $CDCl_3$) δ 35.0, 35.1, 42.1, 51.6, 51.9, 123.4, 125.2, 125.7, 126.2, 127.3, 127.6, 128.8, 131.7, 133.9, 134.2, 172.1, 174.8; MS, 286 (base), 255, 226, 141; IR 3030, 1750, 1730 cm^{-1}. Anal. Calcd for $C_{17}H_{18}O_4$: C, 71.31; H, 6.33. Found: C, 71.49; H, 6.32.

Ethyl 3-methyl-3-(1-naphthyl)propanoate: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.14 (t, J = 7.1 Hz, 3H), 1.41 (d, J = 6.8 Hz, 3H), 2.59 (dd, J = 15.2 Hz, J = 9.0 Hz, 1H), 2.80 (dd, J = 15.2 Hz, J = 5.5 Hz, 1H), 4.02−4.21 (m, 3H), 7.20−8.20 (m, 7H); ^{13}C NMR (50.321 MHz, $CDCl_3$) δ 14.3, 21.3, 30.9, 42.6, 60.4, 122.4, 123.1, 125.5, 125.6, 126.1, 127.0, 129.0, 131.2, 134.1, 141.8, 172.6; MS, 242, 155 (base); IR 1735 cm^{-1} ; HMRS for $C_{16}H_{18}O_2$ calcd 242.317, found 242.131.

Dimethyl α-(*p*-*tert*-butylphenyl)succinate: mp 53.2 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.27 (s, tBu), 2.60 (dd, J = 17.1 Hz, J = 5.1 Hz, 1H), 3.16 (dd, J = 17.1 Hz, J = 10.2 Hz, 1H), 3.63 (s, 6H), 4.02 (dd, J =10.2 Hz, J = 5.1 Hz, 1H), 7.14 (d, J = 8.5 Hz, 2H), 7.29 (d, J = 8.5 Hz, 2H); ^{13}C NMR (50.321 MHz, $CDCl_3$) δ 31.2 (3C), 34.3, 37.5, 46.5, 51.7, 52.1, 125.7 (2C), 127.2 (2C), 134.5, 150.4, 172.0, 173.5; MS, 279, 247, 219, 203 (base); IR 1740 cm^{-1}. Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 68.69; H, 7.96.

Dimethyl α-(*p*-acetylphenyl)succinate: mp 72.8−73 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.60 (s, 3H), 2.70 (dd, J = 17.0 Hz, J = 5.7 Hz, 1H), 3.23 (dd, J = 17.0 Hz, J = 9.6 Hz, 1H), 3.68 (s, 3H), 3.70 (s, 3H), 4.17 (dd, J = 9.6 Hz, J = 5.7 Hz, 1H), 7.40 (d, J = 8.3 Hz, 2H), 7.94 (d, J = 8.3 Hz, 2H); ^{13}C NMR (50.321 MHz, $CDCl_3$) δ 26.2, 36.9, 46.7, 51.5, 52.1, 127.8 (2C), 128.6 (2C), 136.2, 142.5, 171.2, 172.3, 197.0; MS, 265, 233 (base); IR 2980, 1740, 1700 cm^{-1}. Anal. Calcd for $C_{14}H_{16}O_5$: C, 63.63; H, 6.10. Found: C, 63.37; H, 6.06.

Registry numbers (supplied by author): ethyl 3-phenylpropanoate, 2021-28-5; ethyl 3-naphthylpropanoate, 38818-50-5; 3-naphthylpropanenitrile, 70067-70-8; ethyl 2-methyl-3-(1-naphthyl)propanoate, 113777-18-7; dimethyl α-phenylsuccinate, 15463-92-0; dimethyl α-(*p*-methoxyphenyl)succinate, 22248-26-6.

JO951195+