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Registry No. **1a**, 127092-00-6; **1b**, 32445-98-0; **1c**, 127092-01-7; **1d**, 130379-05-4; **1e**, 129970-59-8; **2**, 509-14-8; **5a**, 130379-16-7; **5b**, 130379-17-8; **5c**, 130379-18-9; **5d**, 130379-19-0; **5e**, 130379-20-3; **6a**, 130379-23-6; **6b**, 130379-26-9; **6c**, 130379-27-0; **6d**, 130379-28-1; **6e**, 130379-29-2; **7a**, 935-67-1; **7b**, 99334-84-6; **7c**, 55708-37-7; **7d**, 99334-85-7; **7e**, 125847-22-5; **8a**, 130379-14-5; **8d**, 130405-77-5; **8e**, 130379-15-6; **9**, 130379-06-5; **10**, 127092-07-3; **11a**, 78176-20-2; **11e**, 58324-82-6; **12**, 100-17-4; **13**, 91247-60-8; **14**, 130379-11-2; 15, 130379-12-3; $[\mathbf{1a}\cdots\mathbf{2}]_{CT}$, 130379-32-7; $[\mathbf{1b}\cdots\mathbf{2}]_{CT}$, 130379-33-8; $[\mathbf{1c}\cdots\mathbf{2}]_{CT}$, 130379-34-9; $[\mathbf{1d}\cdots\mathbf{2}]_{CT}$, 130379-35-0; $[\mathbf{1e}\cdots\mathbf{2}]_{CT}$, 130379-36-1; [4-*tert*-Butylanisole$\cdots$**2**]$_{CT}$, 130379-10-1; *meso*-3,4-dimethyl-3,4-diphenylhexane, 62678-49-3; *meso*-3,4-dimethyl-3,4-bis(4′-nitrophenyl)hexane, 83294-20-6; *meso*-3,4-dimethyl-3,4-bis(4′-aminophenyl)hexane, 130379-07-6; *meso*-3,4-dimethyl-3,4-bis(4′-diazoniophenyl)hexane ditetrafluoroborate salt, 130379-09-8; trinitromethane, 517-25-9; 2-phenyl-2-propanol, 617-94-7; 2-(4-methoxyphenyl)-2-propanol, 7428-99-1; 2-(trinitromethyl)-4-methylanisole, 108088-84-2; 2-(dinitromethyl)-4-methylanisole, 130379-13-4; 2-nitro-4-methylanisole, 119-10-8; 2-(4′-methoxyphenyl)-2-(trinitromethyl)butane, 130379-21-4; 2-phenyl-2-(trinitromethyl)butane, 130379-22-5; 4-methoxyl-3-acetylbicumene, 130379-24-7; 4-methoxy-3-carboxybicumene, 130379-25-8; 4-methoxy-3-(dinitromethyl)-4′-(trifluoromethyl)-bicumene, 130379-30-5; 4-methoxy-3-(dinitromethyl)-4′-cyanobicumene, 130379-31-6.

Theory and Experimental Illustration of Preparative Electrochemistry Using Redox Catalysis of Electron Transfer Initiated Radical Chain Reactions. Application to the Cross-Coupling between Aryl Halides and Phenoxide Ions

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A general equation predicting the yield of electron transfer initiated radical chain reaction ($S_{RN}1$ and related mechanisms) under preparative electrochemical conditions is given for situations where the electron-transfer activation of the chain is performed by means of a redox mediator. Simple tests, allowing for the choice of proper redox mediator, are given, and their origins established and discussed. The validity and application of this simple model is shown and discussed for the case of the $S_{RN}1$-like reaction involving di-*tert*-butylphenoxide as a nucleophile, to afford biaryls of interest for their properties in nonlinear optics.

Introduction

Electrochemical reduction of aromatic halides or pseudohalides is a very simple means of activating these ubiquitous molecules under perfectly controlled conditions.[1] Thus when the electrode potential is set on the reduction wave of the halide or pseudohalide, an electron is transferred to the aromatic π^* orbital to afford a frangible anion radical, $ArX^{\bullet-}$. Intramolecular (i.e. $\pi^* \rightarrow \sigma^*_{C-X}$) electron transfer[2] results then in the cleavage of the carbon–halogen or pseudohalogen bond to yield quantitatively a σ-radical, $Ar^\bullet$, and the halide or pseudohalide ion:

$$ArX + e \rightarrow ArX^{\bullet-} \quad (1)$$

$$ArX^{\bullet-} \xrightarrow{k_1} Ar^\bullet + X^- \quad (2)$$

In the absence of other reagents, the sequence of reactions (1–2) is generally followed by a second electron transfer[3-5] to the easily reducible σ-radical to give the corresponding highly basic σ-aromatic anion which affords the dehalogenated hydrocarbon.

$$Ar^\bullet + e \rightarrow Ar^- \quad (3a)$$

$$Ar^\bullet + ArX^{\bullet-} \rightarrow Ar^- + ArX \quad (3b)$$

$$Ar^- + BH \rightarrow ArH + B^- \quad (4)$$

With the exception of a few specific cases where a selective reduction is desirable, the whole sequence of reactions 1–4 presents a poor synthetic interest although its mechanistic consequences have been extensively delineated in the past decade.[1-5] However, it regains a considerable synthetic interest provided one is able to suppress the

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(1) See, e.g.: (a) Feoktistov, L. G. In *Organic Electrochemistry*, 2nd ed.; Baizer, M., Lund, H., Eds.; Dekker: New York, 1983; Chapter 7, pp 259–284. (b) Savéant, J. M. *Acc. Chem. Res.* **1980**, *13*, 323. (c) Savéant, J. M. *Proc. of R. A. Welch Foundation Conferences on Chem. Res. XXX. Adv. in Electrochem.*, Houston, 1986, pp 289–336.

(2) (a) Andrieux, C. P.; Savéant, J. M.; D. Zann, *New J. Chem.* **1984**, *8*, 107. (b) Savéant, J. M. *J. Am. Chem. Soc.* **1987**, *109*, 6788.

(3) This is observed in poor H-atom-donating solvents such as liquid ammonia which is considered in this study.[4] In usual organic solvents and/or in the presence of tetraalkylammonium salts, H-atom transfer from the media (SH) is an additional mode of deactivation of $Ar^\bullet$,

$$Ar^\bullet + SH \rightarrow ArH + S^\bullet, \text{ etc.}$$

leading to the hydrogenolysis product.[5] The electron stoichiometry may then be 1 e or 2 e depending on the ease of reduction of the $S^\bullet$ radical vs that of ArX.

(4) (a) Savéant, J. M.; Thiébault, A. *J. Electroanal. Chem.* **1978**, *49*, 335. (b) Teherani, T.; Bard, A. J. *Acta Chem. Scand., Ser. B* **1983**, *B37*, 419.

(5) (a) M'Halla, F.; Pinson, J.; Savéant, J. M. *J. Am. Chem. Soc.* **1980**, *102*, 4120. (b) Amatore, C.; Pinson, J.; Savéant, J. M.; Thiébault, A. *J. Am. Chem. Soc.* **1982**, *104*, 817. (c) Amatore, C.; Badoz-Lambling, J.; Bonnel-Huyghes, C.; Pinson, J.; Savéant, J. M.; Thiébault, A. *J. Am. Chem. Soc.* **1982**, *104*, 1979.

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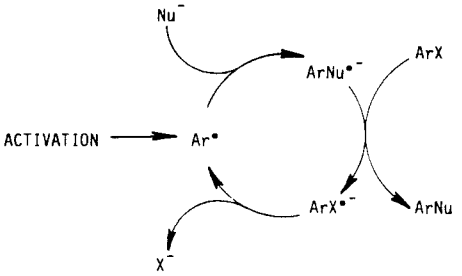
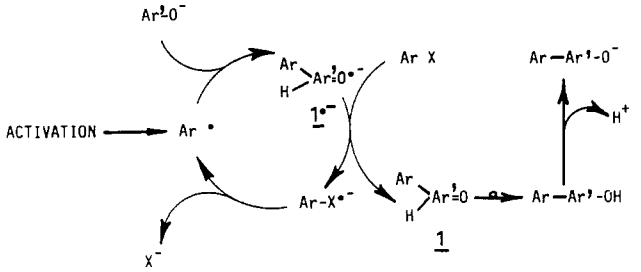
Scheme I



Scheme II



reduction sequence of the σ-aryl radical.[6] Indeed reactions 1 and 2 then amount to a controlled source of highly reactive radicals which can be used as stoichiometric reactants[7] or more importantly to trigger radical chain reactions.[6,8] Therefore electrochemistry would represent a convenient substitute for other techniques which involve difficultly removable reagents and radical initiators, as, e.g., tin hydride.[9]

$$In^{\bullet} + SnH \rightarrow InH + Sn^{\bullet} \quad (5)$$

$$Sn^{\bullet} + ArX \rightarrow SnX + Ar^{\bullet}, \text{ etc.} \quad (6)$$

Indeed it would then present most of the advantages of the photochemical methods involving activation of charge transfer complexes,[10] [ArX, D], where D is a donor present in the reaction medium:

$$[ArX, D] \overset{h\nu}{\rightleftharpoons} [ArX^{\bullet-}, D^{\bullet+}] \quad (7)$$

$$[ArX^{\bullet-}, D^{\bullet+}] \rightarrow ArX^{\bullet-} + D^{\bullet+} \quad (8)$$

$$ArX^{\bullet-} \rightarrow Ar^{\bullet} + X^{-}, \text{ etc.} \quad (9)$$

without the requirement of existence of an adequate charge transfer complex (CTC) and the disadvantage of generally poor quantum yields, arising because of the fast backward electron transfer in eq 7 which anihilates the ion pair before its cage separation in reaction 8.[10a] Because of this latter reason, photochemistry of CTC appears as a poorly efficient source of radicals as soon as their stoichiometric use is desired. However if the photochemical process in reactions 7–9 is considered only for initiating a very efficient radical chain process, a poor quantum yield in the activation sequence (7–9) is no more a serious disadvantage, and may even constitute a serious advantage for photochemical activation of chain reaction via CTC.[10b,11] We have indeed shown that, e.g., for $S_{RN}1$ reactions (see Scheme I), the main deactivation route consists in the reduction of the σ-aryl radical[6] by the two electron-rich chain intermediates, $ArX^{\bullet-}$ and $ArNu^{\bullet-}$.[12] Indeed a poor activating sequence which results in an exceedingly small production of paramagnetic intermediates ($Ar^{\bullet}$, $ArX^{\bullet-}$, $ArNu^{\bullet-}$) amounts to disfavor the termination steps vis-à-vis the chain propagation.[13] Therefore, what appears to be a disadvantage of photochemical initiation can actually be an advantage. This has proven extremely suitable for synthetic purposes, provided the triggered chain is considerably efficient.[14]

On the other hand, the reverse is often true for electrochemical initiation. Indeed, the easy and quantitative production of large fluxes of aryl radicals at the electrode is a tantamount of an easy and quantitative production of reducing species, which then results in a nearly quantitative depletion of the σ-aryl radical, even when the latter escapes from its facile reduction at the electrode surface (reaction 3a).[6,12]

It is seen from the above considerations that photochemical or electrochemical activations will prove worthwhile only when they are associated with extremely efficient radical chains, i.e. those involving an extremely fast chemical reaction of the radical. However this arises for different reasons in each case. For photochemical CTC activation, this is a consequence of generally poor quantum yields. For electrochemical activation, this is required because of the production of large fluxes of radical scavengers ($Ar^{\bullet}$, $ArX^{\bullet-}$, $ArNu^{\bullet-}$). Solutions to both problems exist although they have attracted rather little attention in the past. For example the design of adequate CTC, such as those involving a fast decay of the oxidized donor in eq 7, should prevent the backward electron transfer and result in an increase of the overall quantum efficiency of photochemical activation.[15] Similarly a decrease of the rate

(6) (a) Refences 1b–c. (b) Amatore, C.; Chaussard, J.; Pinson, J.; Savéant, J. M.; Thiébault, A. *J. Am. Chem. Soc.* **1979**, *101*, 6012. (c) Amatore, C.; Savéant, J. M.; Thiébault, A. *J. Electroanal. Chem.* **1979**, *103*, 303. (d) Amatore, C.; Pinson, J.; Savéant, J. M.; Thiébault, A. *J. Am. Chem. Soc.* **1981**, *103*, 6930.

(7) (a) Amatore, C.; Savéant, J. M. *J. Electroanal. Chem.* **1981**, *123*, 203. (b) *Ibid.* **1981**, *125*, 1. (c) *Ibid.* **1981**, *126*, 1. (d) Amatore, C.; M'Halla, F.; Savéant, J. M. *J. Electroanal. Chem.* **1981**, *123*, 219. (e) Amatore, C.; Pinson, J.; Savéant, J. M.; Thiébault, A. *J. Electroanal. Chem.* **1981**, *123*, 231. (f) Chami, Z.; Gareil, M.; Pinson, J.; Savéant, J. M. Thiébault, A. *Tetrahedron Lett.* **1988**, *29*, 639.

(8) (a) Swartz, J. E.; Stenzel, T. T.; *J. Am. Chem. Soc.* **1984**, *106*, 2520. (b) Alam, N.; Amatore, C.; Combellas, C.; Thiébault, A.; Verpeaux, J. N. *Tetrahedron Lett.* **1987**, *28*, 6171. (c) Alam, N.; Amatore, C.; Combellas, C.; Pinson, J.; Savéant, J. M.; Thiébault, A.; Verpeaux, J. N. *J. Org. Chem.* **1988**, *53*, 1496.

(9) See, for instance: (a) Giese, B. In *Radicals in Organic Synthesis: Formation of Carbon–Carbon Bonds*; Pergamon: Oxford, 1986. (b) Pereyre, M.; Quintard, J. P.; Rahm, A. In *Tin in Organic Synthesis*; Butterworths: London, 1986; pp 54–64 and references therein.

(10) (a) See, e.g.: Kochi, J. K. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1227 for a comprehensive discussion on photochemical activation of CTC. For application to $S_{RN}1$ reactions, see: (b) Rossi, R. A.; Rossi, R. H. *Aromatic Nucleophilic Substitution by the $S_{RN}1$ Mechanism*; American Chemical Society: Washington, DC, 1983; ACS Monogr. No. 78. (d) Hoz, S.; Bunnett, J. F. *J. Am. Chem. Soc.* **1977**, *99*, 4690. (e) Bunnett, J. F. *Acc. Chem. Res.* **1980**, *13*, 323. (f) Fox, M. A.; Younathan, J.; Fryxell, G. E. *J. Org. Chem.* **1983**, *48*, 3109. For a more general discussion of electrochemical vs photochemical activation, see the following documented review (g) Julliard, M.; Chanon, M. *Chem. Rev.* **1983**, *83*, 425.

(11) High quantum yields for the sequence of reactions 7–9 would result in too large initiation rates vis-à-vis that of the desired propagating chain sequence. Moreover in the particular context considered here, it would amount to the building up of relatively large concentrations of reducing species, such as $ArX^{\bullet-}$, in the solution, which result in increasing the rate of termination of the chain reaction. See later and ref 6d.

(12) Under electrochemical conditions, direct reduction of $Ar^{\bullet}$ by the electrode consists in an additional important termination step. (a) Amatore, C.; Savéant, J. M. *J. Electroanal. Chem.* **1977**, *85*, 27; **1979**, *102*, 21. (b) References 6a–c and 7.

(13) This arises because the termination reactions are second-order in chain carriers ($Ar^{\bullet} + ArX^{\bullet-} \rightarrow Ar^{-} + ArX$, $Ar^{\bullet} + ArNu^{\bullet-} \rightarrow Ar^{-} + ArNu$, $2Ar^{\bullet} \rightarrow ArAr$) whereas the propagating reactions are first-order chain carriers (Scheme I).[6d]

(14) See, e.g., ref 10b and references therein. For example, compare: (a) electrochemical (ref 8b,c) and (b) photochemical (Beugelmans, R.; Bois-Choussy, M. *Tetrahedron Lett.* **1988**, *29*, 1289) approaches on the same reaction.

(15) See, e.g., Masnovi, J. M.; Sankararaman, S.; Kochi, J. K. *J. Am. Chem. Soc.* **1989**, *111*, 2263 for a discussion of this topic and use of dissociating electron transfer in photochemical CTC activation.

of production of radicals in electrochemical activation should result in a corresponding decreased efficiency of the termination steps involving the reduction of the aryl radical.[16]

In the following we want to show how redox catalysis,[18] that is electrochemical activation involving a suitable electron-transfer mediator, can be used to fulfill the above requirement of efficiency and low fluxes for the activation. This will be elaborated in the case of a $S_{RN}1$-like reaction which amounts to the synthesis of unsymmetrical biaryls via the coupling of a phenoxide and an aromatic halide:[19]

$$ArX + Ar'O^- \rightarrow ArAr'O^- + X^- + H^+ \qquad (10)$$

because of the interest of such biaryls for nonlinear optics.[20] However, most of the results described hereafter are transposable to most situations involving electron-transfer initiation of radical chains provided the termination steps are bimolecular in chain carriers. This is obviously valid for the $S_{RN}1$ and related reactions, but also for other reactions such as those initiated by the trapping of a radical by a double[7f] or triple bond.[21]

Results and Discussion

I. General Considerations on the Use of Mediators. Electron Transfer Activation of Radical Chains Using a Redox Mediator. As explained in the introduction the disadvantage of electrochemical initiation is related to the simultaneous generation of large fluxes of the aryl radical but also of its main scavengers.[22] On the other hand it is often advocated that electrochemistry allows for the control to a high degree of the fluxes of material produced at the electrode via the fine tuning of the electrode potential. Therefore, one could think that setting the electrode potential sufficiently before the reduction peak of the starting organic halide should result in a production of an adequate flux of chain carriers[16] sufficiently large for the chain to have a significant rate of conversion and sufficiently small to minimize the role of the bimolecular termination steps. However this simple "on-paper strategy" does not take into account the very fact that under electrochemical conditions, and for the situation of very fast kinetics considered here, the paramagnetic species exist only in a very thin part of the diffusion layer adjacent to the electrode. Then, as established previously,[6] no significant chain reaction can develop.[23] Under the most favorable conditions, i.e those involving the smallest flux of chain carriers, the main termination step is the direct reduction of the aryl radical by the electrode (reaction 11a).[6] Therefore the maximum

$$ArX \xrightarrow{e} ArX^{\bullet -} \xrightarrow{k_1} Ar^{\bullet} \xrightarrow{\text{electrode}} Ar^- \text{ (termination)} \qquad (11a)$$

$$Ar^{\bullet} \xrightarrow{k_2[Ar'O^-]} \text{etc. (propagation)} \qquad (11b)$$

yield in biaryl is given by eq 12[24] where k_1 and k_2 are defined in eq 11.

$$y_{ArAr'\text{-}O^-} = 1/\{1 + (k_1/k_2[Ar'\text{-}O^-])^{1/2}\} \qquad (12)$$

A way to overcome this built-in problem consists in effecting the reduction of the organic halide far from the electrode surface. This was first recognized for the $S_{RN}1$ reaction when we showed that by setting the electrode potential at the foot of the reduction wave of the substitution product, ArNu (see Scheme I) resulted in a dramatic increase of the substitution yield.[23b] A formally identical approach was then developed by Swartz and Stenzel,[8a] who used an electron transfer mediator, M.

In the absence of the organic halide, the mediator gives rise to a chemically reversible redox system featured in eq 13. In the presence of the organic halide, the endergonic

$$M + e \rightleftharpoons M^{\bullet -} \ (E^\circ_M) \qquad (13)$$

$$M^{\bullet -} + ArX \underset{k_{-o}}{\overset{k_o}{\rightleftharpoons}} M + ArX^{\bullet -} \qquad (14)$$

$$ArX^{\bullet -} \xrightarrow{k_1} Ar^{\bullet} + X^- \qquad (15)$$

electron transfer, in eq 14, takes place because of the continuous removal of the frangible anion–radical $ArX^{\bullet -}$ (eq 15).[18] Then the apparent rate law for the production

(16) (a) On theoretical grounds the flux of production under electrochemical conditions could be adjusted to infinitely small values provided that electrolysis is performed at a potential located sufficiently before that corresponding to the halfwave potential, $E_{1/2}$, of the starting material. For example when the latter undergoes a first-order follow-up reaction controlling the overall electrode process, the current, i, under steady state condition, is given by[17]

$$i = i^{lim}/\{1 + \exp[nF(E - E_{1/2})/RT]\}$$

(i^{lim}, limiting current corresponding to the plateau of the electrochemical wave; $n = +1$, for a reduction, $n = -1$, for an oxidation). On the other hand the current is related to the production rate of the intermediate, I, by[17]

$$i = nFV(d[I]/dt)$$

Therefore, $(d[I]/dt)$ can be formally made as small as possible when $nF(E - E_{1/2}) \gg 0$. (b) However under real practice, background discharge or other uncontrolled electrochemical processes involving unknown impurities will correspond to the main electrochemical processes undergoing at the electrode, as soon as $i \ll i^{lim}$. This usually precludes electrolysis at too small current densities ($i/i^{lim} < 10^{-2}$).

(17) Bard, A. J.; Faulkner, L. R. In *Electrochemical Methods*; Wiley: New York, 1980.

(18) (a) For general description of redox catalysis and its aplication to the determination of rate constants see: Andrieux, C. P.; Savéant, J. M. In *Investigations of Rates and Mechanisms of Reactions*; Bernasconi, C. F., Ed.; Wiley: New York, 1986; Vol. 6, 4/E, Part 2, Chapter 7, pp 305–390. (b) For synthetic applications of redox catalysis, see, e.g., ref 1a. (c) For applications to $S_{RN}1$ or $S_{RN}1$-like reactions, see, e.g., ref 8.

(19) In eqs 10, 29, 38 or Scheme II, a proton is produced as indicated. However it should be understood that under our experimental conditions the proton is trapped by any base present in the medium, including the reactant phenoxide ion or ammonia itself.

(20) Combellas, C.; Gautier, H.; Simon, J.; Thiébault, A.; Tournilhac, F.; Barzoukas, M.; Josse, D.; Ledoux, I.; Amatore, C.; Verpeaux, J. N. *J. Chem. Soc., Chem. Commun.* **1988**, 203.

(21) Amatore, C.; Calas, P.; Gomez, L.; Commeyras, A. *J. Fluorine Chem.*, in press.

(22) I.e., $ArX^{\bullet -}$, $ArNu^{\bullet -}$, etc.[6d]

(23) (a) When k_1 in eq 11a,b is large vis-à-vis the rate of diffusion to and from the electrode, no homogeneous chain may develop,[6a-c] all electron transfers occurring at the electrode. For example the homogeneous chain sequence in Scheme I is then replaced

$$ArX + e \rightarrow ArX^{\bullet -}$$

$$ArX^{\bullet -} \xrightarrow{k_1} Ar^{\bullet} + X^-$$

$$Ar^{\bullet} + Nu^- \xrightarrow{k_2} ArNu^{\bullet -}$$

$$ArNu^{\bullet -} \rightarrow ArNu + e$$

This occurs because $Ar^{\bullet}$ is then generated very close from the electrode surface. If $k_2[Nu^-]$ is not sufficiently large to overcome the rate of reduction of $Ar^{\bullet}$ at the electrode surface, no $S_{RN}1$ reaction takes place. Therefore significant substitution requires[6a-c] $k_2[Nu^-] > k_1$, which implies that $ArNu^{\bullet -}$ is also formed close to the electrode surface where it is immediately oxidized. (b) This remains valid provided that the electrode potential remains less cathodic than the location of the $ArNu/ArNu^{\bullet -}$. In the opposite situation $ArNu^{\bullet -}$ escapes from the close vicinity of the electrode surface and may trigger a homogeneous chain; see, e.g., Amatore, C.; Pinson, J.; Savéant, J. M.; Thiébault, A. *J. Electroanal. Chem.* **1980**, *107*, 59 and 75.

(24) The exponent (1/2) in eq 12 arises because of electrochemical kinetics.[6c] Therefore the analogy of the formulation in eq 11a,b with the relevant homogeneous situation is not total.

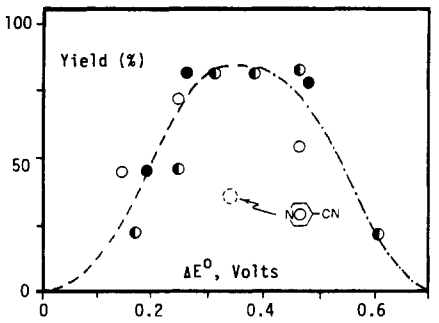


Figure 1. Experimental variation of the yield, y, in biphenyl obtained in indirect electrolysis of arylhalides (○, 3-chlorobenzonitrile; ●, 4-chlorobenzonitrile; and ◐, 3-chloropyridine; 0.038 M) in presence of 2,6-di-*tert*-butylphenoxide (0.225 M) as a function of $\Delta E^\circ = E^\circ_M - E^\circ_{ArX}$, the difference of standard reduction potentials between the mediator and the arylhalide. Liquid ammonia at −38 °C. ((i) The curves are drawn to emphasize the two opposite trends observed for $y = f(\Delta E^\circ)$ (see text and footnote 27). (ii) The dotted circle corresponds to a situation (4-chlorobenzonitrile with 4-cyanopyridine as the mediator), where the mediator is not stable in basic media (see text and compare eq 27)).

of the aryl radical is as given in eq 16, where k_o is small as compared to the diffusion limit (eq 17)

$$(d[Ar^\bullet]/dt)_{prod} = k_1[ArX^{\bullet-}] = k_o[ArX][M^{\bullet-}]\{k_1/(k_1 + k_{dif}[M])\} \quad (16)$$

with[25]

$$k_o = k_{dif} \exp[F(E^\circ_{ArX} - E^\circ_M)/RT] \ll k_{dif} \quad (17)$$

because of the large endergonicity of the electron transfer in reaction 14. Since the bracketted term in the right-hand side of eq 16 is always less than unity, the rate of production of $Ar^\bullet$ is equal to $k_o[ArX][M^{\bullet-}]$ at maximum. Therefore the latter can be adjusted at will by a proper choice of the potential difference between the standard reduction potentials of the halide and the mediator,[26] to allow the radical to be produced far from the electrode surface. Under such conditions the development of the chain reaction in Scheme II is no longer hampered by the electrode, and the most important termination step consists in the reduction of $Ar^\bullet$ by the mediator anion–radical, $M^{\bullet-}$, which is the reducing species present at the largest concentration in the medium.

$$Ar^\bullet \xrightarrow{k_{dif}[M^{\bullet-}]} Ar^- \text{ (termination)} \quad (19a)$$

$$Ar^\bullet \xrightarrow{k_2[Ar'O^-]} \text{etc. (propagation)} \quad (19b)$$

Therefore the instantaneous yield in biaryl (eq 10) is given by[27-28a]

$$y_{biaryl} = k_2[Ar'O^-]/(k_2[Ar'O^-] + k_{dif}[M^{\bullet-}]) = 1/\{1 + (k_{dif}/k_2)[M^{\bullet-}]/[Ar'O^-]\} \quad (20)$$

On the other hand, the electrolysis current, i, is imposed to be a given fraction, f, of the current plateau of the mediator electrochemical wave in the presence of ArX: $i = fi_M^{lim}$.

Then, $[M^{\bullet-}] \approx \epsilon f[M]_o$,[27] where ϵ is a factor less than unity which exact value depends on k_o.[28] When k_o is sufficiently small, ϵ is commensurate to unity. This allow to rewrite eq 20 as[30]

$$y_{biaryl} \approx 1/\{1 + \epsilon\gamma_M(i/i_M^{lim})(k_{dif}/k_2)\} \qquad \epsilon \approx 0.63 \quad (21)$$

where γ_M is the relative concentration of the mediator to that of the phenoxide, i.e. $\gamma_M = [M]/[Ar'O^-]$. In practice f and γ_M can be made as small as 0.1 and 0.01, respectively, for conditions of preparative-scale electrolysis. Therefore yields in biaryl which exceed 90% can be obtained even under conditions where k_2 is 100 times smaller than the diffusion limit rate constant k_{dif}. To be obtained via the direct electrochemical reduction of ArX, similar yields would require that

(25) In eqs 16 and 17, k_{-o} is replaced by the diffusion limit rate constant k_{dif}. This is valid as soon as the electron transfer in eq 14 is sufficiently endergonic. For a thorough discussion of this point, see, e.g.: Schlesner, C. J.; Amatore, C.; Kochi, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 3567.

(26) In the usual practice E°_{ArX} is generally unknown, but only the peak potential in cyclic voltammetry or half-wave potential, $E^{1/2}_{ArX}$, in steady state methods are available. Thus equation 18 may be used as an alternative to eq 17 to estimate k_o, or k_1 when k_o is experimentally determined for a given mediator.[18] In eq 18, δ is the diffusion layer

$$k_o = [k_{dif}/(k_1\delta^2/D)^{1/2}] \exp[F(E^{1/2}_{ArX} - E^\circ_M)/RT] \quad (18)$$

thickness (20–50 μm, under laboratory conditions), and D the average diffusion coefficient of the species involved in the mechanism (in liquid ammonia, $D \approx 5 \times 10^{-5}$ cm^2 s^{-1} at −38 °C). Note that eq 18 supposes that the organic halide electrochemical wave is kinetically controlled by the follow-up reaction in eq 15 (see: Andrieux, C. P.; Savéant, J. M., ref 18a).

(27) (a) The relationship $[M^{\bullet-}] = \epsilon(i/i^{lim})[M]_o$ is valid only when the mediator concentration in the bulk of the solution is not affected by the electrolysis. This supposes that the rate of production of the mediator anion–radical at the electrode does no exceed that of its consumption (via eqs 14 and 19a) within the diffusion layer. This is effective as soon as $k_o[ArX] > 2(D/\delta^2)$, where D is the diffusion coefficient of the mediator and δ the diffusion layer thickness. Under our experimental conditions, $D \approx 5 \times 10^{-5}$ cm^2 s^{-1}, $\delta \approx 30$ μm,[27e] [ArX] < 0.05 M; therefore, the bulk concentration of the mediator is not significantly affected by the electrolysis as soon as $k_o \geq 2 \times 10^2$ M^{-1} s^{-1}. (b) When k_o is smaller than a few tenths of 10^2 M^{-1} s^{-1}, no significant fraction of $M^{\bullet-}$ is consumed within the diffusion layer. The electrolysis then amounts to a net production of $M^{\bullet-}$ in the bulk solution. Under such conditions one obtains:[29]

$$[M^{\bullet-}]/[M]_o \approx (i/i_M^{lim})(AD/V\delta)/(k_o[ArX])$$

(where $A \sim 4$ cm^2 is the electrode surface area and V the volume of the solution), provided that $k_o[ArX] > (AD/V\delta)$, i.e. $k_o \geq 2 \times 10^{-2}$ M^{-1} s^{-1} under our experimental conditions. (c) If k_o is less than this latter value $[M]^{\bullet-}] \approx it/FV$, where t is the electrolysis duration time, provided $t \leq t_{max} = [M]_o(FV/i)$;[29] for $t > t_{max}$, $[M^{\bullet-}] \sim [M]_o$. Note that under the experimental conditions used in this study, $t_{max} \approx 30$ min for $i \approx 100$ mA. Therefore when $k_o < 0.1$ M^{-1} s^{-1}, and after ca. a 30-min electrolysis duration all the mediator present in the cell is reduced, which corresponds to a cathodic shift of the electrode potential which reaches then the aryl halide electrochemical wave. This amounts to perform a direct electrolysis of the organic halide, i.e. under the conditions considered in eqs 11 and 12. (d) To summarize the above discussion (which pertains to cases where $M^{\bullet-}$ undergoes no other chemical route than that considered in the sequence of eqs 13–15; see later, however) one has (i) $k_o > 2(D/\delta^2)/[ArX] \approx 2 \times 10^2$ M^{-1} s^{-1}. Redox catalysis occurs within the diffusion layer and $[M^{\bullet-}] \sim [M]_o(i/i_M^{lim})\epsilon$ with $\epsilon \approx 0.5$.[28] (ii) $2(D/\delta^2) > k_o[ArX] > (AD/V\delta)$, i.e. 2×10^2 M^{-1} s$^{-1} > k_o > 2 \times 10^{-2}$ M^{-1} s^{-1}. Redox catalysis occurs within the bulk of the solution and $[M^{\bullet-}] \approx [M]_o(i/i_M^{lim})\epsilon$, with $\epsilon \approx (AD/V\delta)/(k_o[ArX])$, i.e. $\epsilon \approx 0.1/k_o$, where k_o is expressed in M^{-1} s^{-1}. (iii) $k_o[ArX] < (AD/V\delta)$, i.e. $k_o < 2 \times 10^{-2}$ M^{-1} s^{-1}. No redox catalysis phenomenon occurs. Electrolysis amounts to electrolyse the mediator ($t < t_{max} = [M]_o(FV/i) \sim 30$ min) and then to effect a direct electrolysis of the organic halide. (e) $\delta \sim 30$ μm is estimated for the cell and stirring conditions used in this study from the limiting current observed for the mediator electrochemical wave. Indeed one has[29] $i_M^{lim}/[M]_o = FAD/\delta \approx 6.5$ A mol^{-1} L, with $A \approx 4$ cm^2 and $D \approx 5 \times 10^{-5}$ cm^2 s^{-1}.

(28) (a) Owing to the existence of concentration profiles in the diffusion layer, eq 20 is valid only at a specific distance from the electrode surface. (b) However as soon as k_o is sufficiently small,[28c] $[M^{\bullet-}]$ can be replaced by its average concentration in the diffusion layer, i.e., $[M^{\bullet-}]_{av} \approx [M]_o(i/i_M^{lim})/2$, which corresponds to $\epsilon = 0.63$. (c) When k_o is much larger than $2(D/\delta^2)/[ArX]$, the concentration of $M^{\bullet-}$ corresponds to $\epsilon \ll 1$. Yet these conditions are not considered in the following (see later).

(29) Bard, A. J.; Santhanam, K. S. V. In *Electrochemical Chemistry*; Bard, A. J., Ed.; M. Dekker: New York, 1970; Vol. 4, ppf 220.

(30) Equations 21 and 41 are approximate equations. Indeed complete integration of the relevant partial derivative equations controlling the yield in the diffusion layer yields:

$$y_{biaryl} = 2[\sigma - \ln(1 + \sigma)]/\sigma^2 \quad (21a)$$

with $\sigma = \gamma_M(i/i_M^{lim})(k_{dif}/k_2)$. In the range of σ values of interest for the systems in this study ($\sigma \leq 1$, i.e. $y_{biaryl} \geq 50\%$), eq 21a is approximated, with a precision larger than 3%, by eq 21 or 41 with $\epsilon = 0.63$.

$$k_1 \leq 10^{-2} k_2[\mathrm{Ar'O^-}] \quad (22)$$

as can be easily deduced from eq 12. Taking into account that [Ar'O⁻] is usually about 0.1 M, and considering again that k_2 is 100 times smaller than $k_{dif} = 3 \times 10^{10}$ M^{-1} s^{-1}, fulfillment of the inequality 22, would require that $k_1 \leq 3 \times 10^5$ s^{-1}, a condition generally not satisfied with most of organic halides of interest for synthetic purposes.

Limitation of the Use of Redox Mediators in the Activation of Radical Chains. In the above part we have shown that the use of a redox mediator allows significant yields in biaryls to be obtained even under conditions where a direct electrochemical approach would have failed, provided that the mediator is selected so that the rate constant, k_0, of the electron transfer from $M^{\bullet -}$ to ArX is made small enough, i.e. provided that $\Delta E° = (E°_M - E°_{ArX})$ is sufficiently large. However Figure 1 shows that even if this prediction proves experimentally valid for $\Delta E° \leq 0.4$ V, it fails at higher values of $\Delta E°$.[31] Such a result is easily rationalized when one takes into account the chemical stability of the mediator, M, or of its reduced form, $M^{\bullet -}$, in the reaction medium, under the conditions of electrolysis.[32]

From eq 17, it is seen that large values of $\Delta E°$ correspond to extremely small values of k_0. For example in liquid ammonia at −38 °C, $\Delta E° = 0.35$ V (i.e. at maximum of the curve in Figure 1) corresponds to $k_0 \approx 9 \times 10^2$ M^{-1} s^{-1}, whereas $k_0 \approx 0.5$ M^{-1} s^{-1} is obtained for $\Delta E° = 0.50$ V. Therefore when $\Delta E°$ is increased above 0.3–0.4 V, one can no more neglect other possible reactions of the anion radical $M^{\bullet -}$ of the mediator. Although these latter may be slow enough for not being detected by cyclic voltammetry, they may become significant vis à vis the electron transfer to ArX, as soon as $\Delta E° \sim 0.3$–0.4 V.

$$M^{\bullet -} \xrightarrow{k_0[ArX]} \text{etc. (activation of chain)} \quad (23a)$$

$$M^{\bullet -} \xrightarrow{k} \text{etc. (destruction of mediator)} \quad (23b)$$

For example, in the presence of purposely added phenol, 2,4'-bipyridine (bipy) undergoes an ECE/DISP sequence (eqs 24–26):

$$\text{bipy} + e \rightleftharpoons \text{bipy}^{\bullet -} \quad (24)$$

$$\text{bipy}^{\bullet -} + \text{PhOH} \xrightarrow{k} \text{bipy-H}^{\bullet} + \text{PhO}^- \quad (25)$$

$$\text{bipy-H}^{\bullet} + e \rightleftharpoons \text{bipy-H}^- \quad (26a)$$

and/or

$$\text{bipy-H}^{\bullet} + \text{bipy}^{\bullet -} \rightarrow \text{bipy-H}^- + \text{bipy} \quad (26b)$$

resulting in a total shift from a one-electron reversible process to a two-electron irreversible one as featured by Figure 2. Such an overall two-electron reduction amounts to deplete the mediator concentration. Therefore under our experimental conditions the proton liberated in eq 10 results in protonation of the anion radical of the mediator as soon as k_0, in eq 23a, becomes too small.

Another feature related to large values of $\Delta E°$, is that when k_0 is extremely small, the rate of activation of the chain in Scheme II is very low. This results in a low rate of formation of the biphenyl in eq 10 and therefore corresponds to extremely large duration of electrolysis. This requires that the neutral form of the mediator stands

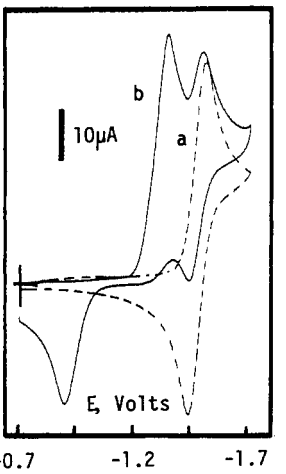
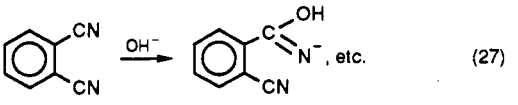


Figure 2. Cyclic voltammetry of 2,4'-bipyridine (22.5 mM) in liquid ammonia (−38 °C) at a gold disk electrode (ϕ 0.5 mm). Scan rate $v = 0.5$ V s^{-1}. Supporting electrolyte, KBr, 0.25 M. Potentials refer to Ag/Ag^+, 0.01 M. (a) 2,4'-Bipyridine alone or in the presence 0.19 M of potassium 2,6-di-*tert*-butylphenoxide. (b) identical with (a) but after addition of ammonium bromide (30 mM), i.e. in the presence of $(tBu)_2PhO^-$, 0.16 M, and $(tBu)_2PhOH$, 0.03 M. Note that curve b corresponds to the superposition of a two-electron irreversible wave (first peak) and a one-electron reversible wave (second peak, identical with that observed in a) because of incomplete titration of the anion radical of 2,4'-bipyridine by the phenol in the diffusion layer.

unaltered for several hours in the reaction medium. Such a requirement is difficultly fulfilled for the molecules prone to be used as redox mediators. Indeed, the presence of electrophores makes them generally vulnerable to basic media over long period of time. For example the presence of a base, such as potassium hydroxide, added to the medium to prevent the protonation of $M^{\bullet -}$ (see above) may then result in the destruction of the mediator, as observed for phthalonitrile in eq 27.



(27)

It is thus seen that when $\Delta E°$ is increased too much, the chemical stability of the mediator or of its anion radical form must be taken into account. Under such conditions the mediator is depleted from the reaction medium faster than the organic halide is converted. Under potentiostatic conditions this would correspond to low conversions of the organic halide but with excellent yields in biphenyl for the small fraction converted. However, under the galvanostatic conditions considered in this study, the disappearance of the mediator couple during the electrolysis results in a progressive shift of the electrode potential toward more cathodic values. As a result as soon as the mediator concentration drops under that needed to supply the current imposed to the cell, the electrode potential reaches the electrochemical wave of the organic halide.[33] Then a direct electrochemical activation is performed, which amounts to convert nearly quantitatively the halide to the hydrocarbon without significant yields in biphenyl (compare eq 12).

Selection of an Adequate Mediator. From what precedes it should be understood that the proper mediator is such that $\Delta E°$ is the largest possible, without resulting, however, in the activation rate, i.e. k_0, being too small with respect to the lifetime of M (or $M^{\bullet -}$) in the reaction me-

(31) For $\Delta E° = 0.4$ V, k_0 is evaluated from eq 17 to be of the order of 1.2×10^2 M^{-1} s^{-1}. Therefore [see footnote 27d, points i and ii] the yield in biaryl should increase (owing to the decrease in ϵ value) with respect to the yields observed at smaller values of $\Delta E°$, rather than decrease as observed in figure 1.[34]

(32) The discussion in footnote 27 considered that $M^{\bullet -}$ was involved only in the "redox catalysis" sequence in eqs 13–15.

(33) Although the reason is quite different, the result is then identical with that predicted in point iii of footnote 27d.

Table I. Determination of $E°_{ArX}$ and k_1 by Redox Catalysis for the Organic Halides Considered in This Study

halide	E^p_{ArX}[a,b]	k_o,[c] M^{-1} s^{-1}	k_1k_o/k_{-o},[c] s^{-1}	$E°_{ArX}$[b]	k_1, s^{-1}
2-chloropyridine	−1.810	7.9×10^2[d]	-	−1.975	6.5×10^8
3-chloropyridine	−1.800	3.3×10^3[d]	-	−1.950	1.7×10^8
4-chloropyridine	−1.805	4.0×10^3[d]	-	−1.940	3.0×10^7
2,5-dichloropyridine	−1.565	2.2×10^2[e]	0.50[e]	−1.705	5.3×10^7[j]
2-chloro-5-cyanopyridine	−1.245	-	10.5[f]	−1.330	$2. \times 10^5$
2-chlorobenzonitrile	−1.430	1.64×10^3[g]	-	−1.585	$1. \times 10^8$
3-chlorobenzonitrile	−1.530	-	7.5[h]	−1.600	4.1×10^4
4-chlorobenzonitrile	−1.525	1.2×10^4[e]	-	−1.640	9.3×10^8
4-chloro(trifluoromethyl)benzene	−1.880	9.2×10^2[d]	-	−1.975	1.5×10^8
2,4-difluorobromobenzene	−1.795	62.5[i]	-	−1.875	$4. \times 10^7$

[a] At 0.2 V s^{-1}. [b] In V vs Ag/Ag^+ 0.01 M, in liquid ammonia at −38 °C. [c] The specific mediator used in each case is indicated for each entry by [d] 2,2′-bipyridine ($E°_M$ = −1.625 V[b]); [e] 4,4′-bipyridine (−1.330 V[b]); [f] phthalonitrile (−1.130 V[b]); [g] 4-cyanopyridine (−1.250 V[b]); [h] 2-cyanopyridine (−1.430 V[b]); [i] 2,4′-bipyridine (−1.475 V[b]); [j] Corresponds to the cleavage of the carbon–chlorine bond in the 2-position.

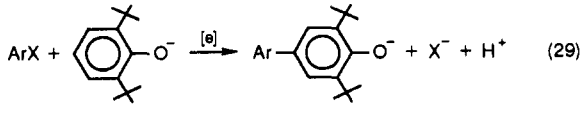
dium.[34] Fulfillment of this requires that the rate of depletion of the mediator (via reactions involving M and $M^{\bullet-}$) is known. This can easily be achieved for the neutral form, M, of the mediator, by following its concentration vs time in the reaction medium without any electrolysis. Thus those candidate-mediators undergoing too fast decay can be eliminated. Estimation of the stability of the reduced form of the mediator is more difficult. Indeed the observation of a perfect chemically reversible cyclic voltammogram for the $M/M^{\bullet-}$ couple is not a warrant of adequateness owing to the large difference between the time scale of cyclic voltammetry (CV)—a few seconds at maximum—and the duration of an electrolysis—from several minutes to several hours, depending on the current density. Therefore, even when the mediators exhibit perfect reversible CV, it is wise to select that one that corresponds to k_o[ArX] being of the order of a few s^{-1} in order to ensure that electron tranfer to ArX is the major route for $M^{\bullet-}$.

From eq 17, with $k_{dif} \approx 3 \times 10^{10}$ M^{-1} s^{-1} as an average value in liquid ammonia (at −38 °C), such a condition corresponds to

$$\Delta E°_{max} = (E°_M - E°_{ArX})_{max} \approx 0.49 + 0.046 \log [ArX]_o \quad (28)$$

where $[ArX]_o$ is the initial bulk concentration of the organic halides, expressed in moles per liter. For the experimental conditions of Figure 1, in which $[ArX]_o \approx$ 0.0375 M, eq 28 affords $\Delta E°_{max} \approx 0.43$ V.

II. Experimental Illustration: Application to the Synthesis of Biaryls via an $S_{RN}1$-like Reaction. Determination of the Standard Reduction Potentials of a Series of Organic Halides of Interest for the Synthesis of Unsymmetrical Biaryls. Table I presents a series of substituted halobenzenes and chloropyridines considered in this study for their interest for the synthesis of unsymmetrical biaryls by coupling to 2,6-di-*tert*-butylphenoxide according to the overall electrocatalytic reaction 29.[19] The choice of the halides in Table I was



(29)

decided to afford two consistent series allowing to test the effect of nature and position of electron-withdrawing groups on the nonlinear optical properties of the biaryls formed in eq 29. For this reason the phenoxide moiety was kept constant in this study.

In the absence of phenoxide, cyclic voltammetry of the monohalides shown in Table I exhibits an irreversible two-electron reduction wave followed at more negative potentials by a reversible one-electron wave. This latter features the reduction of the benzonitrile or pyridine formed via the sequence of reactions (1–4) at the level of the first wave. An essentially identical behavior is observed for the polyhalides, yet involving a succession of irreversible two-electron waves featuring the sequential reduction of each carbon–halide bond.

Direct determination of the standard reduction potential corresponding to the initial electron transfer to the starting organic halide (reaction 30) is hampered by the large magnitude of the rate constant, k_1, corresponding to the cleavage of the anion-radical in eq 31. Peak potential

$$ArX + e \rightleftharpoons ArX^{\bullet-} \ (E°_{ArX}) \quad (30)$$

$$ArX^{\bullet-} \rightarrow Ar^{\bullet} + X^- \ (k_1) \quad (31)$$

variation with the scan rate, v, occurred with a slope of ca. −25 mV per log v, indicating[35a] that the electron transfer in eq 30 is sufficiently fast to be controlled by the follow up reaction 31. Therefore the peak potential, E^p_{ArX}, of the two electron wave is related to the standard reduction potential, $E°_{ArX}$, and to the rate constant, k_1, in eq 31, via the relationship in eq 32.[35b]

$$E^p_{ArX} = \{E°_{ArX} + (RT/2F) \ln k_1\} - (RT/2F)[1.56 - \ln (RT/Fv)] \quad (32)$$

To evaluate $E°_{ArX}$ and k_1 we used redox catalysis. Indeed the increase of the current peak intensity of the CV wave pertaining to any mediator, when recorded in the presence of the organic halide, corresponds to the continuous recycling of the mediator via the sequence of eqs 14 and 15. Therefore the rate constant k_o (when $k_1 \gg k_{-o}$[M] and/or the ratio k_1k_o/k_{-o}, when $k_1 \ll k_{-o}$[M]) can be determined. On the other hand, because of the thermodynamics of the electron transfer in eq 14:

$$E°_{ArX} - E°_M = (RT/F) \ln (k_o/k_{-o}) \quad (33)$$

from which it ensues that

$$\Delta E° = E°_M - E°_{ArX} = (RT/F) \ln k_1 - (RT/F) \ln (k_1k_o/k_{-o}) \quad (34)$$

Therefore, for those systems where k_1k_o/k_{-o} is determined from redox catalysis, linear combination of eqs 32 and 34 affords eq 35. The latter allows the determination

$$E°_{ArX} = 2E^p_{ArX} - E°_M + (RT/F)(1.56 - \ln [(k_1k_o/k_{-o})(RT/Fv)]) \quad (35)$$

(34) When the stability of M or $M^{\bullet-}$ in the reaction medium is sufficient, then the limitation is imposed by the condition iii in footnote 27d. Under our conditions, $k_o < 2.10^{-2}$ M^{-1} s^{-1} corresponds to $\Delta E° > 0.57$ V.

(35) (a) Equation 32 predicts a slope of $(RT/2F) \ln 10 = 23.3$ mV per unit of log v, at −38 °C. (b) See, e.g., Andrieux, C. P.; Savéant, J. M., ref 18a.

Table II. Electrochemical Inducement of Biphenyl Synthesis by a $S_{RN}1$-like Coupling of Organic Halides with 2,6-Di-*tert*-butylphenoxide[a]

halide	y_{direct},[b] %	y_{med},[c] %	k_2,[d] M^{-1} s^{-1}	y^{max}_{direct},[e] %
2-chloropyridine	0	-	$\leq 10^8$	15
3-chloropyridine	50	84[m1]	3.2×10^9	67
4-chloropyridine	-	56[m1/f]	1.2×10^9	75
2-chloro-5-cyano-pyridine	15	77[m2]	2.0×10^9	98
2-chlorobenzonitrile	64	95[m3]	1.0×10^{10}	82
3-chlorobenzonitrile	33	80[m3]	2.8×10^9	99
4-chlorobenzonitrile	22	83[m3]	3.5×10^9	48

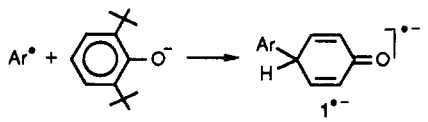
[a] Electrolysis performed at -38 °C in 80 mL of liquid ammonia, 3 mmol of ArX, 18 of mmol 2,6-di-*tert*-butylphenoxide. [b] Yield in biphenyl obtained by direct galvanostatic electrolysis (i = 50 mA) at a Pt cathode. [c] Yield obtained by using a mediator [2 mmol; (m1), 2,4'-bipyridine; (m2), phthalonitrile; (m3), 4,4'-bipyridine] under galvanostatic conditions (i = 50 mA). Except where otherwise stated, yields correspond to the yield in biaryl with respect to the consumed organic halide (conversion between 90 and 95%). See the Experimental Section. [d] Rate constant between the σ-aromatic radical obtained by reductive cleavage of the organic halide, with 2,6-di-*tert*-butylphenoxide. [e] Maximum yield predicted for direct electrolysis on the basis of eq 12 and of the rate constants reported in Tables I and II for a concentration 0.225 M of phenoxide. [f] Conversion (~90%) was not determined accurately; therefore, this yield is given on the basis of the initial organic halide, and constitute a lower limit when compared to other yields in this column.

of $E°_{ArX}$, and therefore of k_1 (via eq 32), from the value of the peak potential of the halide at a given scan rate. When only k_o can be determined, eq 33 is used instead. Indeed as soon as $\Delta E° = E°_M - E°_{ArX}$ is larger than 0.250 V, one can reasonably consider that $k_{-o} \approx k_{dif}$.[25] Therefore one obtains readily

$$E°_{ArX} = E°_M + (RT/F)(\ln k_o - 24.12) \quad (36)$$

When both k_o and (k_1k_o/k_{-o}) can be determined, k_1 can be also obtained by $k_1 = [(k_1k_o/k_{-o})/k_o]k_{dif}$, which is valid again as soon as $k_{-o} \approx k_{dif}$. For 2,5-dichloropyridine where k_o as well as k_1k_o/k_{-o} can be measured, $k_1 = 6 \times 10^7$ s^{-1} is obtained by this method. On the other hand, $k_1 = 5.5 \times 10^7$ is determined through eq 35. For the other halides in Table I, $E°_{ArX}$ and k_1 were determined by application of eq 35 or 36 and 34.

Inducement of Biphenyl Synthesis by Direct Electrolysis. Table II reports the yields of biphenyl obtained upon direct electrolysis, i.e. by imposing a current density so that the electrode potential is set at the foot of the electrochemical wave of the organic halide. The rate constant, k_2, determined by redox catalysis[18a] for the coupling of the σ-aromatic radical, Ar•, generated upon cleavage of the anion radical of the organic halide, with 2,6-di-*tert*-butylphenoxide (eq 37) is also reported in Table II.



(37)

From the values of k_2 and k_1 (reported in Table I) one may evaluate the maximum yield (y^{max}_{direct}, last column in Table II) achievable for biphenyl synthesis, on the basis of eq 12, for a direct electrolysis performed under identical conditions to those in Table II. It is seen by comparison of the experimental (second column) and maximum theoretical yields that, with the exception of 2-chloro-5-cyanopyridine and 3-chlorobenzonitrile, eq 12 provides a reasonable estimate of the experimental yield. However, the latter are always less than those predicted by eq 12, which corresponds to neglecting the participation of the homogeneous reduction of Ar• by $ArX^{•-}$ or $1^{•-}$ (see Scheme II). Such hypothesis supposes that the current density of electrolysis is infinitely small (which is hardly compatible with other experimental requirements) and that k_1 is large enough for the radical Ar• to be produced in the immediate proximity of the electrode surface. For 2-chloro-5-cyanopyridine ($k_1 = 2 \times 10^5$ s^{-1}) or 3-chlorobenzonitrile ($k_1 = 4.1 \times 10^4$ s^{-1}), k_1 is too small for eq 12 to have any validity under the electrolysis conditions considered in Table II.

Biphenyl Synthesis via Indirect Electrolysis Using a Redox Mediator. With the exception of 3-chloropyridine and 2-chlorobenzonitrile, the yields in biphenyl obtained by direct electrolysis of the organic halides in Table II are too small to present any synthetic interest for the electrochemical activation as compared to those obtained using a photochemical one.[36] We therefore decided to investigate the effect of indirect electrolysis.

Choice of the Mediator and Experimental Conditions. As explained in the first part of this paper the yields obtained in mediated electrolysis should be the largest when $\Delta E° = E°_M - E°_{ArX}$ is the largest (eqs 17 and 20).[27] However in selecting a proper mediator, this latter parameter is not the only one to take into account since stability of the mediator or of its reduced form in the medium is obviously an important factor. Most of the problems associated to the stability of the mediator redox couples are related to pH or pH variations in the electrolysis medium. Indeed, when the biphenyl synthesis is efficient, eq 38[19] predicts a progressive acidification of the

$$ArX + PhO^- \rightarrow ArPhO^- + X^- + H^+ \quad (38)$$

medium while electrolysis proceeds. Note in this respect that 2,6-di-*tert*-butylphenol is to be considered as a weak acid in liquid ammonia;[37a] because of resonance and withdrawing effects the biphenyl formed in eq 38 is even stronger. Therefore to avoid protonation[37b,c] of most of the anion radicals of the mediators used in this work, electrolysis must be performed in the presence of an excess of base. For pyridazine or bipyridines mediators, whose neutral forms are stable to strong bases, electrolysis were then performed in the presence of one equivalent (per organic halide) of potassium hydroxide.

These conditions revealed unsuccessful for phthalonitrile or cyanopyridine mediators which undergo hydrolysis of their cyano groups in the presence of a strong base such as potassium hydroxide. Since their reduced forms are stable in the presence of 2,6-di-*tert*-butylphenol/phenoxide buffers, electrolysis using these mediators were performed in the presence of an excess (6-fold vis-à-vis the organic halide) of 2,6-di-*tert*-butylphenoxide.

Taking care of the above conditions, the best mediator was selected so that $\Delta E° \sim 0.30$–0.40,[27,31] which (see discussion in part I) corresponds to the largest efficiency of biphenyl synthesis as evidenced by Figure 1 as well as by Table III in the case of 3-chloropyridine. Electrolysis were then performed in the same cell, at the same current intensity (i = 50 mA) and other experimental conditions

(36) Compare to the yields obtained for the same reaction under homogeneous photochemical activation in ref 14b.

(37) (a) Compare to $pK_a = 3.5$ for PhOH in liquid ammonia at -60 °C. (b) As indicated above (eqs 24–26 and Figure 2) the radical-anion of 2,4'-bipyridine undergoes a rapid protonation in the presence of 2,6-di-*tert*-butylphenol in liquid ammonia. (c) This problem is not specific to the reaction (eq 38) investigated here but arises in any $S_{RN}1$-like reaction involving a nucleophile bearing an acidic hydrogen (HNu^- = $RC(O)CRH^-$, $(NC)_2CH^-$, $RCO_2C(CN)H^-$, $\overline{CH{=}CHCH{=}CHN}^-$, etc.) since owing to resonance, ArNuH is a stronger acid than NuH_2.[19]

$$ArX + HNu^- \rightarrow ArNu^- + X^- + H^+$$

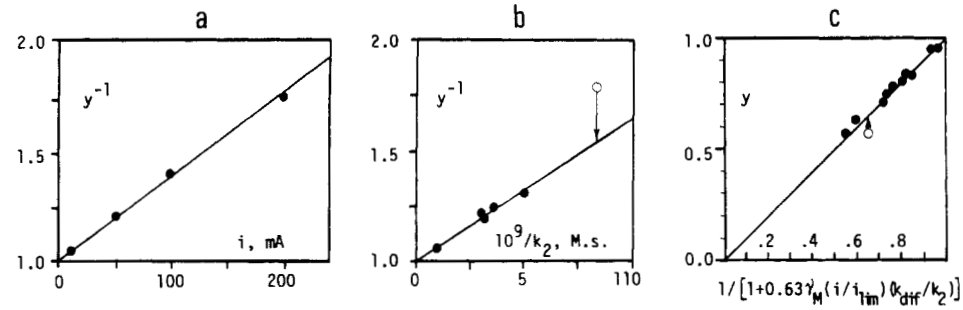


Figure 3. Variation of the yield, y, in biphenyl obtained in indirect electrolysis of aryl halides (0.038 M) in liquid ammonia at −38 °C, in the presence of 0.225 M 2,6-di-*tert*-butylphenoxide. (a) 3-Chloropyridine with 2,2′-bipyridine as the mediator (0.025 or 0.0375 M). Variations of $(1/y)$ vs the imposed electrolysis current intensity, according to eq 39. (b) Variations of $(1/y)$ vs $(1/k_2)$ for the systems in Table II, according to eq 40. The straight line corresponds to the theoretical variation according to the results in Figure 3a (see text). (c) Unifying plot comparing the experimental yields to the predictions of eq 21 [Note that in b or c the open circle represents a system (4-chloropyridine) in which the raw experimental yield is used, without being corrected for incomplete conversion (ca. 90%), whereas the filled circles represent corrected yields. See footnote f in Table II and the Experimental Section].

Table III. Effect of $\Delta E^\circ = E^\circ_M - E^\circ_{ArX}$[a] on the Yield in Biphenyl Obtained by Indirect Electrolysis of 3-Chloropyridine[b] in the Presence of 2,6-Di-*tert*-butylphenoxide[c] in Liquid Ammonia at −38 °C

mediator[d]	E°_M	ΔE°[a]	y,[e] %	k_o, M^{-1} s^{-1}	k_1k_o/k_{-o},[f] s^{-1}
3,3′-bipyridine	−1.755	0.195	23	2.1×10^6	1.1×10^4
2,3′-bipyridine	−1.685	0.265	46	6.5×10^4	3.5×10^2
2,2′-bipyridine	−1.625	0.325	82	3.3×10^3	18
pyridazine	−1.565	0.385	70–80[g]	1.7×10^2[h]	0.95
2,4′-bipyridine	−1.475	0.475	84	1.9[h]	1.1×10^{-2}
4,4′-bipyridine	−1.330	0.620	21	1.4×10^{-3}[h]	8.5×10^{-6}

[a] E° = −1.95 V for 3-chloropyridine. [b] 3 mmol in 80 mL of liquid NH_3. [c] 18 mmol. [d] 2 mmol. [e] Electrolysis performed at a 50 mA current density. [f] Estimated from $(k_o/k_{-o}) = \exp(F\Delta E^\circ/RT)$ and $k_1 = 1.7 \times 10^8$ s^{-1}. [g] Lower yields correspond to a degradation of pyridazine during electrolysis. [h] Not measurable by cyclic voltammetry; the values given are obtained by extrapolation as a function of ΔE°, using eq 17, with $k_{dif} = 3 \times 10^{10}$ M^{-1} s^{-1}.

identical with those used for direct electrolysis. The comparison of the yields (second and third columns in Table II) obtained for each condition demonstrates the large advantage of mediated electrolysis over the direct one when the mediator is adequately chosen (compare Table III, fourth column).

Role of the Current Intensity in Mediated Electrolysis. For the sake of comparison with the yields obtained by direct electrolysis, those reported in Tables II and III were obtained using a mediator and an identical current intensity (50 mA). However eq 21 predicts a dependence of the yield in biphenyl with the current density, through the parameter $f = i/i_M^{lim}$, which compares the current density used in electrolysis, to that, i_M^{lim}, which corresponds to the maximum current density achievable for the mediator. There are several difficulties in accurately determining i_M^{lim} in a preparative cell such as that used in this study.[38] Nevertheless eq 21 can be reformulated as in eq 39, where $\alpha = 0.63(k_{dif}/k_2)([M]_o/i_M^{lim})/[Ar'O^-]$ is a constant provided the concentration of

$$(1/y) = 1 + \alpha i \qquad (39)$$

2,6-di-*tert*-butylphenoxide and that of the organic halide are kept constant.[38b] Figure 3a presents a plot of the yield in biphenyl as a function of the current intensity, under the form in eq 39, for the case of 3-chloropyridine ($k_2 = 3.2 \times 10^9$ M^{-1} s^{-1}), with 2,2′-bipyridine (2 or 3 mM) as the mediator, and $[Ar'O^-] = 0.225$ M. From the slope of the straightline ($\alpha = 4 \times 10^{-3}$ mA^{-1}) obtained in Figure 3a, in agreement with the prediction of eq 39, one obtains $(i_M^{lim}/[M]_o) = 6.5$ A mol^{-1} L. Such a value is in excellent agreement with that, 6 ± 1 A mol^{-1} L,[38b] estimated for the cell and stirring conditions used in this study.

Role of the Rate Constant k_2 on the Yield of Biphenyl in Mediated Electrolysis. In addition to the effect of the current density, eq 21 allows to predict the effect of k_2, the rate constant of coupling of the aryl radical with 2,6-di-*tert*-butylphenoxide. Indeed for a constant current density and a constant excess, γ_M, eq 21 can be rewritten as in eq 40, where $\beta = 0.63(i/i_M^{lim})\gamma_M k_{dif}$. Figure

$$(1/y) = 1 + \beta/k_2 \qquad (40)$$

3b presents a plot of the yields in biphenyl as a function of k_2, under the form of eq 40, for the above halides and experimental conditions (i = 50 mA, $[M]_o$ = 0.025 M, $[Ar'O^-]$ = 0.225 M). Although less precise than the plot in Figure 3a because of the accuracy on k_2 determinations, it is seen that the plot in Figure 3b is in good agreement with the prediction of eq 40, as emphasized by the solid line corresponding to $\beta = 6.5 \times 10^8$ M^{-1} s^{-1} which is obtained introducing $k_{dif} = 3 \times 10^{10}$ M^{-1} s^{-1} and $i_M^{lim}/[M]_o$ = 6.5 A mol^{-1} L, determined above, in β's definition.

The validity of eq 21 can be further substantiated by the unifying plot in Figure 3c which contains all the data already used in Figure 3, parts a and b, together with other data involving variations of the current density for 4-chlorobenzonitrile with 4,4′-bipyridine as the mediator. Indeed it is seen that all the experimental yields obtained in mediated electrolysis agree with the theoretical predictions based on eq 21 with $(i_M^{lim}/[M]_o) = 6.5$ A mol^{-1} L.

Conclusion

The present study shows that even when direct electrolysis affords low yields of biphenyl, indirect electrolysis, that is through the relay of a redox mediator, affords reasonable to excellent yields provided an adequate mediator is chosen. The latter must be selected so that the difference between the reduction potentials of the mediator and of the organic halide is the largest possible, to ensure that the σ-aromatic radical is produced sufficiently far from the electrode surface so that its reduction by the electrode is hampered. However we found that increasing this po-

(38) (a) i_M^{lim} is determined by increasing the current intensity i, while monitoring the potential of the working electrode toward that of the reference. When $i \sim i_M^{lim}$ a dramatic variation of the potential is normally observed,[17] indicating that the electrolysis is now performed on the organic halide wave, rather than on the mediator's one as it was for $i < i_M^{lim}$. However, owing to the resistivity of the solution, this transition of potential is smoothed which results in a large uncertainty on i_M^{lim}. (b) Under our conditions we found that $i_M^{lim}/[M]_o \approx (6 \pm 1)$ A mol^{-1} l; note that this number (i.e. $i_M^{lim}/[M]_o$) represents a constant for the cell considered provided the stirring rate, i.e. the diffusion layer thickness, are maintained constant.

tential difference over 300–400 mV provides no net gain on the yields but may be oppositely associated to a decrease of the yield in biphenyl because of the degradation of the mediator due to the corresponding increase in the electrolysis time. In the experimental practice it may be difficult to select a proper mediator because $E°_{ArX}$, the standard reduction potential of the organic halide, is generally not available owing to the chemical irreversibility of the electrochemical wave. Therefore an alternative way to select an adequate mediator is to scan a series of redox mediators in the presence of the organic halide (~0.01 M) by cyclic voltammetry at a scan rate of ca. 0.2 V s^{-1}. We consider that the most suitable mediator is that with the largest cathodic reduction potential, among those whose cyclic voltammograms are only slightly affected by the presence of the organic halide.[39]

Under these conditions the yield in biphenyl is predicted within a reasonable precision by eq 41,[30] where γ_M = [M]/[phenoxide] is the excess of mediator over the phenoxide reacting with the aryl radical, i the current intensity of electrolysis, i_M^{lim} being the limiting current intensity corresponding to the plateau of the mediator electrochemical wave under the electrolysis conditions. Such an equation shows that a low value of k_2 can be "compensated" by using a low value of γ_M and of (i/i_M^{lim}). Thus good yields of biphenyl (>50%) were obtained even for systems where $(k_2/k_{dif}) \sim 0.03$.

$$y = 1/[1 + 0.63\gamma_M(i/i_M^{lim})k_{dif}/k_2] \qquad (41)$$

Although the above study and conclusions were developed in the context of the synthesis of unsymmetrical biphenyls, it can easily be transposed to other situations involving a radical chain reaction, via the reaction of a radical with a substrate or a nucleophile. In such cases, the kinetic framework is identical with that considered in this study. Thus eq 41 will apply provided that k_2 is replaced by the rate constant of the reaction of the radical with the substrate or the nucleophile.

Experimental Section

Starting chemicals 2,6-di-*tert*-butylphenol, aromatic halides, and mediators are all commercially available and were used without further purification. Kieselgel Merck 60, 230–400-mesh ASTM was used for column chromatography. Analytical chromatography, HPLC, was performed with a LKB 2150 chromatograph equiped with UV detector (λ_{max} 254 nm), using a reverse-phase column Lichrosorb RP-18 (5 μm), 4 × 250 mm, eluted with acetonitrile/water mixtures. The ^1H NMR spectra were recorded on a Brücker 250-MHz spectrometer, the ^{13}C NMR spectra on a Brücker 100-MHz spectrometer, in $CDCl_3$ with Me_4Si as internal standard. A Nermag R-10-10B instrument was used for mass spectra with electronic impact at 70 eV. Combustion analyses were performed by the "Service de microanalyse de l'Université Pierre et Marie Curie", Paris.

All the experiments, cyclic voltammetry as well as preparative electrolyses, were run in an undivided cell filled with 80 mL of liquid ammonia, at −38 °C, and potassium bromide 0.1 M was used as supporting electrolyte. The reference electrode was a Ag/Ag^+ (0.01 M) electrode. The working electrode was a gold disk (0.5 mm diameter) for cyclic voltammetry (CV) and a 3.5 cm^2 platinum grid (1024 mesh per cm^2) for preparative-scale electrolysis. A platinum wire worked as auxiliary electrode for CV whereas a sacrifical magnesium anode was used in preparative experiments.

A solid-state amplifier potentiostat with positive feedback resistance compensation was used together with a function generator (Tacussel TPPRT) and a storage oscilloscope (Schlumberger) or an X-Y recorder (Sefram TGM 164). Ohmic drop compensation was required in the cyclic voltammetry experiments since the resistance between reference and working electrode was currently of the order of 100–200 Ω. For kinetics measurements the mediators and substrates were varied from 10^{-3} to 5×10^{-2} M and the scan rates from 10^{-1} to 5×10^{-1} V s^{-1}.

General Procedure for Direct Electrolysis. To 80 mL of a 0.1 M KBr solution in liquid ammonia, kept at −38 °C, were added first 18 mmol of 2,6-di-*tert*-butylphenol and then 18 mmol of potassium *tert*-butoxide. A 0.225 M concentration of phenoxide was then obtained, close to the solubility limit. To this solution was added 3 mmol of aromatic halide. The electrolysis was carried out at −38 °C, at a constant current intensity (50 mA in standard conditions).

General Procedure for Indirect Electrolysis. Same procedure as described above except that 2 mmol of mediator was added prior to phenol addition. When bipyridines and pyridazine were used, 3 extra mmol of potassium *tert*-butoxide were required.

Workup and Extraction of the Biaryls. At the end of the electrolysis, 18 mmol of ammonium bromide were added to the solution to protonate the phenoxide, and ammonia was allowed to evaporate slowly. The crude reaction mixture was then extracted with 250 mL of dichloromethane leaving a solid residue. This solid mineral residue was dissolved in 100 mL of diluted aqueous nitric acid solution. Titration of the free chloride ions ($AgNO_3$, 0.5 M solution) gave a measurement of the amount of starting aromatic chloride consumed during the electrolysis. The dichloromethane extract was pumped off to dryness, and the organic residue was chromatographed, using petroleum ether, dichloromethane, and diethyl ether mixtures as eluent. Purity of the product was checked by HPLC. Each biarylic product has been isolated and fully characterized. However, in some experiments when only the measurement of the yield was needed, the crude reaction mixture was analyzed by HPLC, and the yield was determined by calibration with an internal standard.

Description of the Products. 3-(3′,5′-Di-*tert*-butyl-4′-hydroxyphenyl)pyridine: mp 167.7 °C; ^1H NMR δ 1.50 (s, 18 H), 5.57 (s, 1 phenolic H), 7.31 (ddd, J = 7.9, 4.8, 0.8 Hz, 1 H), 7.38 (s, 2 H), 7.83 (ddd, J = 7.9, 2.4, 1.6 Hz, 1 H), 8.53 (dd, J = 4.8, 1.6 Hz, 1 H), 8.81 (dd, J = 2.4, 0.8 Hz, 1 H). Anal. Calcd for $C_{19}H_{25}NO$: C, 80.52; H, 8.89; N, 4.94. Found: C, 80.03; H, 8.87; N, 4.77.

4-(3′,5′-Di-*tert*-butyl-4′-hydroxyphenyl)pyridine: mp 244 °C; ^1H NMR δ 1.50 (s, 18 H), 5.42 (s, 1 phenolic H), 7.45 (s, 2 H), 7.45 (dd, J = 8, 2 Hz, 2 H), 8.60 (dd, J = 8, 2 Hz, 2 H). Anal. Calcd for $C_{19}H_{25}NO$: C, 80.52; H, 8.89; N, 4.94. Found: C, 79.94; H, 8.83; N, 4.79.

2-Cyano-3′,5′-di-*tert*-butyl-4′-hydroxy-1,1′-biphenyl: mp 172 °C; ^1H NMR δ 1.50 (s, 18 H), 5.44 (s, 1 phenolic H), 7.43 (td, J = 8, 1.5 Hz, 1 H), 7.44 (s, 2 H), 7.59 (dd, J = 8, 1.5 Hz, 1 H), 7.66 (td, J = 8, 1.5 Hz, 1 H), 7.81 (dd, J = 8 Hz, J = 1, 5 Hz, 1 H); ^{13}C NMR δ 30.3 (6 CH_3), 34.5 (2 C), 111.2 (C), 119.1 (C), 125.7 (2 CH), 126.6 (CH), 129.2 (C), 129.8 (CH), 132.5 (CH), 133.8 (CH), 136.3 (2 C), 146.4 (C), 154.5 (C). Anal. Calcd for $C_{21}H_{25}NO$: C, 82.04; H, 8.20; N, 4.56. Found: C, 82.22; H, 8.33; N, 4.44.

3-Cyano-3′,5′-di-*tert*-butyl-4′-hydroxy-1,1′-biphenyl: mp 127 °C; ^1H NMR δ 1.51 (s, 18 H), 5.42 (s, 1 phenolic H), 7.42 (s, 2 H), 7.56 (td, J = 8, 1.5 Hz, 1 H), 7.64 (dd, J = 8, 1.5 Hz, 1 H), 7.84 (dt, J = 8, 1.5 Hz, 1 H), 7.88 (br s, 1 H); ^{13}C NMR δ 30.1 (6 CH_3), 34.3 (2 C), 112.5 (C), 118.9 (C), 123.7 (2 CH), 129.3 (CH), 129.5 (CH), 130.0 (C), 130.2 (CH), 131.0 (CH), 136.6 (2C), 143.2 (C), 154.2 (C). Anal. Calcd for $C_{21}H_{25}NO$: C, 82.04; H, 8.20; N, 4.56. Found: C, 82.17; H, 8.22; N, 4.37.

4-Cyano-3′,5′-di-*tert*-butyl-4′-hydroxy-1,1′-biphenyl: mp 155 °C; ^1H NMR δ 1.50 (s, 18 H), 5.47 (s, 1 phenolic H), 7.47 (s, 2 H), 7.70 and 7.77 (A_2B_2, J_{app} = 9 Hz, 4 H); ^{13}C NMR δ 30.3 (6 CH_3), 34.4 (2 C), 109.8 (C), 119.0 (C), 124.0 (2 CH), 127.3 (2 CH), 130.4 (C), 132.4 (2 CH), 136.8 (2 C), 146.6 (C), 154.6 (C); m/z 307, 292, 264, 84, 57. Anal. Calcd for $C_{21}H_{25}NO$: C, 82.04; H, 8.20;

(39) (a) In cyclic voltammetry the modification of the mediator reduction wave owing to the processes in eqs 13–15 depends on the magnitude of the dimensionless rate constant $\lambda = k_o[ArX](RT/Fv)$ as compared to unity.[18a] Therefore, at −38 °C and for [ArX] ≈ 0.02 M, $\lambda \approx 1$ corresponds to $k_o \approx (5 \times 10^3)v$, where k_o is expressed in M^{-1} s^{-1} and the scan rate, v, in V s^{-1}. Observation of a slight redox catalysis at v = 0.2 V s^{-1} under the above conditions, then corresponds to $k_o \approx 10^3$ M^{-1} s^{-1} which was shown to be an optimal value for preparative conditions.[27d,34] (b) Worthwhile to mention is that the adequate mediators for preparative conditions are those which seem almost ineffective on the basis of cyclic voltammetry.

N, 4.56. Found: C, 81.87; H, 8.23; N, 4.84.

5-Cyano-2-(3′,5′-di-*tert*-butyl-4′-hydroxyphenyl)pyridine: mp 149.5 °C; ^{1}H NMR δ 1.51 (s, 18 H), 5.57 (s, 1 phenolic H), 7.77 (dd, J = 8.4, 0.8 Hz, 1 H), 7.89 (s, 2 H), 7.91 (dd, J = 8.4, 2 Hz, 1 H), 8.87 (dd, J = 2, 0.8 Hz, 1 H); IR 3500, 2950, 2250, 1600, 1350 cm^{-1}. Anal. Calcd for $C_{20}H_{24}N_2O$: C, 77.88; H, 7.82; N, 9.06. Found: C, 78.33; H, 7.89; N, 9.01.

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Registry No. 2-Chloropyridine, 109-09-1; 3-chloropyridine, 626-60-8; 4-chloropyridine, 626-61-9; 2,5-dichloropyridine, 16110-09-1; 2-chloro-5-cyanopyridine, 33252-28-7; 2-chlorobenzonitrile, 873-32-5; 3-chlorobenzonitrile, 766-84-7; 4-chlorobenzonitrile, 623-03-0; 4-chloro(trifluoromethyl)benzene, 98-56-6; 2,4-difluorobromobenzene, 348-57-2; potassium 2,6-di-*tert*-butylphenoxide, 24676-69-5; 2,2′-bipyridine, 366-18-7; 4,4′-bipyridine, 553-26-4; phthalonitrile, 91-15-6; 4-cyanopyridine, 100-48-1; 2-cyanopyridine, 100-70-9; 2,4′-bipyridine, 581-47-5; 3,3′-bipyridine, 581-46-4; 2,3′-bipyridine, 581-50-0; pyridazine, 289-80-5; 3-(3′,5′-di-*tert*-butyl-4′-hyroxyphenyl)pyridine, 129708-80-1; 4-(3′,5′-di-*tert*-butyl-4′-hydroxyphenyl)pyridine, 129708-81-2; 2-cyano-3′,5′-di-*tert*-butyl-4′-hydroxy-1,1′-biphenyl, 118720-23-3; 3-cyano-3′,5′-di-*tert*-butyl-4′-hydroxy-1,1′-biphenyl, 129708-82-3; 4-cyano-3′,5′-di-*tert*-butyl-4′-hydroxy-1,1′-biphenyl, 114460-19-4; 5-cyano-2-(3′,5′-di-*tert*-butyl-4′-hydroxyphenyl)pyridine, 114460-18-3; 2,6-di-*tert*-butylphenol, 128-39-2.

Direct Synthesis of Carboxylic Acids from Organoboranes[1]

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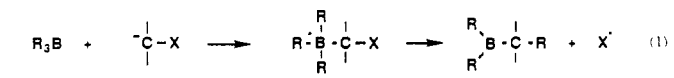
Direct synthesis of carboxylic acids through a two carbon atom homologation from organoboranes has been achieved, by the reaction with the dianion of phenoxyacetic acid. It is now possible to synthesize alkanoic, alkenoic, or alkynoic acids, from the corresponding alkenes, dienes, or enynes, respectively, via hydroboration. The reaction is tolerant of various functional groups present in alkenes, thus giving the corresponding carboxylic acids with chloro, sulfide, ether, acetal, and thioacetal functionalities in good yields.

Introduction

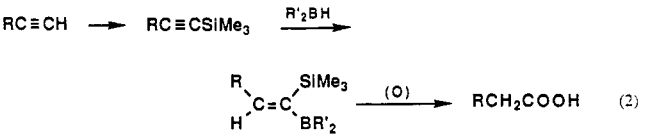
Since the discovery of the hydroboration reaction, the chemistry of organoboranes has been rapidly developed. Many fascinating features have been discovered and applied to the syntheses[2] of a wide variety of organic molecules. The use of organoboranes for carbon–carbon bond formation is well documented.[3] Most of these reactions involve the formation of tetracoordinate organoborates ("ate" complexes) between the electron-deficient boron and a nucleophilic carbon atom.[4] The complex formation is followed by the 1,2-intramolecular migration of an alkyl group from the boron atom to the adjacent carbon atom. These anionic rearrangements occur either with substitution of leaving group (eq 1) or by addition to a carbon–carbon or carbon–heteroatom multiple bond activated by an electrophile.



(1)

A wide variety of functional derivatives like aldehydes, ketones, esters, nitriles, etc.[5,6] have been synthesized, via this methodology. However, there was no successful report of the direct synthesis of carboxylic acids via carbon homologation from organoboranes. In our continued efforts to achieve this feat, we reported[1] the first direct synthesis of carboxylic acids by the reaction of organoboranes with the dianion of phenoxyacetic acid. We now describe, in full, the results of our systematic investigations.

Carboxylic acids are important biological molecules and synthetic materials. Zweifel and Backlund[7] have reported the conversion of alkynes to monosubstituted acetic acids via silylation, hydroboration, and oxidation (eq 2). With



(2)

this method, the alkyl groups of organoboranes are not used as the alkyl source. From the same laboratory, the high yield method illustrated in eq 3 has been published.[8a] Although this is a very useful reaction, it does not offer homologation capability.

Brown et al.[5] and Hooz and Morrison[6] have reported the synthesis of esters by a carbon–carbon homologation se-

(1) Preliminary accounts of this work have appeared: (a) Dhillon, R. S.; Hara, S.; Suzuki, A. Abstracts of the 46th Annual Meeting of the Chemical Society of Japan, Part II, 1982, p 674. (b) Hara, S.; Kishimura, K.; Suzuki, A. *Tetrahedron Lett.* **1978**, 2891.

(2) Brown, H. C. *Hydroboration*; Benjamin: New York, 1962. Second printing with Nobel Lecture, Benjamin/Cummings: Reading, MA, 1980.

(3) For example, Pelter, A.; Smith, K.; Brown, H. C. *Borane Reagents*; Academic Press: London, 1988.

(4) (a) Suzuki, A. *Top. Curr. Chem.* **1983**, *112*, 67. (b) Negishi, E. *J. Organomet. Chem.* **1976**, *108*, 281.

(5) (a) Brown, H. C.; Rogic, M. M.; Rathke, M. W.; Kabalka, G. W. *J. Am. Chem. Soc.* **1968**, *90*, 818. (b) Weill-Raynal, J. *Synthesis* **1976**, 633.

(6) Hooz, J.; Morrison, G. F. *Can. J. Chem.* **1970**, *48*, 868 and references cited therein.

(7) Zweifel, G.; Backlund, S. J. *J. Am. Chem. Soc.* **1977**, *99*, 3184.

(8) (a) Zweifel, G.; Arzoumanian, H. *J. Am. Chem. Soc.* **1967**, *89*, 291. (b) Brown, H. C.; Imai, T. *J. Org. Chem.* **1984**, *49*, 892. (c) Periasamy, M.; Narayana, C.; Anitha, N. *Indian J. Chem.* **1986**, *25B*, 844.

0022-3263/90/1955-6356$02.50/0