ORGANIC
LETTERS

2012
Vol. 14, No. 5
1314–1317

Novel Triarylimidazole Redox Catalysts: Synthesis, Electrochemical Properties, and Applicability to Electrooxidative C–H Activation

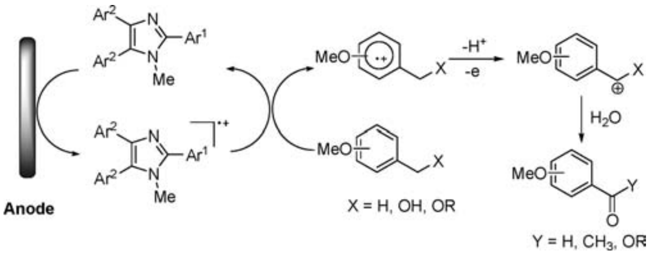
Cheng-chu Zeng,*,† Ni-tao Zhang,† Chiu Marco Lam,‡ and R. Daniel Little*,‡

College of Life Science & Bioengineering, Beijing University of Technology,
Beijing 100124, China, and Department of Chemistry & Biochemistry, University of
California—Santa Barbara, Santa Barbara, California 93106, United States

zengcc@bjut.edu.cn; little@chem.ucsb.edu

Received January 24, 2012

ABSTRACT



A new class of metal-free, easy to synthesize redox catalysts based on a triarylimidazole framework is described. With those synthesized thus far, one can access a potential range of ca. 410 mV. They proved to be useful mediators for the activation of benzylic C–H bonds under mild conditions.

Electroorganic chemistry provides convenient access to the chemistry of radical ions. Its unique ability to effect charge reversal (umpolung) makes it possible to achieve bond constructions that are otherwise very difficult to accomplish.[1] The transformations can be carried out either directly or indirectly. In the former, the redox reaction of interest occurs at the electrode, while the latter uses an electron transfer mediator. When the mediator is oxidized (or reduced) at the electrode, then it can serve as a homogeneous electron transfer agent toward the substrate. Use of a mediator frequently means that the chemistry can be carried out at a potential that is less than that needed for the direct process. Mediators come in many varieties including, for example, metal ions, organometallic complexes, halides, and polycyclic aromatics.[2]

Since Nelson and co-workers first demonstrated that *para*-substituted triarylamines are electrochemically stable,[3] these compounds have found applicability as photoconductors,[4] light emitting devices,[5] and in optical data storage.[6]

---

† Beijing University of Technology.

‡ University of California—Santa Barbara.

(1) For organoelectrochemical synthesis, see reviews: (a) Schäfer, H. J. *C. R. Chimie* **2011**, *14*, 745. (b) Yoshida, J.; Kataoka, K; Horcajada, R.; Nagaki *A. Chem. Rev.* **2008**, *108*, 2265. (c) Duñach, E.; Medeiros, M. J; Olivero, S. *New J. Chem.* **2006**, *30*, 1534. (d) Sperry, J. B.; Wright, D. L. *Chem. Soc. Rev.* **2006**, *35*, 605. (e) Frontana-Uribe, B. A.; Little, R. D.; Ibanez, J. G.; Palma, A.; Vasquez-Medrano, R. *Green Chem.* **2010**, *12*, 2099. (f) Little, R. D.; Moeller, K. D. *Electrochem. Soc. Interface* **2002**, *11*, 36. For recent excellent examples of organoelectrochemical synthesis, see: (g) Sperry, J. B.; Wright, D. L. *J. Am. Chem. Soc.* **2005**, *127*, 8034. (h) Xu, H.; Moeller, K. D. *J. Am. Chem. Soc.* **2008**, *130*, 13542. (i) Tang, F.; Moeller, K. D. *J. Am. Chem. Soc.* **2007**, *129*, 12414. (j) Tajima, T.; Kurihara, H.; Fuchigami, T. *J. Am. Chem. Soc.* **2007**, *129*, 6680. (k) Matsumoto, K.; Fujie, S.; Ueoka, K.; Suga, S.; Yoshida, J.-I. *Angew. Chem., Int. Ed.* **2008**, *47*, 2506. (l) Anderson, L. A.; Redden, A.; Moeller, K. D. *Green. Chem.* **2011**, *13*, 1652. (m) Tang, F.; Moeller, K. D. *Tetrahedron* **2009**, *65*, 10863. (n) Madelaine, C.; Six, Y.; Buriez, O. *Angew. Chem., Int. Ed.* **2007**, *46*, 8046–8049. (o) Ashikari, Y.; Nokami, T.; Yoshida, J. *J. Am. Chem. Soc.* **2011**, *133*, 11840.

(2) For indirect electrolysis, see reviews: (a) Ogibin, Y. N.; Elinson, M. N.; Nikishin, G. I. *Russ. Chem. Rev.* **2009**, *78*, 89. (b) Steckhan, E. *Angew. Chem., Int. Ed. Engl.* **1986**, *28*, 683. (c) Steckhan, E. *Top. Curr. Chem.* **1987**, *142*, 1.

(3) (a) Seo, E. T.; Nelson, R. F.; Fritsch, J. M.; Marcoux, L. S.; Leedy, D. T.; Adams, R. N. *J. Am. Chem. Soc.* **1966**, *88*, 3498. (b) Ambrose, J. F.; Carpenter, L. L.; Nelson, R. F. *J. Electrochem. Soc.* **1975**, *122*, 876.

10.1021/ol300195c © 2012 American Chemical Society

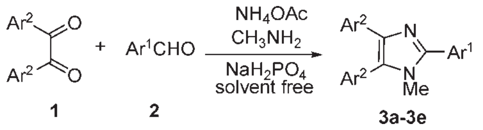
Triarylamines have also served as redox mediators for a host of interesting transformations. For example, Steckhan applied triarylamines to the deprotection of dithioacetals, the oxidation of alcohols and alkyl benzenes, and so on.[7] Fry and co-workers studied the anodic oxidation of alkenes bearing one or more strongly electron-withdrawing substituents.[8] We have also performed the triarylamine-mediated rearrangement of housanes and have used the transformation as the key step in the total synthesis of daucene.[9]

Despite the great success of triarylamines as redox catalysts and in materials research, the synthesis of substituted frameworks can be problematic. Positional isomers are frequently generated, and tedious chromatographic separation may be required.[10] Also, the low solubility of nitro-substituted triarylamines in organic solvents restricts their application.

Given these shortcomings, we sought to develop a new class of organic redox catalysts subject to the conditions that they be (a) easy to synthesize, (b) metal-free, and (c) capable of providing access to a wide range of potentials. In this manuscript we report that systems based on a triarylimidazole framework fulfill these conditions and demonstrate their applicability to the oxidation of methoxy-substituted benzyl alcohols and benzyl ethers.

The synthetic route used to access the mediators is shown in Table 1. Thus, by following a known procedure,[11] a mixture of benzils (**1**), aldehydes (**2**), methylamine, and ammonium acetate in the presence of a catalytic amount of sodium dihydrogen phosphate was heated to 150 °C under solvent-free conditions. The reaction proceeds smoothly to afford the desired triarylimidazoles in 85−92% yield (see Supporting Information).

Table 1. Synthesis and Peak Potentials of Imidazole Mediators



med.	Ar^1	Ar^2	P_{ox}^1 (V)	P_{ox}^2 (V)	P_{ox}^3 (V)	P_{red} (V)
3a	*p*-BrPh	Ph	1.26	1.54	1.80	1.19
3b	*p*-BrPh	*p*-MeO-Ph	1.00	1.27	1.48	0.92
3c	*p*-BrPh	*p*-BrPh	1.30	1.58	1.84	1.17
3d	*p*-MeO-Ph	Ph	1.15	1.32	1.70	0.71
3e	*p*-MeO-Ph	*p*-MeO-Ph	0.89	1.15	1.36	1.05

Cyclic voltammetry was performed first in order to observe the electrochemical behavior of the aryl imidazoles. The cyclic voltammogram (CV) of triarylimidazole **3a** exhibits three oxidation peaks at 1.26, 1.54, and 1.80 V vs Ag/AgCl and one cathodic peak at 1.19 V when 0.1 M $LiClO_4/CH_3CN$ was used as the supporting electrolyte (see Supporting Information (SI)). We were pleased to discover that the first oxidation peak and the reduction peak are quasi-reversible with the current being slightly smaller during the reduction scan. These observations indicate that the initially formed cation radical is stable on the CV time scale. Of additional interest is the fact that following an initial decrease in current during the first three scans, the system settles down and the curve remains quasi-reversible; we have gone to 20 scans without observing a significant change (see SI). This behavior contrasts sharply with that for triphenylamine since its aminium cation radical is known to dimerize thereby leading to a nonreversible redox couple. It is noteworthy that the voltammogram is completely irreversible when the imidazole nitrogen is not alkylated (viz., NH vs NCH_3); this is reasonable since the cation radical ought to be strongly acidic and capable of protonating the starting material.

Similar CV behaviors were also observed for *N*-methyl substituted triarylimidazoles, **3b**−**3e**, and the results are summarized in Table 1. Note that the P_{ox}^1 values can be correlated with the electronegativity of the substituents, viz., the more electron-donating the substituent(s), the easier the substrate is to oxidize. Notice too that these five systems allow access to a potential range of 410 mV; compare, for example, structures **3c** and **3e**.

We envisioned that, similar to substituted triarylamines, our systems might be able to serve as redox catalysts. To explore this hypothesis, the electrochemical behavior of triarylimidazole **3a** in the presence of *p*-methoxy benzyl alcohol (**4a**) and an excess of lutidine was investigated. As shown in Figure 1, the anodic peak current for **3a** increases slightly when an excess of **4a** is present (compare curves **a** and **b**). When lutidine is added, the anodic peak current for **3a** increases dramatically while the cathodic peak current disappears (curve **c**). Since the substrate (**4a**) and base are not oxidizable at the potentials shown in Figure 1 (the peak potential of *p*-methoxy benzyl alcohol and 2,6-lutidine are 1.52 and 1.89 V vs Ag/AgCl, respectively), the enhanced anodic current results from its re-entering the catalytic cycle in the manner illustrated in Scheme 1; it is referred to as a "catalytic current". These observations provide clear evidence that the mediator serves as the hole carrier and

---

(4) Stolka, M.; Yanus, J. F.; Pai, D. M. *J. Phys. Chem.* **1984**, *88*, 4707.

(5) Thomas, B.; David, C.; Muller, M. G.; Klaus, M.; Oskar, N. *Macromol. Rapid Commun.* **2000**, *21*, 583.

(6) Moerner, W. E.; Silence, S. M. *Chem. Rev.* **1994**, *94*, 127.

(7) (a) Brinkhaus, K. G.; Steckhan, E.; Schmidt, W. *Acta Chem. Scand., Ser. B* **1983**, *37*, 499. (b) Schmidt, W.; Steckhan, E. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 673. (c) Schmidt, W.; Steckhan, E. *Angew. Chem., Int. Ed.* **1979**, *18*, 801. (d) Dapperheld, S.; Steckhan, E. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 780. (e) Platen, M.; Steckhan, E. *Chem. Ber.* **1984**, *117*, 1679. (f) Haberl, U.; Steckhan, E.; Blechert, S.; Wiest, O. *Chem.—Eur. J.* **1999**, *5*, 2859.

(8) (a) Wu, X.; Davis, A. P.; Lambert, P. C.; Steffen, L. K.; Toy, O.; Fry, A. J. *Tetrahedron* **2009**, *65*, 2408. (b) Mayers, B. T.; Fry, A. J. *Org. Lett.* **2006**, *8*, 411. (c) Wu, X.; Davis, A. P.; Fry, A. J. *Org. Lett.* **2007**, *9*, 5633.

(9) (a) Park, Y. S.; Wang, S. C.; Tantillo, D. J.; Little, R. D. *J. Org. Chem.* **2007**, *72*, 4351. (b) Gerken, J. B.; Wang, S. C.; Preciado, A. B.; Park, Y. S.; Nishiguchi, G.; Tantillo, D. J.; Little, R. D. *J. Org. Chem.* **2005**, *70*, 4598. (c) Park, Y. S.; Little, R. D. *J. Org. Chem.* **2008**, *73*, 6807.

(10) (a) Wu, X.; Dube, M. A.; Fry, A. J. *Tetrahedron Lett.* **2006**, *47*, 7667. (b) Lartia, R.; Allain, C.; Bordeau, G.; Schmidt, F.; Fiorini-Debuisschert, C.; Charra, F.; Teulade-Fichou, M.-P. *J. Org. Chem.* **2008**, *73*, 1732.

(11) Karimi-Jaberi, Z.; Barekat, M. *Chin. Chem. Lett.* **2010**, *21*, 1183.

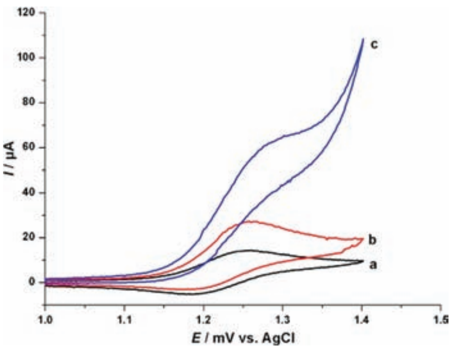


Figure 1. Cyclic voltammogram of triarylimidazole **3a** in the absence and presence of *p*-methoxy benzyl alcohol (**4a**) and lutidine at a glassy carbon working electrode, platinum wire counter and Ag/AgCl reference electrodes, in 0.1 M of $LiClO_4$/CH_3CN, scan rate: 0.1 V/s. (curve a) 1 mmol/L **3a**; (curve b) 1 mmol/L **3a**, 20 mmol/L **4a**; (curve c) 1 mmol/L **3a**, 20 mmol/L **4a**, 50 mmol/L lutidine.

Scheme 1. Catalytic Cycle

$$\text{mediator} = \text{M} \rightleftharpoons \text{M}^{\bullet+}$$

$$\text{M}^{\bullet+} + \text{substrate} \rightleftharpoons \text{M} + (\text{substrate})^{\bullet+}$$

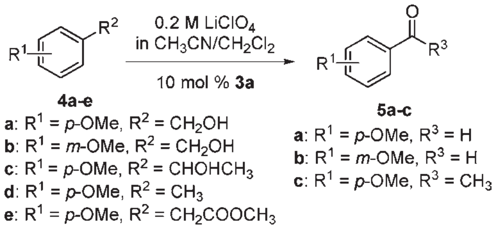
that the neutral form is regenerated following oxidation of the substrate. It also indicates that the added base has a large effect on the catalysis (vide infra).

To further demonstrate the applicability of triarylimidazoles as redox catalysts, preparative scale electrolysis of a series of benzylic alcohols, **4a**–**4e**, was performed using 10 mol % of the mediator **3a** and 2,6-lutidine (5 equiv) as a base in CH_3CN/CH_2Cl_2 (v/v = 4:1) with lithium perchlorate serving as the supporting electrolyte. The transformations were carried out at a controlled potential that matched that of the mediator (i.e., at 1.26 V = $P_{ox}{}^1$ for **3a**), and not that of the substrate (1.52 V vs Ag/AgCl for **4a**). When charge was allowed to pass, a greenish color appeared immediately at the surface of the working electrode (Pt mesh) and diffused into the bulk solution. The addition of substrate led to an immediate color change from green to pink (see SI).

We were delighted to discover that the transformation proceeded smoothly, converting **4a** to *p*-methoxybenzaldehyde (**5a**) in a 65% isolated yield (entry 1, Table 2). To confirm that the outcome was due to electron transfer between the mediator and substrate, a control experiment was performed using identical conditions, but in the absence of the mediator. Only background levels of current were observed, and no reaction took place.

In order to explore the generality and scope of the reaction, other examples were investigated. As shown in Table 2, under the exactly same conditions, *m*-methoxybenzyl alcohol, **4b**, delivered *m*-methoxybenzaldehyde in a 60% yield (entry 2). This example constituted a meaningful challenge for the mediator in that the oxidation potential for the substrate **4b** (1.68 V vs Ag/AgCl) is ca. 420 mV more positive than that of the mediator, **3a** (1.26 V). The chemistry also proved applicable to secondary alcohols. Compound **4c**, for example, was oxidized to the corresponding ketone in a good yield (entry 3). Alkylbenzenes can also be indirectly oxidized; for example, *p*-methoxybenzaldehyde was generated from 1-methoxy-4-methylbenzene, **4d**, under the same reaction conditions albeit in diminished yield (entry 4).

Table 2. Oxidation Potentials of Substrates **4a**–**4e** and Yields of the Oxidation Products Using **3a** as a Redox Mediator



entry	substrate	substrate P_{OX} vs Ag/AgCl (V)	product	yield (%)
1	**4a**	1.52	**5a**	65
2	**4b**	1.68	**5b**	60
3	**4c**	1.66	**5c**	64
4	**4d**	1.53	**5a**	44
5	**4e**	1.75	–	–

It is worth noting that, for an efficient electron transfer to occur, the difference between the oxidation potential of the mediator and substrate should not be "too large". When it is, no observable reaction takes place.[7f,12] This proved to be the case with **4e**; here, the 490 mV difference between the potentials of the mediator **3a** and substrate **4e** proved to be an unsurmountable thermodynamic impasse (entry 5).

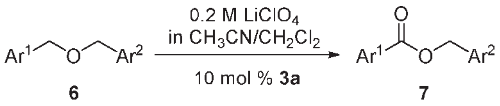
Based upon the results described thus far and the seminal works of Steckhan and co-workers,[7] we propose that the products arise from the oxidative activation of benzylic C–H bonds (note Scheme 2). This hypothesis suggests that the indirect oxidation of unsymmetrically substituted ethers, wherein one of the groups is an electron-rich benzyl unit, ought to lead to an oxocarbenium which can then undergo nucleophilic addition. To explore this hypothesis, *p*-methoxybenzyl ethers **6** were subjected to indirect oxidation in the presence of 0.1 mL of water using 10 mol % of **3a** as a redox catalyst. As shown in Table 3, for all *p*-methoxy substituted substrates **6a**–**6f**, differing by less than 320 mV of the oxidation potentials of **3a**, moderate yields of the corresponding 4-methoxybenzoate (42–55%) were isolated, along with a trace amount of

---

(12) Miranda, J. A.; Wade, C. J.; Little, R. D. *J. Org. Chem.* **2005**, *70*, 8017.

4-methoxybenzaldehyde; good to excellent yields were obtained based on the recovered substrates (column 7 of Table 3). The electron transfer did not occur when **6g** and **6h** were examined, presumably because the difference between their oxidation potential and that of **3a** was too large (> 500 mV).

Table 3. Oxidation Potentials of Benzyl Ether **6** and Yields of Benzoate **7**



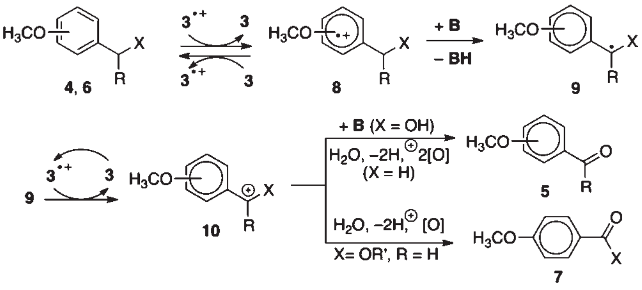
sub.	Ar^1	Ar^2	P_{OX} (V)	prod.	yield (%)[a]	yield (%)[b]
6a	*p*-MeO-Ph	*p*-BrPh	1.54	**7a**	55	87
6b	*p*-MeO-Ph	*p*-ClPh	1.58	**7b**	54	89
6c	*p*-MeO-Ph	Ph	1.54	**7c**	40	92
6d	*p*-MeO-Ph	*m*-BrPh	1.57	**7d**	42	88
6e	*p*-MeO-Ph	*p*-MePh	1.57	**7e**	45	86
6f	*p*-MeO-Ph	*p*-MeO-Ph	1.56	**7f**	50	89
6g	*m*-MeO-Ph	*p*-BrPh	1.74	–	–	–
6h	*m*-MeO-Ph	*m*-BrPh	1.77	–	–	–

[a] Isolated. [b] The yield based on the recovered starting material.

A mechanism that accounts for the formation of both **5** and **7** is shown in Scheme 2. It begins with oxidation of triarylimidazole **3** at the anode. The resulting cation radical then accepts an electron from the substrate, either **4** or **6**, to afford a new cation radical **8** and regenerate the mediator, **3**. Subsequent deprotonation by lutidine, **B**, and oxidation of the resulting benzylic radical **9** leads to **10**. When X = OH, its reaction with lutidine affords **5**, while a sequence involving capture by water, loss of two protons, and oxidation leads to **5** when X = H and benzoate **7** when X = OR′. The prominent influence of lutidine on the voltametric behavior shown in Figure 1 presumably reflects its role in the conversion of **8** to **9**. That transformation shifts the original redox equilibrium toward **9** and facilitates catalyst turnover ($\mathbf{3}^{+\bullet}$ to **3**).

In summary, we have uncovered a new class of organic redox catalysts based on a triarylimidazole framework. The systems are easy to synthesize and are capable of accessing a reasonable range of potentials simply by adjusting the substituent pattern on the aromatic rings. The mediators exhibit quasi-reversibility, and a catalytic current is observed for the oxidation of benzyl alcohol in the presence of lutidine. The preparative scale experiments demonstrate that they can be used to catalytically mediate the oxidation of *p*-methoxybenzyl alcohols and benzyl ethers. We are hopeful that our systems will find additional uses in materials science and in industrial settings. Further demonstration of their applicability to radical cation versions of [4 + 2] and [2 + 2] cycloaddition is currently being developed in our laboratory.

Scheme 2. Plausible Mechanism for the Triarylimidazole Induced Oxidation of **4** and **6**



Acknowledgment. This work was supported by Grants for C.C.Z. from the National Natural Science Foundation of China (No. 20772010), Beijing Natural Science Foundation (No. 7112008), the National Basic Research Program of China (No. 2009CB930200), and the Beijing City Education Committee (KM201010005009). R.D.L. thanks Amgen for an educational donation, the UCSB Academic Senate Council on Research and Instructional Resources, the National Science Foundation PIRE-ECCI Program, and Dr. Timothy Gallagher for discussions of imidazoles.

Supporting Information Available. Experimental details; spectral data for **3b** and **3c**; photo during reaction; CV of **3a**. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.