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Electrooxidative Cyclization of Hydroquinolyl Alcohols, Hydroquinolylamines, and Dimethyl Aminomalonates

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Several hydroquinolyl alcohols and amines were electrochemically oxidized in methanol in the presence of sodium methoxide and potassium iodide to afford the corresponding intramolecular cyclization products. Furthermore, several amino malonates were electrochemically oxidized to yield the corresponding heterocyclic compounds through an intramolecular carbon–carbon bond formation in the presence of sodium cyanide in methanol.

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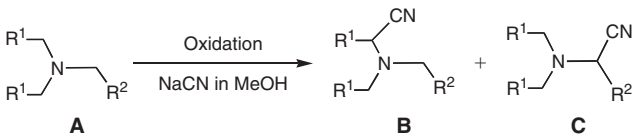
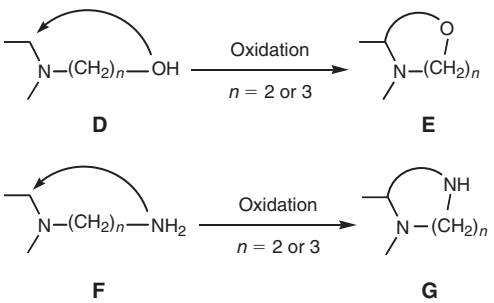
Introduction

An important and unique technique in organic synthesis is the electrochemical process, which can be carried out under very mild reaction conditions without the use of harsh oxidizing or reducing reagents.[1] Our laboratories have employed such electrochemical techniques in the oxidation of organic compounds, in particular, nitrogenous compounds such as amines, enamines, and hydrazones.[2] For tertiary aliphatic amines, it is well known that the α-carbon of the nitrogen atom can be activated under appropriate anodic conditions.[3] Although numerous reports describe the characteristic behaviour of amines in the preparation of organic compounds, studies that examine the electrooxidative intramolecular cyclization of amines are limited.[4] Chiba and coworkers have reported on the electrooxidative cyanation of tertiary aliphatic amine **A**, as illustrated in Scheme 1, in which the α-carbon of amine **A** is attacked by a cyano anion (formed from sodium cyanide, which is employed as the electrolyte) to yield a mixture of the corresponding nitriles **B** and **C**.[5]

From their report, we reasoned that a similar nucleophilic attack on the α-carbon of a nitrogen atom could be achieved using the oxygen atom of a hydroxy group or the nitrogen atom of an amino group. Specifically, amino alcohol **D** and diamine **F** would produce the corresponding intramolecular heterocyclic compounds **E** and **G**, respectively, as illustrated in Scheme 2.



Scheme 1. Electrooxidative cyanation of tertiary aliphatic amines.



Scheme 2. Electrooxidative cyclization of amino alcohols and diamines.

Results and Discussion

Initially, because of the simple synthetic procedures, numerous amino alcohols **D** and diamines **F** were examined. In these cases, the expected corresponding cyclized products **E** and **G** are presumably stable against methanolysis and hydrolysis. Based on the preliminary results, hydroquinolyl and hydroisoquinolyl alcohols (Scheme 3, compounds **1** and **3**, respectively) and amines (Scheme 3, compounds **7** and **10**, respectively) were chosen as the starting substrates. As shown in Scheme 3, amino alcohols **1** and **3** resulted in the formation of an intramoleclar carbon–oxygen bond to afford the expected heterocyclic type-**E** compounds (**2** and **4**, respectively). In contrast, diamines **7** and **10** afforded heterocyclic imino amines **8** and **11**, respectively, instead of the expected type-**G** diamines.

Investigations on the electrooxidation of hydroquinolyl and hydroisoquinolyl alcohols (Scheme 3, compounds **1** and **3**, respectively) and amines (Scheme 3, compounds **7** and **10**, respectively) began with the optimization of the reaction conditions. Using 2-(3,4-dihydroquinolin-1(2*H*)-yl)ethanol **1a** as a model substrate, electrooxidation reactions were performed in the presence of various supporting electrolytes, as listed in Table 1, to yield the corresponding fused-ring heterocyclic compound 2,3a,4,5-tetrahydro-1*H*-oxazolo[3,2-*a*]quinoline **2a**.

In the presence of basic electrolytes, such as NaOAc, NaCN, NaOH, and NaOMe (runs 1–4), the yields of **2a** varied from 25 to 80%. Increased basicity of the electrolyte resulted in high

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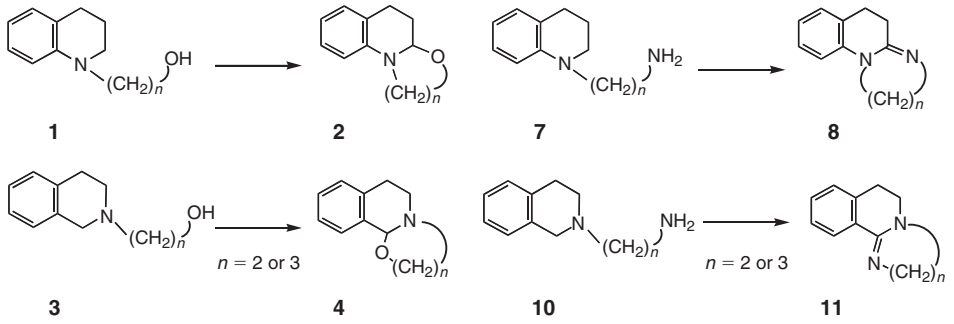
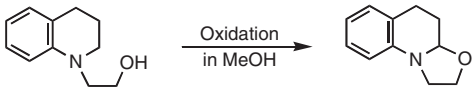


Scheme 3. Electrooxidative cyclization of hydroquinolyl alcohols and diamines.

Table 1. Influence of supporting electrolytes for the cyclization of amino alcohol 1a

Reaction conditions: **1a** (5 mmol), MeOH (40 mL), current passed (2.0 F mol^{-1}), constant current (0.3 A), ~15°C



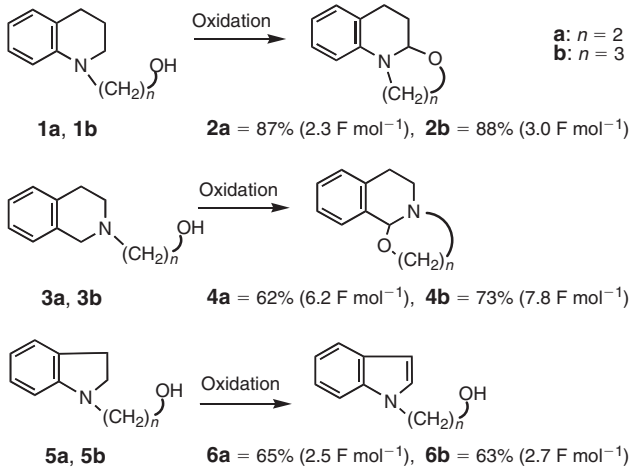
Run	Supporting electrolyte	Amount used [mmol]	Recovery[A] of **1a** [%]	Yield[A] of **2a** [%]
1	NaOAc	10	37	25
2	NaCN	10	14	50
3	NaOH	10	4	70
4	NaOMe	10	17	80
5	$LiClO_4$	10	59	1
6	*p*-$TsONEt_4$	8	15	2
7	KBr	10	23	7
8	KI	10	22	23
9	KI + NaOMe	5 + 5	4	93

[A]Recovery of **1a** and yields of **2a** were determined by GC analysis.

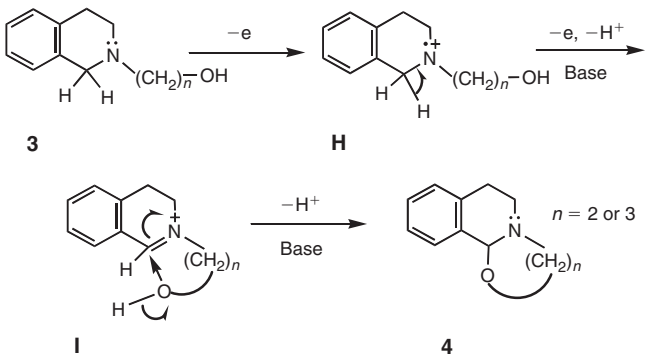
yields of **2a**. In contrast, neutral electrolytes, such as $LiClO_4$, tetraethylammonium *p*-toluenesulfonate, KBr, and KI (runs 5–8), gave very poor yields of **2a**. In such cases, the purification procedures resulted in the recovery of unreacted **1a** and/or the deposit of considerable amounts of dark brownish material on the silica gel column. It is noteworthy that, although the presence of NaOMe or KI afforded **2a** with yields of 80% (run 4) and 23% (run 8), respectively, the concurrent use of both electrolytes resulted in an improved yield of 93% (run 9). Our studies showed that varying the amount of KI, over a range of 2 to 10 mmol, did not affect the yield of **2a** (90 and 91%, respectively), whereas using an excessive amount of NaOMe (20 vs 5 mmol) decreased the yield of **2a** (73 vs 93%, respectively).

Based on the yields listed in Table 1, the corresponding optimal reaction conditions were employed for the electrooxidation of other hydroquinolyl alcohols **1b**, **3a**, and **3b**, as shown in Scheme 4. During the course of the electrooxidation reactions, the composition of the reaction mixture was monitored using gas chromatography (GC) analysis to determine whether the reaction had reached completion.

Significantly higher amounts of electrical current were required for the electrooxidation of aliphatic amines **3** than that for the aromatic amines **1**, for example, substrates **1a** and **1b** required electric currents of 2.3 F mol^{-1} (62 min) and 3.0 F mol^{-1} (81 min), respectively, to form the corresponding



Scheme 4. Electrooxidation of the tetrahydroquinolyl alcohols, tetrahydroisoquinolyl alcohols, and indolinyl alcohols. *Reaction conditions:* substrate (5 mmol), NaOMe (5 mmol), KI (5 mmol), MeOH (40 mL), constant current (0.3 A), ~15°C. Isolated yields are shown.



Scheme 5. Proposed scheme of the oxidative cyclization of quinolyl alcohols.

heterocyclic products in good yields (87 and 88%, for **2a** and **2b**, respectively), whereas substrates **3a** and **3b** required electric currents of 6.2 F mol^{-1} (167 min) and 7.8 F mol^{-1} (210 min), respectively, to form the products in moderate yields (62 and 73% for **4a** and **4b**, respectively). As a note, in the cases of **3a** and **3b**, the oxygen atom on the hydroxy group carried out the nucleophilic attack selectively on the benzylic carbon, which is presumably because of the stable molecular structure of the conjugated intermediate (Scheme 5).

As shown in Scheme 5, the most reasonable pathway for the cyclization of tetrahydroisoquinolyl alcohol **3** to **4** can be described as three reaction steps: (i) loss of one electron from the lone electron pair of the nitrogen atom of substrate **3** to the anode to form cationic radical **H**; (ii) immediate one-electron oxidation and deprotonation to form iminium ion **I**; and then (iii) subsequent nucleophilic attack by the oxygen atom of the hydroxy group. Essentially, substrate **3** loses two protons and two electrons (two-electron oxidation) during the course of the reaction. During these steps, NaOMe would serve as the base in facilitating the deprotonation of both cation radical **H** and the hydroxy group of **I**.

Interestingly, electrooxidations of indolinyl alcohols **5a** and **5b** under similar reaction conditions resulted in the dehydrogenation products **6a** (65%) and **6b** (63%), respectively (Scheme 4), instead of the expected heterocyclic compounds. Apparently, the electrooxidation of **5** favours aromatization over cyclization to afford the corresponding indolyl alcohol **6**,[6] presumably by a reaction pathway as shown in Scheme 6.

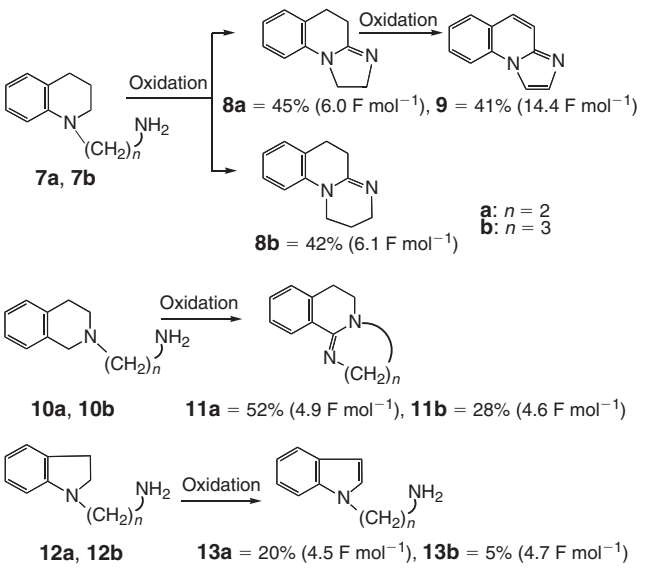
Although the pathway is initially identical to that of **1** and **3**, the formation of iminium ion **K** allows the deprotonation of the benzilic carbon to afford indole derivatives **6**.

In reference to the cyclized product obtained from **1** and **3** by electrooxidation, Schneider and coworkers first reported the formation of **4a** using 3,4-dihydroquinoline as the starting substrate.[7] Consequently, the conversion of **4a** into several useful derivatives were investigated.[8] Lohray and coworkers were able to obtain **2a** in a yield of 56% by reduction of the amide esters.[9]

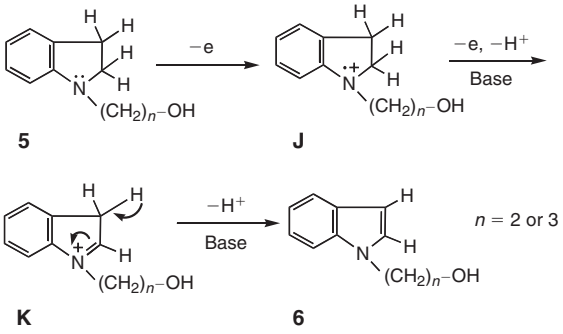
The electrochemical oxidations of hydroquinolyl- and hydroisoquinolyl-amines (**7** and **10**, respectively) were carried out under optimal reaction conditions (NaOMe–KI in MeOH system) that were independently determined using **7b** as a model substrate. Not only were the yields low, but the main products were the unexpected cyclized imino amines **8b**, **9**, and **11**, which can be attributed to the further oxidized products of the first expected compound type-**G** (Scheme 2). In the case of **7a**, after the passage of 6.0 F mol^{-1} of electric current, the corresponding cyclized imino amine **8a** was formed in a yield of 45% (determined by GC analysis). Interestingly, however, after the passage of 14.4 F mol^{-1} of electricity, fused aromatic compound **9** was obtained as the final product, as shown in Scheme 7. While monitoring the conversion of **8a** into **9** using GC analysis, a peak that would correspond to either intermediate **M** or **N** (Scheme 8) was observed. Unfortunately, isolation of the compound was unsuccessful.

In the case of **10a** and **10b**, a selective nucleophilic attack on the carbon at the benzilic position, similar to that of amino alcohol **3**, resulted in the formation of imino amines **11a** (52%) and **11b** (28%), respectively. Except for **8a**, imino amines **8b**, **11a**, and **11b** resisted further oxidation, in spite of excessive amounts of electric current passed, to form the oxidized products such as **9**. In comparison with the electrooxidation process, Finch and coworkers produced an **L**-type product (Scheme 8) in a yield of 27% from **7b** using mercuric acetate as the oxidant.[10] Moreover, Wendelin and coworkers reported on the three-step synthesis of the picrates of **8a** and **8b** using 3,4-dihydroquinoline-2(1*H*)-thioine as the starting substrate.[11] As a note, the electrooxidation of indolinylamines **12a** and **12b** resulted in only very poor yields of dehydrogenation products **13a** (20%) and **13b** (5%) along with a large amount of tar-like material. The proposed mechanism that describes the aromatization of tetrahydroquinolylamine **7a** to **9** through the partially oxidized product **8a** is shown in Scheme 8.

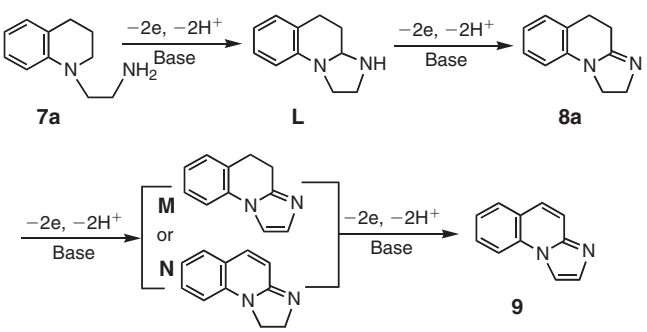
In order to produce **8a**, substrate **7a** would lose four protons and four electrons. In the formation of **9**, however, substrate **7a** must lose a total of eight protons and eight electrons (eight-electron oxidation). Although expected product **8a** could



Scheme 7. Electrooxidation of the tetrahydroquinolylamines, tetrahydroisoquinolylamines, and indolinylamines. *Reaction conditions:* substrate (5 mmol), NaOMe (5 mmol), KI (5 mmol), MeOH (40 mL), constant current (0.3 A), ~15°C. Isolated yields are shown, except for **8a**.



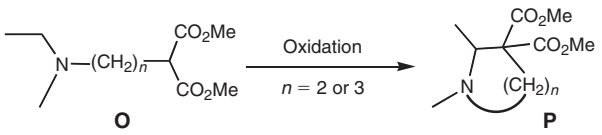
Scheme 6. Proposed scheme of the oxidative aromatization of indolinyl alcohols.



Scheme 8. Proposed scheme of the oxidative aromatization of quinolylamine **7a**.

not be isolated, the reaction mechanism for formation of the **L**-type compound from substrate **7a** should resemble that of the amino alcohols. In every step, NaOMe would serve as the base in facilitating the deprotonation.

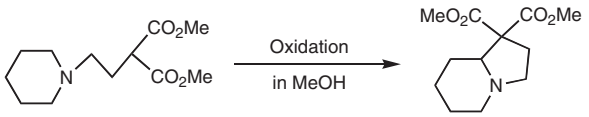
Furthermore, we have also investigated the electrooxidation of dimethyl aminomalonates **O**. As shown in Scheme 9, the electrooxidation resulted in a carbon–carbon bond formation between the carbon at the α-position of the nitrogen atom and the active methine carbon of the dimethyl malonate moiety to give the intramolecular cyclization product **P**.[12]



Scheme 9. Electrooxidative cyclization of aminomalonates.

Table 2. Influence of supporting electrolytes for the cyclization of aminomalonate 14c

Reaction conditions: **14c** (5 mmol), MeOH (40 mL), constant current (0.3 A), current passed (2.6 F mol^{-1}), ∼15°C



Run	Supporting electrolyte	Amount used [mmol]	Yield[A] of **15c** [%]
1	NaOH	20	4
2	*p*-TsONEt$_4$	10	4
3	KBr	20	5
4	KI	20	5
5	LiClO$_4$	20	6
6	NaOAc	20	10
7	NaOMe	20	10
8	NaOMe	5	25
9	NaCN	20	63

[A]Yields of **15c** were determined by GC analysis.

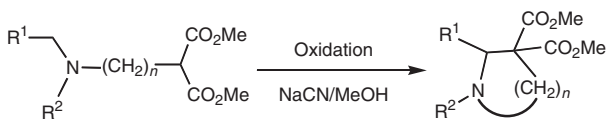
To optimize the reaction conditions of the cyclization of **O** to **P**, electrooxidations were performed using dimethyl 2-(piperidin-1-yl)ethylmalonate **14c** as the model substrate to yield the corresponding fused-ring heterocyclic dimethyl hexahydroindolizine-1,1-dicarboxylate **15c**. At first, the electrooxidations were examined in the presence of various supporting electrolytes, as listed in Table 2. In the presence of NaOH (run 1) or neutral salts (runs 2–5), the yields were less than 10%. The yield improved slightly using an equimolar amount of NaOMe (run 8). Unfortunately, the concurrent use of NaOMe and KI, which gave favorable results earlier, did not function as a suitable electrolyte system for the cyclization of compound **14c**. In the cases of low yields of **15c** (runs 1–8), approximately 50% of **14c** was recovered unchanged and/or a considerable amount of tar-like material remained after evaporation of the reaction mixture. Surprisingly, the use of NaCN as the supporting electrolyte resulted in the highest yield (63%, run 9). Because the amount of NaCN, over the wide range of 5 to 40 mmol, did not affect the yield of **15c** (63 and 61%, respectively), it can be assumed that NaCN does not directly relate to this cyclization mechanism. Moreover, during the first half of the electrooxidation, the yield of **15c** increased in proportion to the current passed (18%, 0.5 F mol^{-1}; 36%, 1.0 F mol^{-1}; 52%, 1.5 F mol^{-1}); during the final stages of the electrooxidation, however, the rate of increase gradually declined (58%, 2.0 F mol^{-1}). The highest yield of 63% was obtained after passage of ∼2.6 F mol^{-1} (70 min), at which point almost all of **14c** was oxidized. Cyanation adducts (type-**B** and/or **C** compounds in Scheme 1) were not detected during the electrooxidation of **14c**.[5]

The results of electrooxidations of aminomalonates **14a**–**g**, using the optimal reaction conditions as described above, are shown in Table 3. All of the substrates were consumed after passing 2.5 to 3.0 F mol^{-1} of electric current. As listed in Table 3, the corresponding cyclization product can be obtained, not only from five- and six-membered cyclic aminomalonates **14a**–**e**, but also from non-cyclic aminomalonates **14f** and **14g**. The products were isolated as a slightly yellow viscous oil with yields of 45% (**15a**) to 71% (**15b**).

Although most of the products obtained in this reaction are new compounds, similar skeletons are widely found in plants,[13] and hence have attracted widespread attention as targets of organic synthesis.[14] Among such syntheses, two

Table 3. Electrooxidation of the dimethyl aminomalonates

Reaction conditions: **14** (5 mmol), NaCN (10 mmol), MeOH (40 mL), constant current (0.3 A), ∼15°C

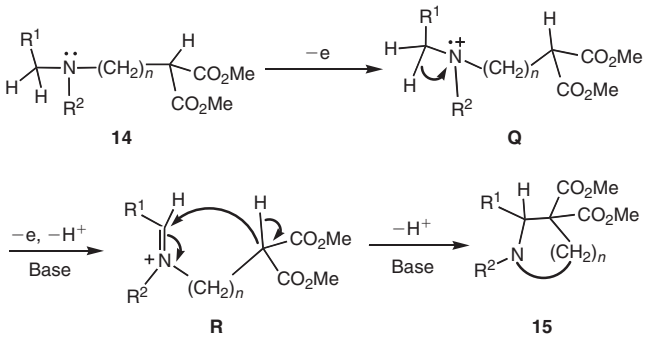


Substrate **14**	R^1	R^2	*n*	Current passed [F mol^{-1}]	Yield[A] of **15** [%]
14a	–(CH$_2$)$_3$–		2	2.6	45 (53)
14b	–(CH$_2$)$_3$–		3	2.5	71 (73)
14c	–(CH$_2$)$_4$–		2	2.6	59 (63)
14d	–(CH$_2$)$_4$–		3	2.5	53 (62)
14e	–CH$_2$CH(CH$_3$)CH$_2$CH$_2$–		2	2.8	68 (72)
14f	Et	Pr^n	2	2.7	61 (71)
14g	Pr^n	Bu^n	2	3.0	60 (66)

[A]Isolated yields based on **14**. Values in parentheses were determined by GC analysis.

notable examples include the iminium salt from α-amino acid decarboxylation[15] or the anodically prepared carbamate;[16] unfortunately, their syntheses require multi-step reactions. A reaction pathway of this cyclization is proposed in Scheme 10. Up to the formation of iminium ion **R**, the pathway for both amino alcohol and diamine should be identical. A nucleophilic attack by an active methine carbon of a malonate moiety in the activated **R** would produce cyclization product **15** under basic conditions.

Although the role of NaCN remains unclear, in this reaction, NaCN may serve as a suitable base and facilitate the deprotonation of both cation radical **Q** and the methine carbon of **R**. Essentially, substrate **14** loses two protons and two electrons (two-electron oxidation) during the course of the reaction.



Scheme 10. Proposed scheme of the oxidative cyclization of aminomalonates.

Conclusions

In conclusion, our studies have demonstrated the electrooxidation of hydroquinolyl alcohols, hydroquinolylamines, and amino malonates toward the synthesis of several heterocyclic compounds. Although the actual yields depend upon the structure of the substrates, our methodology is advantageous as follows: (i) the absence of oxidants and/or special reagents; (ii) very mild reaction conditions; (iii) availability of the substrates; and (iv) simple, one-pot procedure.

Experimental

All electrooxidation products were identified from their physical and/or spectroscopic data. Hydroquinolyl alcohols and amines were synthesized by typical *N*-alkylation of hydroquinoline with the corresponding chloro alcohol or chloro amine, respectively. The aminomalonates were prepared by a three-step reaction from the corresponding secondary amine: (i) *N*-alkylation of the amine by chloro alcohol to yield amino alcohol; (ii) bromination of the amino alcohol by concentrated hydrobromic acid in toluene to yield the hydrobromide salt of the bromo amine; and (iii) reaction between the salt and dimethyl malonate in MeOH in the presence of NaOMe to give the dimethyl aminomalonate.[17]

Preparative-scale electrooxidations were carried out in a tall 50 mL beaker equipped with a fine frit cup (porosity ∼100 μm) as the cathode compartment with a nickel coil (diameter 0.8 mm, length 220 mm) as the cathode, and an insert cylindrical platinum net (diameter 32 mm, height 35 mm, 55 mesh) as the anode. Amino alcohols **1**, **3**, **5** (5 mmol) and diamines **7**, **10**, **12** (5 mmol) were electrooxidized in MeOH (40 mL) in the presence of KI (0.83 g, 5 mmol) and NaOMe (5 mmol). In the case of the dimethyl aminomalonates **14**, the substrate (5 mmol) was electrooxidized in MeOH (40 mL) that contained NaCN (0.49 g, 10 mmol). In all cases, the electrooxidation was carried out using a constant current of 0.3 A. During the course of the electrooxidation, the anolyte was magnetically stirred and the temperature of the cell was maintained at ∼15°C. Upon completion of the electrooxidation, the reaction mixture was treated using a three-fold increase in the amount of anolyte. The combined reaction mixture was concentrated under vacuum at ∼45°C to remove most of the methanol, and then treated with water (∼20 mL). The resulting oily layer was extracted using ether (3 × 60 mL), the ether layers were combined, washed with aqueous sodium thiosulfate solution (in the case of **15**, brine), and dried over magnesium sulfate. Following removal of the solvent, the residue was purified by silica gel column chromatography (diameter 25 mm, length 500 mm, diethyl ether as the elution solvent; in the case of **15a**, 7:3 ether/MeOH was used) or by distillation under reduced pressure.

*2,3a,4,5-Tetrahydro-1*H*-oxazolo[3,2-*a*]quinoline* ***2a***

Bp 108–110°C (2 mmHg). ν_{max} (neat)/cm^{-1} 2939, 2864, 1605, 1504, 1460, 1346, 1312, 1061, 1053, 1001, 746. δ_H ($CDCl_3$) 1.4–1.9 (m, 1H, CH_2), 2.1–2.4 (m, 1H, CH_2), 2.6–2.9 (m, 2H, CH_2), 3.2–3.6 (m, 2H, CH_2), 3.8–4.3 (m, 2H, CH_2), 4.7–4.9 (m, 1H, CH), 6.4–6.8 (m, 2H, ArH), 6.9–7.3 (m, 2H, ArH). δ_C ($CDCl_3$) 24.76 (CH_2), 26.18 (CH_2), 47.36 (CH_2), 65.68 (CH_2), 87.96 (CH), 111.90 (CH), 116.99 (CH), 122.33 (C), 127.37 (CH), 128.07 (CH), 143.87 (C). *m/z* 175 (M^+, 87%), 174 (100), 145 (26), 144 (25), 132 (21), 130 (17), 118 (14), 117 (27), 91 (18), 77 (13). Found: 175.0993 [M^+]. Calc. for $C_{11}H_{13}NO$: 175.0997.

*1,2,3,4a,5,6-Hexahydro[1,3]oxazino[3,2-*a*]quinoline* ***2b***

Bp 110–112°C (1.5 mmHg). Mp 39–41°C (recrystallized from EtOH). ν_{max} (neat)/cm^{-1} 2953, 2845, 1603, 1495, 1458, 1315, 1263, 1171, 1076, 1061, 748. δ_H ($CDCl_3$) 1.2–1.5 (m, 1H, CH_2), 1.7–2.1 (m, 3H, CH_2), 2.4–3.4 (m, 3H, CH_2), 3.7–4.3 (m, 3H, CH_2), 4.6–4.8 (m, 1H, CH), 6.4–6.8 (m, 2H, ArH), 6.9–7.3 (m, 2H, ArH). δ_C ($CDCl_3$) 23.67 (CH_2), 24.43 (CH_2), 28.38 (CH_2), 46.91 (CH_2), 67.84 (CH_2), 85.96 (CH), 112.84 (CH), 118.13 (CH), 125.62 (C), 127.09 (CH), 128.68 (CH), 143.91 (C). *m/z* 189 (M^+, 100%), 188 (50), 170 (13), 158 (26), 146 (29), 132 (36), 131 (72), 130 (52), 91 (13), 77 (11). Found: 189.1179 [M^+]. Calc. for $C_{12}H_{15}NO$: 189.1154.

*3,5,6,10b-Tetrahydro-2*H*-oxazolo[2,3-*a*]isoquinoline* ***4a***

Mp 50–52°C (recrystallized from EtOH). ν_{max} (neat)/cm^{-1} 1464, 1394, 1290, 1078, 1057, 1016, 991, 889, 777, 746. δ_H ($CDCl_3$) 2.5–4.0 (m, 8H, CH_2), 5.19 (s, 1H, CH), 6.8–7.5 (m, 4H, ArH). δ_C ($CDCl_3$) 29.73 (CH_2), 45.65 (CH_2), 54.73 (CH_2), 62.18 (CH_2), 90.40 (CH), 126.28 (CH), 128.07 (CH), 128.23 (CH), 128.84 (CH), 132.14 (C), 134.95 (C). *m/z* 175 (M^+, 69%), 174 (100), 145 (53), 130 (25), 117 (53), 115 (26), 103 (15), 91 (21), 77 (17), 56 (16). Found: 175.0973 [M^+]. Calc. for $C_{11}H_{13}NO$: 175.0997.

*2,3,4,6,7,11b-Hexahydro[1,3]oxazino-[2,3-*a*]isoquinoline* ***4b***

Bp 114–116°C (1.5 mmHg). ν_{max} (neat)/cm^{-1} 2947, 2839, 1464, 1393, 1371, 1294, 1142, 1086, 964, 885, 745. δ_H ($CDCl_3$) 1.2–1.5 (m, 1H, CH_2), 1.8–3.4 (m, 7H, CH_2), 3.7–4.3 (m, 2H, CH_2), 4.87 (s, 1H, CH), 7.0–7.4 (m, 4H, ArH). δ_C ($CDCl_3$) 22.97 (CH_2), 29.08 (CH_2), 46.22 (CH_2), 53.22 (CH_2), 68.33 (CH_2), 89.95 (CH), 125.95 (CH), 127.29 (CH), 127.78 (CH), 128.31 (CH),

132.20 (C), 134.83 (C). *m/z* 189 (M^+, 38%), 188 (77), 158 (37), 146 (100), 145 (31), 133 (46), 132 (66), 131 (42), 130 (35), 104 (79). Found: 189.1174 [M^+]. Calc. for $C_{12}H_{15}NO$: 189.1154.

*2-(1*H*-Indol-1-yl)ethanol* ***6a***

Bp 141–142°C (2.5 mmHg). ν_{max} (neat)/cm^{-1} 3380, 1510, 1481, 1464, 1362, 1337, 1315, 1063, 764, 743. δ_H ($CDCl_3$) 1.94 (br s, 1H, OH), 3.69 (t, *J* 7, 2H, CH_2), 4.07 (t, *J* 7, 2H, CH_2), 6.4–6.5 (m, 1H, ArH), 6.9–7.3 (m, 4H, ArH), 7.5–7.7 (m, 1H, ArH). δ_C ($CDCl_3$) 48.54 (CH_2), 61.61 (CH_2), 101.31 (CH), 109.34 (CH), 119.51 (CH), 120.98 (CH), 121.59 (CH), 128.35 (CH), 128.68 (C), 136.09 (C). *m/z* 161 (M^+, 38%), 131 (10), 130 (100), 103 (7), 77 (8). Found: 161.0841 [M^+]. Calc. for $C_{10}H_{11}NO$: 161.0841.

*3-(1*H*-Indol-1-yl)propan-1-ol* ***6b***

Bp 148–150°C (2 mmHg). ν_{max} (neat)/cm^{-1} 3380, 2941, 1510, 1485, 1464, 1337, 1315, 1065, 1015, 743. δ_H ($CDCl_3$) 1.87 (quin., *J* 7, 2H, CH_2), 2.7 (br s, 1H, OH), 3.38 (t, *J* 7, 2H, CH_2), 4.09 (t, *J* 7, 2H), 6.6–6.7 (m, 1H, ArH), 7.1–7.6 (m, 4H, ArH), 7.8–7.9 (m, 1H, ArH). δ_C ($CDCl_3$) 32.58 (CH_2), 42.51 (CH_2), 59.29 (CH_2), 101.07 (CH), 109.34 (CH), 119.23 (CH), 120.90 (CH), 121.39 (CH), 127.90 (CH), 128.56 (C), 135.97 (C). *m/z* 175 (M^+, 45%), 131 (36), 130 (100), 117 (7), 103 (7), 89 (7), 77 (8). Found: 175.0993 [M^+]. Calc. for $C_{11}H_{13}NO$: 175.0997.

*2,3,5,6-Tetrahydro-1*H*-pyrimido[1,2-*a*]quinoline* ***8b***

Bp 136–138°C (1.5 mmHg). ν_{max} (neat)/cm^{-1} 2941, 2854, 1655, 1649, 1637, 1456, 1392, 1313, 1265, 752. δ_H ($CDCl_3$) 2.02 (quin., *J* 6, 2H, CH_2), 2.4–3.0 (m, 4H, CH_2), 3.2–3.7 (m, 4H, CH_2), 6.6–7.4 (m, 4H, ArH). δ_C ($CDCl_3$) 21.91 (CH_2), 26.18 (CH_2), 32.33 (CH_2), 43.49 (CH_2), 43.86 (CH_2), 112.23 (CH), 120.94 (CH), 126.48 (C), 127.29 (CH), 127.70 (CH), 141.55 (C), 153.15 (C). *m/z* 186 (M^+, 93%), 185 (100), 158 (17), 130 (41), 118 (8), 103 (8), 91 (8), 77 (10), 65 (5), 51 (4). Found: 186.1191 [M^+]. Calc. for $C_{12}H_{14}N_2$: 186.1157.

*Imidazo[1,2-*a*]quinoline* ***9***

Bp 156–158°C (2 mmHg). ν_{max} (neat)/cm^{-1} 1612, 1535, 1447, 1420, 1317, 806, 752. δ_H ($CDCl_3$) 6.8–7.5 (m, 4H, ArH), 7.6–8.0 (m, 4H, ArH). δ_C ($CDCl_3$) 110.96 (CH), 115.00 (CH), 115.53 (CH), 117.23 (CH), 123.26 (C), 124.57 (CH), 125.83 (C), 128.60 (CH), 128.96 (CH), 132.55 (CH), 143.91 (C). *m/z* 168 (M^+, 100%), 140 (7), 128 (14), 114 (11), 101 (4), 84 (9), 75 (3), 63 (3). Found: 168.0666 [M^+]. Calc. for $C_{11}H_8N_2$: 168.0687.

*2,3,5,6-Tetrahydroimidazo[2,1-*a*]isoquinoline* ***11a***

Bp 127–129°C (2 mmHg). ν_{max} (neat)/cm^{-1} 2945, 2845, 1616, 1461, 1410, 1339, 1283, 1258, 1016, 739. δ_H ($CDCl_3$) 2.6–3.5 (m, 6H, CH_2), 3.7–4.0 (m, 2H, CH_2), 7.0–8.2 (m, 4H, ArH). δ_C ($CDCl_3$) 28.95 (CH_2), 45.49 (CH_2), 52.65 (CH_2), 53.14 (CH_2), 126.19 (C), 126.56 (CH), 126.68 (CH), 127.86 (CH), 130.67 (CH), 136.98 (C), 162.39 (C). *m/z* 172 (M^+, 59%), 171 (100), 169 (7), 156 (5), 144 (10), 130 (4), 115 (8), 89 (3), 77 (4), 56 (4). Found: 172.1003 [M^+]. Calc. for $C_{11}H_{12}N_2$: 172.1000.

*3,4,6,7-Tetrahydro-2*H*-pyrimido[2,1-*a*]isoquinoline* ***11b***

Bp 140–142°C (2 mmHg). ν_{max} (neat)/cm^{-1} 2934, 2843, 1622, 1601, 1576, 1456, 1418, 1366, 1308, 741. δ_H ($CDCl_3$) 1.93 (quin., *J* 6, 2H, CH_2), 2.7–3.0 (m, 2H, CH_2), 3.1 –3.4 (m, 4H, CH_2), 3.5–3.8 (m, 2H, CH_2), 7.0–8.2 (m, 4H, ArH). δ_C ($CDCl_3$) 22.07 (CH_2), 28.95 (CH_2), 44.79 (CH_2), 48.13 (CH_2), 48.62 (CH_2), 126.19 (CH), 126.52 (CH), 127.21 (CH), 129.41 (CH), 131.28 (C), 135.97 (C), 151.89 (C). *m/z* 186 (M^+, 95%), 185 (100), 171 (12), 158 (11), 157 (21), 131 (23), 130 (24), 116 (8), 103 (10), 77 (8). Calc. for $C_{12}H_{14}N_2$: 186.1157. Found: 186.1155 (M^+).

*2-(1*H*-Indol-1-yl)ethanamine* ***13a***

ν_{max} (neat)/cm^{-1} 2936, 1670, 1609, 1510, 1464, 1398, 1313, 1084, 1013, 741. δ_H ($CDCl_3$) 1.28 (br s, 2H, NH_2), 2.93 (t, *J* 7, 2H, CH_2), 4.01 (t, *J* 7, 2H, CH_2), 6.3–6.6 (m, 1H, ArH), 6.8–7.4 (m, 4H, ArH), 7.5–7.8 (m, 1H, ArH). δ_C ($CDCl_3$) 41.94 (CH_2), 49.39 (CH_2), 101.23 (CH), 109.29 (CH), 119.35 (CH), 120.94 (CH), 121.47 (CH), 127.99 (CH), 128.68 (C), 136.05 (C). *m/z* 160 (M^+, 43%), 132 (9), 131 (63), 130 (100), 117 (5), 103 (10), 77 (12), 63 (3), 51 (3), 30 (13). Calc. for $C_{10}H_{12}N_2$: 160.1000. Found: 160.0974 [M^+].

*3-(1*H*-Indol-1-yl)propan-1-amine* ***13b***

ν_{max} (neat)/cm^{-1} 2934, 2870, 1670, 1609, 1508, 1464, 1313, 1244, 1186, 743. δ_H ($CDCl_3$) 1.55 (br s, 2H, NH_2), 1.91 (quin., *J* 7, 2H, CH_2), 2.65 (t, *J* 7, 2H, CH_2), 4.16 (t, *J* 7, 2H, CH_2), 6.4–6.6 (m, 1H, ArH), 6.8–7.4 (m, 4H, ArH), 7.5–7.8 (m, 1H, ArH). δ_C ($CDCl_3$) 33.68 (CH_2), 39.34 (CH_2), 43.78 (CH_2), 101.12 (CH), 109.29 (CH), 119.23 (CH), 120.94 (CH), 121.39 (CH), 127.70 (CH), 128.64 (C), 136.01 (C). *m/z* 174 (M^+, 57%), 156 (20), 144 (15), 131 (100), 130 (65), 117 (26), 89 (11), 77 (12), 63 (5), 30 (20). Found: 174.1162 [M^+]. Calc. for $C_{11}H_{14}N_2$: 174.1157.

Dimethyl Tetrahydropyrrolizine-1,1-dicarboxylate ***15a***

ν_{max} (neat)/cm^{-1} 2955, 2874, 1734, 1456, 1437, 1265, 1225, 1198, 1134, 1076. δ_H ($CDCl_3$) 1.1–2.7 (m, 9H, CH, $CH_2 \times 4$), 2.8–3.2 (m, 2H, CH_2), 3.73 (s, 3H, CH_3), 3.76 (s, 3H, CH_3). δ_C ($CDCl_3$) 23.62 (CH_2), 26.35 (CH_2), 28.71 (CH_2), 32.70 (CH_2), 52.37 (CH_3), 52.82 (CH_3), 55.50 (CH_2), 63.65 (C), 68.70 (CH), 170.66 (C=O), 171.64 (C=O). *m/z* 227 (M^+, 41%), 196 (44), 168 ($M^+ - CO_2Me$, 23), 140 (45), 127 (22), 108 (19), 84 (40), 83 (100), 55 (47), 42 (23). Found: 227.1140 [M^+]. Calc. for $C_{11}H_{17}NO_4$: 227.1158.

Dimethyl Hexahydroindolizine-8,8-dicarboxylate ***15b***

ν_{max} (neat)/cm^{-1} 2953, 2789, 1732, 1435, 1304, 1261, 1217, 1115, 1080, 1000. δ_H ($CDCl_3$) 1.4–2.8 (m, 11H, CH, $CH_2 \times 5$), 2.9–3.3 (m, 2H, CH_2), 3.70 (s, 3H, CH_3), 3.75 (s, 3H, CH_3). δ_C ($CDCl_3$) 21.18 (CH_2), 22.60 (CH_2), 26.18 (CH_2), 32.45 (CH_2), 51.88 (CH_3), 52.29 (CH_3), 53.26 (CH_2), 55.10 (CH_2), 57.01 (C), 67.76 (CH), 169.97 (C=O), 171.56 (C=O). *m/z* 241 (M^+, 42%), 210 (39), 182 ($M^+ - CO_2Me$, 55), 122 (28), 97 (100), 96 (75), 83 (40), 82 (36), 69 (58), 41 (25). Found: 241.1313 [M^+]. Calc. for $C_{12}H_{19}NO_4$: 241.1314.

Dimethyl Hexahydroindolizine-1,1-dicarboxylate ***15c***

Mp 56–58°C. ν_{max} (KBr)/cm^{-1} 2924, 2793, 1730, 1441, 1271, 1248, 1150, 1117, 1088, 1003. δ_H ($CDCl_3$) 0.9–2.8 (m, 11H, CH, $CH_2 \times 5$), 3.0–3.3 (m, 2H, CH_2), 3.73 (s, 3H, CH_3), 3.74 (s, 3H, CH_3). δ_C ($CDCl_3$) 24.31 (CH_2), 24.84 (CH_2), 28.02 (CH_2), 31.19 (CH_2), 52.33 (CH_3), 52.45 (CH_3), 53.39 (CH_2), 53.83 (CH_2), 61.94 (C), 69.31 (CH), 170.95 (C=O), 172.04 (C=O). *m/z* 241 (M^+, 47%), 210 (55), 182 ($M^+ - CO_2Me$, 93), 150 (24), 122 (27), 98 (41), 97 (100), 69 (38), 59 (28), 41 (23). Found: 241.1305 [M^+]. Calc. for $C_{12}H_{19}NO_4$: 241.1314.

Dimethyl Hexahydroquinolizine-1,1-dicarboxylate ***15d***

ν_{max} (neat)/cm^{-1} 2937, 2858, 1732, 1445, 1304, 1257, 1150, 1108, 1036, 997. δ_H ($CDCl_3$) 1.1–2.6 (m, 13H, CH, $CH_2 \times 6$), 2.8–3.1 (m, 2H, CH_2), 3.71 (s, 3H, CH_3), 3.74 (s, 3H, CH_3). δ_C ($CDCl_3$) 22.32 (CH_2), 24.76 (CH_2), 25.13 (CH_2), 26.92 (CH_2), 32.21 (CH_2), 51.96 (CH_3), 52.57 (CH_3), 55.58 (CH_2), 57.70 (CH_2), 58.35 (C), 66.09 (CH), 170.29 (C=O), 171.80 (C=O). *m*/*z* 255 (M^+, 30%), 224 (29), 196 ($M^+ - CO_2Me$, 32), 124 (26), 111 (79), 97 (38), 96 (25), 83 (100), 55 (21), 41 (14). Found: 255.1505 [M^+]. Calc. for $C_{13}H_{21}NO_4$: 255.1471.

Dimethyl 7-Methylhexahydroindolizine-1,1-dicarboxylate ***15e***

ν_{max} (neat)/cm^{-1} 2953, 2795, 1734, 1456, 1437, 1273, 1233, 1200, 1150, 1084. δ_H ($CDCl_3$) 0.95 (d, *J* 7, 3H, CH_3), 1.0–2.8 (m, 10H, CH × 2, $CH_2 \times 4$), 3.0–3.3 (m, 2H, CH_2), 3.73 (s, 3H, CH_3), 3.74 (s, 3H, CH_3). δ_C ($CDCl_3$) 21.99 (CH_3), 31.23 (CH), 31.60 (CH_2), 33.51 (CH_2), 36.32 (CH_2), 52.33 (CH_3), 52.45 (CH_3), 52.98 (CH_2), 53.10 (CH_2), 61.77 (C), 69.18 (CH), 170.91 (C=O), 172.00 (C=O). *m*/*z* 255 (M^+, 26%), 224 (31), 196 ($M^+ - CO_2Me$, 60), 164 (15), 112 (81), 111 (100), 96 (23), 69 (25), 59 (21), 41 (19). Found: 255.1441 [M^+]. Calc. for $C_{13}H_{21}NO_4$: 255.1471.

Dimethyl 2-Ethyl-1-propylpyrrolidine-3,3-dicarboxylate ***15f***

Bp 108–110 (1.5 mmHg). ν_{max} (neat)/cm^{-1} 2959, 2876, 1736, 1456, 1435, 1267, 1232, 1194, 1157, 1072. δ_H ($CDCl_3$) 0.89 (t, *J* 7, 3H, CH_3), 0.92 (t, *J* 7, 3H, CH_3), 1.2–1.7 (m, 3H, CH, CH_2), 2.0–2.8 (m, 6H, CH_2), 3.0–3.4 (m, 2H, CH_2), 3.71 (s, 3H, CH_3), 3.74 (s, 3H, CH_3). δ_C ($CDCl_3$) 10.91 (CH_3), 11.85 (CH_3), 22.15 (CH_2), 25.37 (CH_2), 32.62 (CH_2), 51.19 (CH_2), 52.25 (CH_3), 52.65 (CH_3), 58.23 (CH_2), 63.57 (C), 69.43 (CH), 170.38 (C=O), 172.33 (C=O). *m*/*z* 257 (M^+, 8%), 229 (15), 228 ($M^+ - Et$, 100), 198 ($M^+ - CO_2Me$, 28), 159 (5), 140 (12), 114 (9), 84 (8), 59 (7). Found: 257.1556 [M^+]. Calc. for $C_{13}H_{23}NO_4$: 257.1627.

Dimethyl 1-Butyl-2-propylpyrrolidine-3,3-dicarboxylate ***15g***

Bp 124–126 (1.5 mmHg). ν_{max} (neat)/cm^{-1} 2957, 2934, 2874, 2808, 1736, 1456, 1435, 1269, 1223. δ_H ($CDCl_3$) 0.90 (t, *J* 7, 3H, CH_3), 0.91 (t, *J* 7, 3H, CH_3), 1.1–1.7 (m, 9H, $CH_2 \times 4$, CH), 1.9–2.8 (m, 4H, CH_2), 3.0–3.5 (m, 2H, CH_2), 3.71 (s, 3H, CH_3), 3.73 (s, 3H, CH_3). δ_C ($CDCl_3$) 14.09 (CH_3), 14.42 (CH_3), 19.79 (CH_2), 20.61 (CH_2), 31.19 (CH_2), 32.62 (CH_2), 34.90 (CH_2), 51.23 (CH_2), 52.25 (CH_3), 52.69 (CH_3), 55.38 (CH_2), 63.67 (C), 68.04 (CH), 170.46 (C=O), 172.37 (C=O). *m*/*z* 285 (M^+, 10%), 254 (15), 243 (27), 242 ($M^+ - Pr$, 100), 226 ($M^+ - CO_2Me$, 3), 200 (10), 140 (23), 114 (9), 98 (14), 59 (8), 42 (9). Found: 285.1926 [M^+]. Calc. for $C_{15}H_{27}NO_4$: 285.1940.

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