Radical Cycloaddition by Nickel(II) Complex-Catalyzed Electroreduction. A Method for Preparation of Pyrrolopyridine and Pyrrolopyrrole Derivatives

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Cycloalkano[*a*]pyrroles were obtained by reductive radical cycloaddition of 1-(2-iodoethyl)pyrrole and activated olefins or by cyclization of 1-(ω-iodoalkyl)pyrroles, through electroreduction of the iodides using nickel(II) complex as an electron-transfer catalyst.

Key words sequential radical reaction; indirect electroreduction; nickel(II) complex; cycloalkano[*a*]pyrrole; 1-(2-iodoethyl)pyrrole

Within the past two decades, there has been a remarkable development in the synthetic applications of tin hydride-mediated free radical chemistry.[1] However, applications of this chemistry to aromatic systems have been limited mainly to the formation of aryl–aryl bonds.[2] On the other hand there have been a number of investigations on the homolytic substitutions or cyclizations of electron-rich carbon aromatics or heteroaromatics conducted under oxidative conditions using oxidants such as manganese(III) acetate, Fe^{2+}/H_2O_2,[3c] and Et_3B/O_2,[3b,d] where the oxidation of the intermediate σ radical to the substituted product occurs smoothly under the conditions applied.[3] However, even under the weakly oxidative conditions the homolytic substitutions or cyclizations of pyrrole derivatives by simple alkyl radicals have not been studied so extensively, unlike those by electrophilic radicals. This might be partly because simple alkyl radicals are more difficult than electrophilic radicals to generate with Fe^{2+}/H_2O_2 or Et_3/O_2.[3d,4] We have shown that nickel(II) complex-catalyzed electroreductive method for radical generation is a general method which can produce various types of carbon-centered radicals.[5]

We now report that this electroreductive method allows the direct synthesis of pyrrolopyridine-8-carboxylate and -8-carbonitrile starting from 1-(2-iodoethyl)pyrrole and activated olefins. We also report the intramolecular cyclization of the radicals generated from 1-(ω-iodoalkyl)pyrroles and 1-(4-iodobutyl)indole, which were examined to investigate further the nature of the radical cyclization onto heteroaromatic compounds in the present catalytic electroreduction.

Results and Discussion

The reactions were conducted by controlling (*a*) the sequential cycloaddition of the pyrrolylethyl radical with the activated olefins; or (*b*) the cyclization of ω-pyrrolylalkyl radicals, which should proceed as shown in Chart 1.

The electrolysis for the sequential reactions was conducted by using 3 mmol of a pyrrole (**1a**—**1f**) (1 mmol of pyrrole in the case of cyclization of ω-pyrrolylalkyl radicals), 1 mmol of an olefin, 0.05—0.2 mmol of a nickel complex, $Ni(II)(tmc)(ClO_4)_2$,[6,7] with a graphite plate as a cathode and a zinc plate as an anode[8] both in an undivided and a divided cell at room temperature. The cell was wrapped in aluminum foil since the starting iodides are sensitive to light. As anticipated, the tetrahydropyrrolopyridine derivatives were formed in reasonable yields for two-step reaction. The results are summarized in Table 1. As shown in Table 1, the total yields of the adduct, 1-(4-substituted butyl)pyrroles **3** and pyrrolopyridine derivatives **4** (runs 1, 1′, 2′ and 2″), show that more than

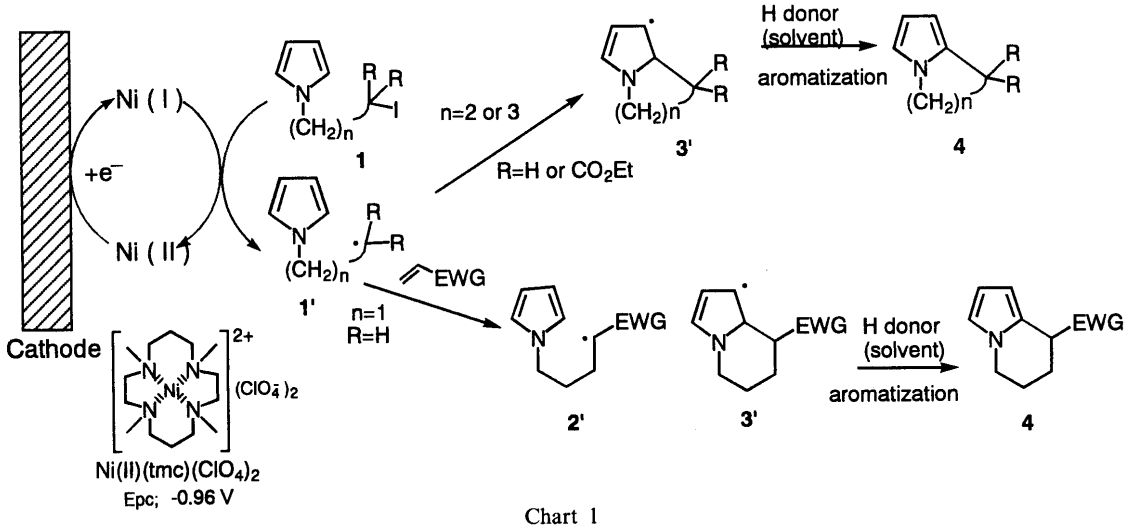

Chart 1

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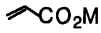
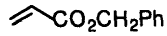
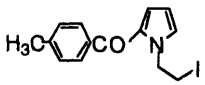
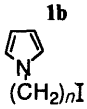
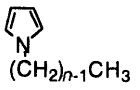
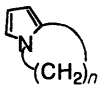
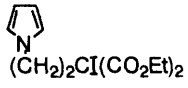
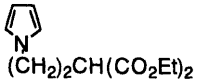
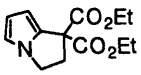
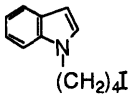
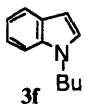
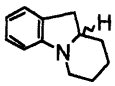
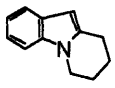
Table 1. Nickel (II) Complex-Catalyzed Electroreductive Cycloaddition of 1-(2-Iodoethyl)pyrrole with Electron-Deficient Olefins and Cyclization of 1-(ω-Iodoalkyl)pyrroles and -indole[a]

Run	Pyrrole or Indole (1 mmol)	EWG (3 mmol)	Product Yield (%)[b] 3	4	5
	 [c]		**3a1**	**4a1**	**5a1**
1[d]			(14)	(26)	(6)
1′			(27)	(37)	(12)
	1a				
			**3a2**	**4a2**	
2[d]	**1a**		(9)	(25)	(4)
2′			(51)	(34)	(0)
2″[e]			(30)	(36)	
3	**1a**		**3a3**	**4a3**	(0)
			(7)	(23)	
4	**1a**		**3a4**		
			(73)	(0)	(8)
			**3b**	**4b**	
5			(9)	(10)	(0)
	1b				
					
	1c $n=4$	**3c**	**4c**	**5c**	
6		f)	(49)[g]	(0)	
6′[e]		(12)	(20) (75)[g]	(0)	
6″[h]		(30)	(trace)		
	1d $n=3$	**3d**	**4d**	**5d**	
7[e]		(9)	(9)	(6)	
7′[e]		(34)[g]	(25)[g]		
7″[e]		f)	(55)[g,i]		
					
	1e	**3e**	**4e**		
8[j]		(40)	(33)		
8′[e]		(80)	(0)		
					
	1f	**3f**	**4f′**	**4f**	**5f**
9[e]		(14)	(33)[k]	(18)	(0)

a) Electrolysis in DMSO using a divided cell unless otherwise noted. For conditions, see the text. b) Isolated yield based on the iodides unless otherwise stated. c) **1c** exhibits a reductive peak at *ca.* −2.25 V *vs.* SCE. d) Electrolysis in an undivided cell. e) Electrolysis in DMF. f) Detected by TLC, but not determined. g) Determined by GLC. h) Electrolysis in DMF in the presence of 1.2 eq of Ph_2PH. i) Electrolysis at 70 °C. j) Electrolysis in acetonitrile. **1g** Exhibits its reductive peak at *ca.* −0.8 V *vs.* SCE and so Co(cyclam)Cl_3 was used as a catalyst in the electrolysis. k) Stereochemistry not determined.

60% of the initial radical, 2-(1-pyrrolyl)ethyl radical **1′** underwent 1,4-addition to the activated olefin and about half of the resulting adduct radical cyclized onto the pyrrole ring to provide **4**. The other part of the adduct radical seems to be trapped by the solvent to give **3** (Table 1) or reduced at the cathode to the corresponding carbanion followed by protonation to provide **3**, since the α- carbonyl and α-cyanosubstituted alkyl radicals could be considered to be more reducible than simple alkyl radicals. The reaction with methacrylonitrile gave a large amount of the adduct **3a4** and did not provide the corresponding pyrrolopyridine derivative, probably because of steric hindrance at the cyclization stage. As shown in run 5, substitution of an electron-withdrawing *p*-tolyl group on the pyrrole ring reduced the homolytic cyclization of the electrophilic radical to give **4b**. The electrolysis in *N*,*N*-dimethylformamide (DMF) affords the cyclized derivatives **4a** in nearly same or rather better yields than those in dimethyl sulfoxide (DMSO), and so electrolysis of **1c**—**f** was conducted in DMF except for runs 7″ and 8. When the 4-(1-pyrrolyl)butyl radical was generated from 1-(4-iodobutyl)pyrrole **1c** it cyclized onto the pyrrole ring to give a pyrrolopyridine **4c** in a good yield[9] along with a small amount of the reduction product, 1-butylpyrrole **3c**. When the electrolysis of **1c** was performed in the presence of 1.2 eq of a hydrogen donor, diphenylphosphine

(Ph_2PH),[10] only a trace amount of **4c** was detected on GLC and **3c** was formed in 30% yield, in contrast to the results of the reactions where rapid cyclization was involved.[5a,d] This implies that cyclization onto the pyrrole ring is relatively slow at room temperature. The yield of a pyrrolopyrrole **4d** was lower than that of a pyrropyridine **4c**, probably because of the increase in the ring strain. However, the electrolysis of **1d** at an elevated temperature (70 °C) increased the yield of **4d** to 55%. When electrolysis of a diethylmalonate **1e** was conducted in DMF using more reducible Co(III)(cyclam)Cl_3 (E_{pc}; −0.45 V *vs.* saturated calomel electrode (SCE) as a catalyst, taking into consideration that **1e** is much more reducible (E_{pc}; −0.8 V *vs.* SCE) than simple alkyl iodides (E_{pc}; *ca.* −2.25 V *vs.* SCE), a reduction product **3e** was provided in 80% yield and the cyclized product **4e** was not obtained. Electrolysis of **1e** in acetonitrile, however, provided a pyrrolopyrrole **4e** in 33% yield, which could be attributed to the longer lifetime of the malonyl radical **1′** (Chart 1, R = CO_2Et) in acetonitrile. However, a 3-iodopyrrolopyrrole derivative was not formed contrary to the results of catalytic electroreduction of α-iodoacetyl amides in acetonitrile, which provided iodinated 2-pyrrolidinones *via* iodine-atom transfer mechanism.[5e,11] The iodine-atom transfer from iodomalonates to radical centers has been considered to be essentially diffusion-controlled.[11a] The observation that 3-iodopyrrolopyrrole was not formed suggests that the cyclization of **1′** to give **3′** is much slower than the conversion of the iodomalonate **1e** by an electron-transfer from Co(II)(cyclam)Cl_2 to the iodomalonate **1e** to give a malonyl radical **1′**. This consequently would reduce the iodine-atom transfer to the cyclized radical **3′** from the starting iodomalonate. Next, the electrolysis of 1-(4-iodobutyl)indole **1f** was examined to test further the nature of the cyclization onto indole ring. Radical cyclization of **1f** gave 1-butylindole **3f**, a tetrahydropyridoindole **4f** and one of the stereoisomers of the hexahydropyridoindole **4f′**.

A final stage in the formation of substituted products such as **4** involves the formal elimination of two hydrogen atoms. Similar formal elimination of a hydrogen atom to give the product has been shown to be involved in the tin hydride mediated[2] or electrochemically induced[12] intramolecular radical substitution of phenyl radical onto an adjacent benzene ring,[2] as well as the intramolecular cyclization of α-benzamidoyl radicals,[13a] or phenylcarbamoyl radicals.[13b,c] However, the mechanism of the formal elimination of a hydrogen atom has not been established, except for that tentatively proposed by Bowman and co-workers for Bu_3SnH mediated reductive cyclization of aryl radicals onto thioamides.[2d]

An indoline derivative **4f′** seems to be a usual product formed by a hydrogen transfer from the solvent to the final σ-radical.[14] The formation of the pyridoindoline **4f′** seems to suggest that the cycloalkano[*a*]pyrroles **4** (**a**—**f**) were generated through loss of H_2 from the corresponding unstable cycloalkane[*a*]-2-pyrroline derivatives. The oxidation of the σ radical **3′** at the anode (Zn) and/or by Zn ion followed by deprotonation to give the final products seems unlikely, since the electrolysis provided the cyclized products in better yields in a divided cell than in an undivided cell (runs 1 and 1′, and runs 2 and 2′).

In this work, we have demonstrated that the present simple one-step route to (8-substituted)tetrahydropyrrolopyridines could be a useful alternative to other methods,[15] and that the cyclizations of ω-pyrrolylalkyl radicals onto a pyrrole ring proceed smoothly under catalytic electroreductive conditions designed to minimize the competitive hydrogen transfer from the solvent or further reduction of the ω-pyrrolylalkyl radicals.

Experimental

Instrumentation NMR spectra were taken on a JEOL EX-270, JEOL GX-500 or Varian VXR-200 instrument. The *J*-values are given in hertz (Hz). IR spectra were taken on a JASCO Valor III instrument. Cyclic voltammetry was performed with a three-electrode system employing a linear scanning unit (Huso Electronical System HECS 321B) equipped with a potentiostat (Hokuto Denko PS-55B). Constant current electrolysis was carried out with a potentio-galvanostat (Hokuto Denko HA105S), and the quantity of electricity was recorded with a coulometer (Hokuto Denko HF-201). Analytical gas chromatography was performed on a JEOL JGC-20K equipped with FID using a glass column (2 m × 3 mm i.d.) packed with 5% polyethylene glycol (PEG) 20M.

Materials 1-(2-Chloroethyl)pyrrole, acrylonitrile, methacrylonitrile, methyl acrylate and indole were purchased and used as received.

1-(2-Iodoethyl)-1*H*-pyrrole (1a) **1a** was prepared by means of the halogen exchange reaction.[3b] NaI (3.00 g, 20 mmol) was added to 1-(2-chloroethyl)-1*H*-pyrrole (1.30 g, 10 mmol) in acetonitrile (50 ml) under nitrogen at room temperature and the mixture was heated under reflux for 48 h. The reaction mixture was cooled to room temperature, diluted with water and extracted with Et_2O. The extract was successively washed with 5% aqueous $Na_2S_2O_3$, and saturated aqueous $NaHCO_3$, brine, and dried over $MgSO_4$. Purification by silica gel chromatography (hexane–AcOEt, 100:1) provided **1a** as colorless oil (1.77 g, 68%). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 3.38 (2H, m, CH_2I), 4.24 (2H, t, *J* = 6.6, CH_2N), 6.18 (2H, m, H-3, H-4), 6.68 (2H, m, H-2, H-5).

1-(2-Iodoethyl)-2-toluoyl-1*H*-pyrrole (1b) **1b** was prepared by mean of the halogen exchange reaction[3b] of 1-(2-chloroethyl)-2-toluoyl-1*H*-pyrrole, which had been prepared by *p*-toluoylation of 1-(2-chloroethyl)-1*H*-pyrrole.[16] The halogen exchange reaction was performed using NaI (3.63 g, 24.2 mmol), 1-(2-chloroethyl)-2-toluoyl-1*H*-pyrrole (3.00 g, 12.1 mmol) in the same way as described for **1a**. Purification by silica gel column chromatography (hexane–AcOEt, 20:1) afforded **1b** as a colorless oil (2.09 g, 51%). IR ν_{max}^{KBr} cm^{-1}: 1680 (CO). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 2.43 (3H, s, CH_3), 3.57 (2H, t, *J* = 7.0, CH_2I), 4.68 (2H, t, *J* = 7.0, CH_2N), 6.19 (1H, dd, $J_{3,4}$ = 4.0, $J_{4,5}$ = 2.5, H-4), 6.80 (1H, dd, $J_{3,4}$ = 4.1, $J_{2,5}$ = 1.6, H-3), 7.02 (1H, t, *J* = 2, H-5), 7.30 (2H, d, *J* = 8.3, ArH), 7.71 (2H, *J* = 8.3, ArH).

1-(4-Iodobutyl)-1*H*-pyrrole (1c) This compound was prepared in the same manner as described for 1-(3-iodopropyl)-1*H*-indole[14] using pyrrole (2.01 g, 30 mmol), 1,4-diiodobutane (10.83 g, 35 mmol), potassium *tert*-butoxide (4.90 g, 35 mmol) and 18-crown-6 (0.80 g, 3 mmol) in dry ether under nitrogen. Purification by silica gel column chromatography (hexane–AcOEt, 20:1) gave **1c** as a pale yellow oil (2.25 g, 30%). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.69—1.96 (4H, m, $CH_2C\underline{H}_2C\underline{H}_2CH_2$), 3.15 (2H, t, *J* = 6.6, CH_2I), 3.91 (2H, t, *J* = 6.6, CH_2N), 6.14 (2H, t, *J* = 2.0, H-3, H-4), 6.64 (2H, t, *J* = 2.0, H-2, H-5).

1-(3-Iodopropyl)-1*H*-pyrrole (1d) This compound was prepared by halogen exchange reaction from 1-(4-chloropropyl)-1*H*-pyrrole, which had been prepared according to a literature method[17] by the reaction of sodium pyrrolide (2.48 g, 37 mmol) and 4-chlorobutyl toluene-*p*-sulfonate (10 g, 37 mmol) in dry dimethoxyethane (DME) (30 ml) under nitrogen at room temperature. Purification by silica gel column chromatography (hexane–AcOEt, 20:1) gave **1d** as a pale yellow oil (1.67 g, 44%). ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 2.18 (2H, q, *J* = 6.27, $CH_2C\underline{H}_2CH_2$), 3.05 (2H, t, *J* = 6.27, CH_2I), 3.99 (2H, t, *J* = 6.27, CH_2N), 6.13 (2H, t, *J* = 2.0, H-3, H-4), 6.66 (2H, t, *J* = 2.0, H-2, H-5).

1-[3,3-Bis(ethoxycarbonyl)-3-iodopropyl]-1*H*-pyrrole (1e) **1e** was prepared in the same manner as described for diethyl methyliodomalonate.[11a] 1-(3,3-Diethoxycarbonylpropyl)-1*H*-pyrrole[3b] (1.4 g, 5.4 mmol) in dry tetrahydrofuran (THF, 10 ml) was added to a THF solution containing NaH (60% in oil, 0.4 g, 10 mmol) at 0 °C. The flask was

wrapped in a aluminum foil, and all subsequent operations were performed in the dark. The reaction mixture was stirred for 1 h at room temperature, then *N*-iodosuccinimide (NIS) (0.4 g, 10 mmol) in dry THF (20 ml) was added dropwise at −78 °C. The reaction mixture was warmed to room temperature, and **1e** was separated by silica gel column chromatography (hexane–AcOEt, 5 : 1) in the dark to afford an orange oil, which was unstable and decomposed to 1-(3,3-diethoxycarbonylpropyl)-1*H*-pyrrole, liberating iodine within a week. (0.8 g, 39%). ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 1.33 (6H, t, J=6.9, C$\underline{H}_3$CH$_2$), 2.69 (2H, t, J=7.6, CH$_2$Cl), 4.10 (2H, t, J=7.6, CH$_2$N), 4.27 (4H, q, J=6.9, CH$_3$C$\underline{H}_2$), 6.16 (2H, t, J=2.0, H-3, H-4), 6.71 (2H, t, J=2.0, H-2, H-5).

1-(4-Iodobutyl)-1*H*-indole (1f) **1f** was preparedin the same manner as described for 1-(3-iodopropyl)-1*H*-indole[14] using indole (2.27 g, 19.37 mmol), 18-crown-6 (0.51 g, 1.93 mmol), potassium *tert*-butoxide (2.39 g, 21.29 mmol) and 1, 4-diiodobutane (11.99 g, 38.7 mmol) in dry Et_2O. Purification of the crude product by silica gel chromatography (hexane–AcOEt, 20 : 1) provided **1f** as a pale yellow oil (2.70 g, 48%). ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 1.76—1.87 (2H, m, C$\underline{H}_2$CH$_2$I), 1.89—2.03 (2H, m, C$\underline{H}_2$CH$_2$N), 3.15 (2H, t, J=6.9, CH$_2$I), 4.16 (2H, t, J=6.9, CH$_2$N), 6.52 (1H, d, J=3.3, ArH), 7.08—7.16 (2H, m, ArH), 7.20—7.25 (1H, m, ArH), 7.30 (1H, d, J=8.3, ArH), 7.75 (1H, d, J=7.6, ArH).

Benzyl Acrylate Aqueous 25% NaOH (70 ml) and acrylic acid (3.6 g, 50 mmol) were successively added to hexamethylphosphoric triamide (HMPA) (50 ml) and the mixture was stirred for 1 h. Benzyl bromide (8.5 g, 50 mmol) was added dropwise over 5 min period, and the reaction mixture was stirred for 18 h. Then 5% HCl (100 ml) was added, and the whole was extracted with Et_2O. The organic layer was washed with brine, and dried over $MgSO_4$. Purification by silica gel column chromatography provided the acrylate as a colorless oil. ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 5.20 (2H, s, C$\underline{H}_2$Ph), 5.85 (1H, dd, J=10, 1.6, C$\underline{H}$H=CH), 6.17 (1H, dd, J=17, 10, CH$_2$C$\underline{H}$), 6.46 (1H, dd, J=17, 1.6, CH$\underline{H}$=CH), 7.35 (5H, m, ArH).

1-Butyl-1*H*-pyrrole (3c) This pyrrole was prepared by the same method as described for **1c**, using pyrrole (2.60 g, 38.7 mmol), iodobutane (11.0 g, 59.8 mmol), 18-crown-6 (1.02 g, 3.96 mmol), and potassium *tert*-butoxide (4.78 g, 42.58 mmol) in dry ether. Purification of the crude product by silica gel column chromatography (hexane–AcOEt, 80 : 1) provided **3e** as a pale yellow oil (1.6 g, 34%). ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 0.92 (3H, t, J=7.3, CH$_3$), 1.30 (2H, m, C$\underline{H}_2$CH$_3$), 1.73 (2H, m, C$\underline{H}_2$CH$_2$N), 3.85 (2H, t, J=7.2, CH$_2$N), 6.12 (2H, t, J=2.0, H-3, H-4), 6.63 (2H, t, J=2.0, H-2, H-5).

1-Propyl-1*H*-pyrrole (3d) This pyrrole was prepared by the same method as described for 1-butyl-1*H*-pyrrol, using pyrrole (2.35 g, 35.1 mmol) and iodopropane (6.56 g, 38.6 mmol). Purification of the crude product by silica gel column chromatography (hexane–AcOEt, 20 : 1) provided **3d** as a pale yellow oil (2.0 g, 52%). ^{1}H-NMR (270 Mz, $CDCl_3$) δ: 0.91 (3H, t, J=7.26, CH$_3$), 1.79 (2H, sextet, J=7.26, C$\underline{H}_2$CH$_3$), 3.83 (2H, t, J=7.26, C$\underline{H}_2$N), 6.14 (2H, t, J=2.1, H-3, H-4), 6.65 (2H, t, J=2.1, H-2, H-5).

1-[3,3-Bis(ethoxycarbonyl)propyl]-1*H*-pyrrole (3e) **3e** was prepared in the same manner as described for 1-[3,3-bis(ethoxycarbonyl)propyl]-2-benzoyl-1*H*-pyrrole,[3b] using sodium hydride (60% in oil, 1 g, 25 mmol), diethyl malonate (4.0 g, 25 mmol) and 1-(2-iodoethyl)-1*H*-pyrrole (5.53 g, 25 mmol) in dry DMF at 0 °C. Purification of the crude product by silica gel column chromatography (heaxane–AcOEt, 50 : 3) provided **3e** as colorless oil (4.94 g, 78%). ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 1.28 and 1.30 (6H, t, J=6.9, CH$_2$C$\underline{H}_3$), 2.34 (2H, q, J=6.9, CH$_2$C$\underline{H}_2$CH$_2$), 3.24 (1H, t, J=7.3, C$\underline{H}$CH$_2$), 3.97 (2H, t, J=6.9, CH$_2$N), 4.20, 4.21 (4H, q, J=7.3, C$\underline{H}_2$CH$_3$), 6.14 (2H, t, J=2.0, H-3, H-4), 6.63 (2H, t, J=2.0, H-2, H-5). Co(III)(cyclam)Cl$_3$[18a] and Ni(II)(tmc)(ClO$_4$)$_2$[18b] were prepared according to the literature methods.

Constant Current Electrolysis Electroreductions were carried out using 10 or 20 ml of DMSO, DMF or acetonitrile containing tetraethylammonium perchlorate (0.1 M) in an undivided or a divided cell with the iodide (1 mmol) and the activated olefin (3 mmol), nickel(tmc)$(ClO_4)_2$ (0.05 mmol) at a constant current of 3 mA (current density *ca.* 0.24 mA cm^{-2}) between a graphite cathode and a zinc anode (undivided cell) or a platinum anode (divided cell) under an inert gas at ambient temperature until 1.04—1.20 F/mol of electricity based on the iodide was consumed. The products were extracted with Et_2O from the electrolyte, after dilution with saturated aqueous NH_4Cl or brine, and separated by silica gel column chromatography. Spectra data and analytical results of the products are as follows.

Methyl 5-(1-Pyrrolyl)valerate (3a1) An oil. IR ν_{max}^{KBr} cm^{-1}: 1736 (CO). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.51—2.19 (4H, m, CH$_2$C$\underline{H}_2$C$\underline{H}_2$CH$_2$), 2.30 (2H, t, J=7.3, CH$_2$CO), 3.72 (3H, s, CH$_3$O), 3.90 (2H, m, CH$_2$N), 6.13 (2H, m, H-3, H-4), 6.63 (2H, m, H-2, H-5).

5-(1-Pyrrolyl)valeronitrile (3a2) IR ν_{max}^{KBr} cm^{-1}: 2247 (CN). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.42—2.01 (4H, m, CH$_2$C$\underline{H}_2$C$\underline{H}_2$CH$_2$), 3.93 (2H, t, J=6.6, CH$_2$CN), 3.39 (2H, m, CH$_2$N), 6.14 (2H, m, H-3, H-4), 6.64 (2H, t, J=2.0, H-2, H-5).

Benzyl 5-(1-Pyrrolyl)valerate (3a3) An oil. IR ν_{max}^{KBr} cm^{-1}: 1734 (CO). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.68—1.88 (4H, m, CH$_2$C$\underline{H}_2$C$\underline{H}_2$CH$_2$), 2.38 (2H, t, J=7.0, CH$_2$CO), 3.89 (2H, t, J=7.0, CH$_2$N), 5.03 (2H, s, CH$_2$Ph), 6.15 (2H, m, H-3, H-4), 6.64 (2H, t, J=2.0, H-2, H-5).

2-Methyl-5-(1-pyrrolyl)valeronitrile (3a4) An oil. IR ν_{max}^{KBr} cm^{-1}: 2237 (CN). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.28 (3H, d, J=7.0, C$\underline{H}_3$CH), 1.40—2.10 (4H, m, CH$_2$C$\underline{H}_2$C$\underline{H}_2$CH$_2$), 2.49 (1H, t, J=6.6, CHCN), 3.92 (2H, t, J=6.8, CH$_2$N), 6.14 (2H, m, H-3, H-4), 6.63 (2H, t, J=2.1, H-2, H-5).

3c (an oil) and **3d** (an oil) which were separated from the crude products by column chromatography, showed ^{1}H-NMR spectra (cited above) identical with those of standard samples synthesized separately. The yield of **3d** was determined by GLC analysis using a column packed with PEG 20M (2 m × 3 mm i.d.) at 140 °C and hexadodecane as an internal standard.

Methyl 5,6,7,8-Tetrahydropyrrolo[1,2-*a*]pyridine-8-carboxylate (4a1) An oil. Found: C, 66.55; H, 7.28; N, 7.59. Calcd. for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. IR ν_{max}^{KBr} cm^{-1}: 1736 (CO). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.80—2.19 (4H, m, H-6, H-7), 3.73 (3H, s, CH$_3$O), 3.84—3.96 (3H, m, H-5, H-8), 6.03 (1H, m, H-1), 6.14 (1H, t, J=3.3, H-2), 6.55 (1H, t, J=2.2, H-3).

5,6,7,8-Tetrahydropyrrolo[1,2-*a*]pyridine-8-carbonitrile (4a2) An oil. IR ν_{max}^{KBr} cm^{-1}: 2247 (CN). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.85—2.66 (4H, m, H-6, H-7), 3.94 (2H, m, H-5), 4.04 (1H, m, H-8), 6.17 (2H, d, J=2.0, H-1, H-2), 6.58 (1H, t, J=2.2, H-3). ^{13}C-NMR (67.8 MHz, $CDCl_3$): 21.69 (C-7), 25.82 (C-6), 26.09 (C-8), 44.62 (C-5), 106.81 (C-1), 108.96 (C-2), 120.31 (C-3).

Benzyl 5,6,7,8-Tetrahydropyrrolo[1,2-*a*]pyridine-8-carboxylate (4a3) An oil. Found: C, 75.10; H, 6.82; N, 5.29. Calcd for $C_{16}H_{17}NO_2$: C, 75.28; H, 6.71; N, 5.49. IR ν_{max}^{KBr} cm^{-1}: 1736 (CO). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.80—2.44 (4H, m, H-6, H-7), 3.89—3.97 (3H, m, 2 × H-5, H-8), 5.17 (2H, s, CH$_2$Ph), 6.03 (1H, m, H-1), 6.13 (1H, t, J=3.1, H-2), 6.55 (1H, J=2.2, H-3), 7.33—7.37 (5H, m, ArH).

Methyl 5,6,7,8-Tetrahydro-3-toluoylpyrrolo[1,2-*a*]pyridine-8-carboxylate (4b) An oil. IR ν_{max}^{KBr} cm^{-1}: 1736 (CO). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.80—2.42 (4H, m, H-6, H-7), 2.42 (3H, s, ArC$\underline{H}_3$), 3.76 (3H, s, CH$_3$O), 3.95 (1H, t, J=6.4, H-8), 4.48 (2H, m, H-5), 6.12 (1H, d, J=4.0, H-1), 6.72 (1H, t, J=4.0, H-2), 7.25 (2H, d, J=8.25, ArH), 7.70 (2H, d, J=8.25, ArH).

5,6,7,8-Tetrahydropyrrolo[1,2-*a*]pyridine (4c) An oil. **4c** seemed stable to heating and showed a peak height proportional to concentration on GLC analysis at 150 °C using ethyl phenylacetate as internal standard. However, it decomposed slowly on purification by silica gel column chromatography. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 1.74—1.86 (2H, m, H-7), 1.88—2.0 (2H, m, H-6), 2.78 (2H, t, J=5.9, H-8), 3.94 (2H, t, J=5.9, H-5), 5.83 (1H, m, H-1), 6.16 (1H, t, J=2.6, H-2), 6.65 (1H, t, J=2.0, H-3). ^{13}C-NMR (67.8 MHz, $CDCl_3$): 21.51 (C-7), 23.27 (C-6), 23.87 (C-8), 45.29 (C-5), 103.83 (C-1), 107.42 (C-2), 118.49 (C-3), 129.13 (C-8a).

1,2-Dihydro-3*H*-pyrrolo[1,2-*a*]pyrrole (4d) An oil. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 2.49 (2H, q, J=6.6, H-2), 2.83 (2H, t, J=6.6, H-1), 3.94 (2H, t, J=6.9, H-3), 5.80 (1H, m, H-7), 6.21 (1H, t, J=2.6, H-6), 6.61 (1H, t, J=2.3, H-5). ^{13}C-NMR (67.8 MHz, $CDCl_3$) δ: 24.05 (C-2), 27.91 (C-1), 46.17 (C-3), 98.74 (C-7), 128.08 (C-6), 113.55 (C-5). The yield of **4d** was determined by GLC under the same condition used for analysis of **3d**.

Diethyl 1,2-Dihydro-3*H*-pyrrolo[1,2-*a*]pyrrole-1,1-dicarboxylate (4e) A colorless oil. Found: C, 61.97; H, 6.85; N, 5.56. Calcd for $C_{13}H_{17}NO_4$: C, 62.13; H, 6.82; N, 5.57. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.27 (6H, t, J=6.8, CH$_3$), 3.04 (2H, t, J=6.8, CH$_2$C), 4.07 (2H, t, J=6.8, CH$_2$N), 4.22 (4H, q, J=6.8, C$\underline{H}_2$CH$_3$), 6.14 (1H, d, J=2.6, H-7), 6.25 (1H, t, J=2.6, H-6), 6.62 (1H, d, J=2.6, H-5). ^{13}C-NMR (67.8 MHz, $CDCl_3$): 13.96 (CH$_3$), 36.68 (C-2), 44.84 (C-3), 61.91 (C$\underline{H}_2$CH$_3$), 102.84 (C-5), 112.94 (C-6), 115.02 (C-7), 169.47 (CO).

1-Butyl-1*H*-indole (3f) An oil. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 0.94 (3H, t, J=7.6, Me), 1.25—1.41 (2H, m, C$\underline{H}_2$Me), 1.82 (2H, q, J=7.3,

$C\underline{H}_2CH_2N$), 4.13 (2H, t, J=7.3, CH_2N), 6.48 (1H, d, J=3.3, H-3), 7.06—7.23 (3H, m, H-2, H-5, H-6), 7.35 (1H, d, J=7.9, H-7), 7.63 (1H, d, J=7.9, H-4).

1,2,3,4-Tetrahydropyrido[1,2-*a*]indole (4f) A solid, mp 53—55 °C. Found: C, 83.98; H, 7.93; N, 8.09. Calcd for: $C_{12}H_{13}N$: C, 84.17; H, 7.65; N, 8.18. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 1.84—1.92 (2H, m, H-2), 2.04—2.12 (2H, m, H-3), 2.97 (2H, t, J=6.3, H-1), 4.04 (2H, t, J=6.3, H-4), 6.19 (1H, s, H-10), 7.04—7.16 (2H, m, H-7, H-8), 7.25 (1H, J=8.3, H-6), 7.52 (1H, d, J=8.2, H-9). ^{13}C-NMR (67.8 MHz, $CDCl_3$): 21.24 (C-2), 23.43 (C-3), 24.24 (C-1), 42.28 (C-4), 97.45 (C-10), 108.50 (Ar), 119.55 (Ar), 120.07 (Ar), 128 (Ar, 9a or 5a), 136 (Ar, 5a or 9a), 137.14 (Ar, 10a).

1,2,3,4,10,10a-Hexahydropyrido[1,2-*a*]indole (4f') Stereochemistry not determined, a solid, mp 33 °C. Found: C, 82.83; H, 8.90; N, 8.31. Calcd. for $C_{12}H_{15}N$: C, 83.19; H, 8.73; N, 8.08. ^{1}H-NMR (270 MHz, $CDCl_3$, ^{1}H–^{1}H COSY) δ: 1.32—1.76 (4H, m, H-1, H-2), 1.83—1.91 (2H, m, H-3), 2.56 (1H, dd, J=15.0, 11.2, H-10), 2.64 (1H, dd, J=11.2, 3.3, H-10′), 2.94 (1H, dd, J=4.9, 7.5, H-4), 3.18 (1H, ddd, J=14.9, 7.5, 2.6, H-4′), 3.61 (1H, dt, J=11.2, 2.3, H-10a), 6.42 (1H, d, J=7.6, H-6), 6.62 (1H, t, J=7.6, H-9), 7.05 (2H, t, J=7.6, H-7, H-8). ^{13}C-NMR (67.8 MHz, $CDCl_3$): 24.39 (C-2), 24.62 (C-3), 30.68 (C-1), 35.53 (C-10), 45.14 (C-4), 65.21 (C-10a), 105.77 (C-6), 117.41 (C-9), 124.40 (C-8), 127.17 (C-7).

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References and Notes

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