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Electrochemical Carboxylation of Some Heteroaromatic Compounds

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Thirty heteroaromatic compounds have been investigated by cyclic voltammetry (CV) and/or preparative scale electrolysis (PSE) in the absence and presence of carbon dioxide. The rate constants of dehalogenation of the primarily formed anion radical of halogenated heterocycles were estimated from cyclic voltammetric data; these data indicated that carboxylation without loss of chlorine is possible under cyclic voltammetric conditions when the rate constant for cleavage is less than about 10^4 s^{-1}. PSE confirmed that such halogenated heterocycles may be reductively carboxylated without loss of halogen. In the competition between cleavage and carboxylation low temperatures favour the latter reaction.

Electrochemical reductive carboxylation has been described for a number of substrate types, including polycyclic aromatic hydrocarbons,[1] ketones,[2] acetylenes,[1] olefins,[3-8] alkyl halides,[9] and azomethine compounds.[10-12] Compared to carboxylations through organometallic derivatives the electrochemical carboxylation is simpler and has the advantage that it might be applicable to the preparation of compounds bearing substituents which are not compatible with the preparation of organometallic compounds.

The synthesis of carboxylated derivatives of heterocyclic compounds is of interest, *e.g.* for the preparation of potential new drugs, so the electrochemical carboxylation reaction was investigated by means of cyclic voltammetry (CV) and preparative scale electrolysis (PSE) using some *N*-heteroaromatic compounds as substrates; a number of halogenated compounds have been included in order to investigate the possibility of carboxylation of such compounds without loss of halogen.

The compounds investigated were: Quinoline (*1*), the following quinoline derivatives, 2-chloro- (*1a*), 4-chloro-2,7,8-trimethyl- (*1b*), 4,7-dichloro- (*1c*), 5-chloro-8-methyl- (*1d*), 5-chloro-8-methoxy-(*1e*), 6-chloro- (*1f*), 6-chloro-2-methyl- (*1g*), 6-chloro-8-methyl-(*1h*), 7-chloro- (*1i*), 7-chloro-6-methyl- (1*j*), 7-chloro-4-methoxy- (*1k*), 7-chloro-8-methyl- (*1l*), 8-chloro-6-methyl-(*1m*), 3-bromo- (*1n*), 2-methoxy-(*1o*), 8-methoxy-2-methylquinoline (*1p*), 1-(4-quinolyl)ethanol (*1q*), quinoxaline (*2*), 2-chloroquinoxaline (*2a*), 2,3-dichloroquinoxaline (*2b*), 6-chloroquinoxaline (*2c*), 5-chloro-4,7-phenanthroline (*3*), 3-chloro-6-methylpyridazine (*4a*), 3-chloro-6-phenylpyridazine (*4b*), 3,6-diphenylpyridazine (*4c*), 4-chloroquinazoline (*5*), and 2-chloro-4,6-dimethylpyridine (*6*).

The compounds were investigated by cyclic voltammetry (CV) and/or preparative electrolysis.

RESULTS

Cyclic voltammetry. CV was performed both in the absence and the presence of carbon dioxide in a range of sweep rates (v) from $0.4-10^3$ V s^{-1}. The medium was *N*,*N*-dimethylformamide (DMF) with tetrabutylammonium iodide (TBAI) as supporting electrolyte.

CV without CO_2. The halogenated compounds could be divided into 3 classes according to their behaviour in CV which depended on the rate of the cleavage of the carbon–chlorine bond in the initially formed anion radical.

Class A comprises compounds with a fast cleavage reaction of the anion radical (rate constant, $k_c > 2\times10^5$ s^{-1}), class B compounds with medium fast cleavage ($10 < k_c < 2\times10^5$ s^{-1}), and class C

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Table 1. Cleavage rates k_c of halogenated anion radicals and CV-data of some *N*-heteroaromatic compounds with and without CO_2. Conditions: Hanging mercury drop electrode, reference electrode SCE, medium DMF/TBAI, E_p measured at $v = 10$ V s^{-1}.

Substrate	CO_2			$+CO_2$ (0.2 M)		
	k_c/s^{-1}	$-dE_p$ (d log v)$^{-1}$/mV	$-E_p$/V	$-dE_p$ (d log v)$^{-1}$/mV	$-E_p$/V	ΔE_p/mV
1a	$>2\times10^5$	29.4	1.800	29.4	1.800	0
1c 4–Cl	$>2\times10^5$	29.2	1.604	31.8	1.604	0
7–Cl	1.1×10^4	31.8	1.863			
1d	7.3×10^3	28.0	1.868	27.9	1.845	23
1e	3.7×10^3	26.0	1.910	29.9	1.861	49
1f	1.1×10^4	27.7	1.870	46.1	1.816	54
1g	1.5×10^4	30.0	1.935	31.2	1.907	28
1h	2.3×10^4	29.8	1.919	29.3	1.883	36
1i	1.0×10^5	29.7	1.894	37.7	1.826	68
1j	7.6×10^4	27.9	1.892	39.0	1.836	56
1l	1.1×10^5	30.5	1.915	28.0	1.897	18
1m	1.0×10^3	29.0	1.910	20.0	1.858	52
2a	2.5×10^2	29.5	1.360[a]	21.5	1.307[a]	53
2b 2–Cl	2.1×10^2	30.6	1.207[a]	31.2	1.306[a]	68
3–Cl		30.1	1.374[a]			
2c	<1		1.430[a]	28.5	1.330[a]	100
3	1.3×10^3	30.0	1.753	29.7	1.675	78
4a	$>2\times10^5$	34.5	1.822	36.4	1.809	13
4b	$>2\times10^5$	29.5	1.719	29.5	1.719	0
5	$>2\times10^5$	30.3	1.460	27.7	1.468	−8
6	$>2\times10^5$	60	1.839	60	1.831	8

[a] $v = 1$ V s^{-1}.

compounds with a cleavage reaction which is slow on the time scale of CV ($k_c < 10$ s^{-1}).

The compounds of class A (*1a*, first cleavage of *1c*, *4a*, *4b*, *5*, and *6*) show at all v ($v \leqq 10^3$ V s^{-1}) an irreversible peak followed by a reversible peak (except *1c*, which has two irreversible peaks and one reversible one). dE_p (d log v)$^{-1}$ is about −30 mV for the first peak for $v < ca.\ 10^2$ V s^{-1}; at higher v the slope increases.

The compounds of class B (second cleavage of *1c*, *1d*, *1e*, *1f*, *1g*, *1h*, *1i*, *1j*, *1l*, *1m*, *2a*, *2b*, *3*) show a behaviour in CV at low v similar to that of the class A compounds, dE_p (d log v)$^{-1}$ ~ −30 mV. At higher v the scan outruns the cleavage reaction and an anodic peak corresponding to the first reduction peak appears; at the same time the reversible peaks of the parent heterocycle disappear; in a certain range of v dE_p (d log v)$^{-1} = 0$. The rate constant k_c of the cleavage can be calculated from the v at the intersection between the two lines, dE_p (d log v)$^{-1} = -30$ mV and dE_p (d log v)$^{-1} = 0$.[13] The results are listed in Table 1.

2c belongs to class *C*; on CV the first reduction is reversible at $v < 200$ V s^{-1} and no reduction wave of quinoxaline is seen. At $v > 200$ V s^{-1} the peak separation increases.

Table 2. Cleavage rate k_c of halogenated anion radicals at different temperatures. ΔE_p is the difference in peak potential of the substrate in the presence and absence of CO_2.

Compound	T/K	k_c/s^{-1}	ΔE_p/mV
1f	297	1.1×10^4	54
1f	273	8.2×10^2	61
1f	253	9×10^1	67
1m	297	1×10^3	52
1m	293	3.6×10^2	60
1m	253	3×10^1	68
4b	297	$>2\times10^5$	0
4b	273	2×10^4	15
4b	253	3×10^3	25

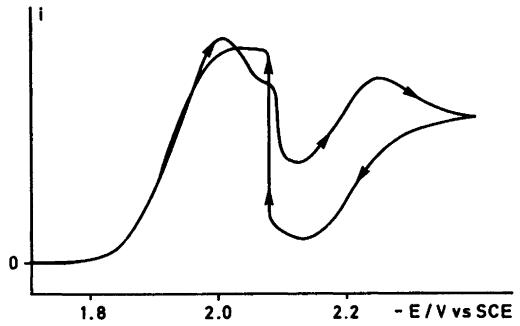


Fig. 1. CV of 7-chloro-6-methylquinoline in DMF/0.1 M TBAI, $v = 0.04$ V s^{-1}.

The cleavage rate of the halogenated anion radicals is dependent on the temperature; in Table 2 the cleavage rates k_c are given for some anion radicals of halogenated *N*-heterocycles at different temperatures. A decrease in the temperature of 20 °C lowers the cleavage rate by a factor of approximately 10.

In some cases, especially pronounced for *1j*, the CV-curves are irregular at low v ($v < 0.08$ V s^{-1}), Fig. 1. This has been observed at a mercury electrode in DMF/TBAI or $TBABF_4$ and to a lesser degree at a glassy carbon electrode in DMF/TBAI. A pronounced effect was not observed in acetonitrile or dimethylsulfoxide. A classical polarogram in DMF/TBAI shows a "dip" in the same potential region as in CV. A somewhat similar phenomenon was recently observed.[14]

CV in the presence of CO_2. Under these conditions the first peak of all the compounds becomes irreversible, and only for a few compounds is it possible to observe the appearance of a small reoxidation peak at very high v ($v > 5 \times 10^3$ Vs^{-1}), but no reliable measurements could be made at such a high v. dE_p (d log v)$^{-1}$ was about -30 mV in most cases, but some showed deviations from that value (Table 1). The peak potential of the first peak shifted for many of the compounds towards less negative potentials; the shifts, ΔE_p, are listed in Tables 1 and 2.

Preparative carboxylations. A number of quinoline derivatives have been reduced electrochemically in DMF saturated with CO_2; after the reduction the product mixture was treated with an alkylating agent, in most cases methyl or ethyl chloride. The carboxylation reaction gave in general a complex mixture of products; only the major products were isolated. Some alkyl and alkoxy substituted, halogenated, and side chain substituted heterocycles were chosen as examples for the preparative carboxylations. The results are listed in Table 3.

DISCUSSION

CV indicates that with the exception of *1q* all the compounds are reduced at less negative potentials than CO_2 so the coupling is likely to be a nucleophilic attack of the substrate anion radical on CO_2.

In the absence of CO_2 the follow-up reaction of the anion radical of the halogenated compounds is a cleavage of the carbon–halogen bond. The cleavage rates listed in Table 1 indicate that halogens positioned in the heterocyclic ring are cleaved faster than halogens in the fused benzene ring. It is well-known that the former compounds are much more susceptible to nucleophilic attack than the latter.

The rate of the cleavage of a halogen in a given position could be imagined to be connected with the unpaired π-electron density of the anion radical at that position. These electron densities may be obtained from the C–H hyperfine coupling constants in the ESR-spectrum; the ESR-spectra of the chlorinated quinolines have not been obtained due to their short life-time. For $1^{\cdot -}$ the coupling constants decrease along the sequence: Position 4 > 5 > 8 > 2 > 7 > 3 > 6,[15] whereas the cleavage rates decrease in the following sequence: Position 2 ~ 4 > 7 > 6 > 5 > 8. If the introduction of a halogen does not change the sequence of the coupling constants of the quinoline derivatives, there seems to be little connection between the two sequences.

It has been observed[16] that the rate of cleavage in a series of chlorinated heterocyclic compounds was lower the more positive the reduction potential was. This is roughly substantiated, but it must be emphasized that the position of the halogen is very important for k_c.

In the presence of CO_2 the first peak potential of the members of class A is changed only slightly or not at all. This indicates that for class A carboxylation is not significantly faster than cleavage so that the rate of the follow-up reaction is not changed in the presence of CO_2; one can thus not expect a carboxylation of these compounds without loss of halogen. The simplest criterion for a member of class A is that no significant change in E_p occurs on addition of CO_2. *4a* shows a shift of 13 mV showing that it is a borderline case between class A and B.

The shift towards positive potentials is significant for the first peak of class B and C compounds in

Table 3. Products from the reductive carboxylation of some substituted *N*-heterocyclic compounds. Potentials measured *vs.* SCE.

Substrate	$-E$/V	Products	Yield/%
1p	2.2	4-Ethoxycarbonyl-8-methoxy-2-methylquinoline (*7*)	25
		4-Ethoxycarbonyl-3-hydroxy-8-methoxy-2-methyl-quinoline (*8*)	5
		3,4-Di(ethoxycarbonyl)-1,2,3,4-tetra-hydro-8-methoxy-2-methylquinoline (*9*)	30
1o	2.5	3,4-Dihydro-4-methoxycarbonyl-2-quinolinone (*10*)	50
		3,4-Dihydro-3,4-di(methoxycarbonyl)-2-quinolinone (*11*)	5
1a	2.0	*1*	50
		2-Ethoxycarbonylquinoline	20
1b		4-Ethoxycarbonyl-2,7,8-trimethylquinoline (*12*)	25
1n	1.95	3-Methoxycarbonylquinoline (*13*)	32
1f	2.0	6-Chloro-4-methoxycarbonylquinoline (*14*)	50
		6-Chloro-2-methoxycarbonylquinoline (*15*)	5
1g	2.0	6-Chloro-4-methoxycarbonyl-2-methylquinoline (*16*)	25
1g[a]	2.0	2-Methylquinoline (*17*)	90
2	1.7	1,4-Dihydro-1,4-di(methoxycarbonyl) quinoxaline (*18*)	65
2b	1.3	6 (or/and) 7-Chloro-2-methoxycarbonyl quinoxaline	60
		6-Chloro-1,4-dihydro-1,4-di(methoxycarbonyl) quinoxaline (*19*)	5
1k	2.0	2,2'-bi(7-Chloro-4-methoxyquinolyl) (*20*)	20
1q	2.85	Ethyl 2-(4-quinolyl)propionate (*21*)	36
		Ethyl 2-(2-ethoxycarbonyl-4-quinolyl) propionate	12
4c	2.0	1,2,5,6-Tetrahydro-1,2-di(methoxy-carbonyl)-3,6-diphenylpyridazine (*23a*)	12
		1,2,5,6-Tetrahydro-1,4-di(methoxy-carbonyl)-3,6-diphenylpyridazine (*23b*)	35
		1,2,5,6-Tetrahydro-2,4-di(methoxycarbonyl)-3,6-diphenylpyridazine (*23c*)	10
4b[b]	2.0	4,5-Dihydro-4-methoxycarbonyl-6-phenyl pyridazin-3(2H)-one (*25*)	26

[a] Without CO_2. [b] $t = -20$ °C.

the presence of CO_2. The shift, ΔE_p, is interpreted as being caused by a faster follow-up reaction in the presence of CO_2 and to be a measure of how much faster carboxylation is compared to cleavage under these conditions. In DMF saturated with CO_2 ($[CO_2] \sim 0.1 - 0.2$ M)[17] compounds of class B and C are thus expected to be carboxylated with only minor loss of halogen.

CV indicates that k_c decreases on lowering the temperature whereas the follow-up reaction in the presence of CO_2 still is fast on the time scale of CV; ΔE_p increases as T decreases. CV thus suggests the possibility that a compound from class A would behave as a class B compound at lower temperatures. A similar shift might be possible by increasing the CO_2 pressure.

The influence of substituents on the cleavage rate has not been investigated systematically, so it is not known yet whether the rather surprising finding that $1d^{\cdot -}$ cleaves faster than $1e^{\cdot -}$ is general. One would expect that the methoxy group of *1e* would promote the cleavage compared to the methyl group of *1d* by donating electrons to the ring. It might, however, be pointed out that under certain conditions a methoxy substituent in a benzene ring may act as an electron attracting group in an anion radical due to the $\pi - \sigma^*$ interaction in the orthogonal conformation of the methoxy group.[18]

The reductive carboxylation produces initially a dihydro derivative; most of the products isolated from the quinolines are, however, either substituted quinolines or tetrahydroquinolines. The dihydro-

quinolines are reactive compounds which may be either oxidized to quinolines during work-up or, being enamines, attacked by oxygen to form oxygen-substituted products. The latter process is probably responsible for part of the loss of material in the form of a number of difficultly separable products, which may undergo further conversion on column chromatography.

The carboxylation of *1p* exemplifies that. The formation of 4-ethoxycarbonyl-8-methoxy-2-methyl-quinoline (*7*) indicates position 4 as the preferred point of attack, at least when position 2 is blocked. The initially formed 4-ethoxycarbonyl-1,4-dihydro-8-methoxy-2-methylquinoline (*7a*) is oxidized to a mixture of *7* and its 3-hydroperoxy derivative (*7b*); alkaline degradation of *7b* could give a carbonyl group at C−3 which would enolize to 4-ethoxycarbonyl-3-hydroxy-8-methoxy-2-methylquinoline (*8*). The third isolated product, 3,4-di(ethoxycarbonyl)-1,2,3,4-tetrahydro-8-methoxy-2-methylquinoline (*9*) may be formed by further reductive carboxylation of *7a* after tautomerization to the 1,2-dihydro derivative (*7c*) which, being an activated olefin, would be carboxylated β to the ester group, *i.e.* at C−3.

The carboxylation of *1o* to 3,4-dihydro-4-methoxycarbonyl-2-quinolinone (*10*) can be explained through formation of the expected 1,4-dihydro-2-methoxy-4-methoxycarbonylquinoline (*10a*) which might tautomerize to the 3,4-dihydro derivative (*10b*); *10b* is an iminoether which would be hydrolyzed to *10*. The dicarboxylated product, 3,4-dihydro-3,4-di(methoxycarbonyl)-2-quinolinone (*11*) could either be formed analogously to *9* followed by oxidation or by carboxylation of the anion of *10b*.

The reactions of *1a*, *1b* and *1n* (class A compounds) are analogous; the carboxylation takes place at the position from which the halogen is leaving. CV indicates that the loss of halide is very fast; the primarily formed anion radical loses the halide before it has diffused away from the electrode. The resulting radical accepts then an electron, probably from the electrode, less likely from an anion radical. The anion thus formed attacks CO_2. Some of the radicals may abstract a hydrogen atom from the medium thus forming *1*.

In the absence of CO_2 halogen is reductively removed; in a dihalogenated compound, such as *1c* or *2b*, it is possible to remove one halogen selectively (*1c*→*1i*; *2b*→*2a*).

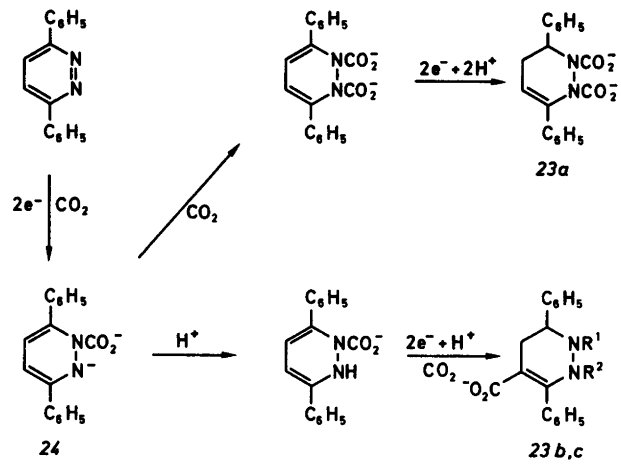
CV of the compounds in class B (and C) indicates that the carboxylation reaction for these compounds is a faster follow-up reaction than the cleavage, so under voltammetric conditions a carboxylation takes place without loss of halogen. Preparative reductions show that this also is the case under preparative conditions in DMF saturated with CO_2 ($[CO_2] \sim 0.2$ M).[17] It has not been investigated whether a higher CO_2-pressure could improve the yields in the cases where the compounds were on the borderline between class A and B, but reductive carboxylation of a class A compound, *4b*, at low temperatures (−20 °C) to 4,5-dihydro-4-methoxycarbonyl-6-phenylpyridazin-3(2*H*)-one (*25*) proved it possible to introduce a carboxyl group in the pyridazine ring without reductive loss of chlorine; the chlorine was, however, lost during work up by hydrolysis to the corresponding hydroxyl compound. $[CO_2]$ of the saturated solution in DMF increases on lowering the temperature; both the increase in $[CO_2]$ and the decrease in cleavage rate favour carboxylation in the competition with cleavage.

The product distribution from carboxylation of *1f* shows that even if position 2 is unsubstituted, the major product is carboxylated in the 4-position and only a minor part at C−2. This might be connected with the higher unpaired π-electron density at C−4 compared to C−2.[15]

The reductive carboxylation, followed by methylation of *4c* yields a mixture of dicarboxylated tetrahydropyridazines from which 1,2,5,6-tetrahydro-1,2-di(methoxycarbonyl)-3,6-diphenylpyridazine (*23a*), 1,2,5,6-tetrahydro-1,4-di(methoxycarbonyl)-3,6-diphenylpyridazine (*23b*), and 1,2,5,6-tetrahydro-2,4-di(methoxycarbonyl)-3,6-diphenylpyridazine (*23c*) were isolated. *4c* may initially form a carboxylated 1,2-dihydropyridazine anion (*24*) which may be either protonated or carboxylated. These compounds are derivatives of 1,4-diphenylbutadiene which is reduced at a potential slightly more negative than that of *4c*; the reduction is performed at −2.0 V so the dihydro compounds could be reduced and carboxylated further to the isolated compounds.

Reductive removal of a side-chain hydroxy or amino group from a carbon α to an activated position in a π-electron deficient heterocyclic compound is well-known.[19] In *1q* the hydroxyl group is lost in a two-electron reduction and the resulting carbanion reacts with CO_2 to ethyl 2-(4-quinolyl)propionate (*21*). *21* may be further carboxylated to ethyl 2-(2-ethoxycarbonyl-4-quinolyl)propionate (*22*).

In conclusion, the results show that electro-



Scheme 1. *23b*, $R^1=CO_2^-$, $R^2=H$; *23c*, $R^1=H$, $R^2=CO_2^-$.

chemical carboxylation may be used even if the substrate bears halogen substituents, provided the rate of cleavage is not too high ($k_c < 10^4\ s^{-1}$). Low temperatures favour carboxylation in the competition with cleavage. In general, higher yields of carboxylated compounds are obtained at low temperatures, and some of the yields reported here could probably be raised by using low-temperature electrolysis.

EXPERIMENTAL

The apparatus for fast cyclic voltammetry was constructed at the University of Aarhus; the construction was similar to those published.[20,21] The potentiostats were from Ultraschalltechnique, Halle, and Tage Juul Electronics, Copenhagen.

The following quinolines were made by the Skraup synthesis:[22,23] *1d*, *1e*,[24] *1f*,[25] *1g*,[26] *1h*,[27] *1i*,[28] *1j*,[29] *1l*,[30] *1m*,[29] *1p*.[31] *1b* was prepared from 2,3-dimethylaniline analogous to Ref. 32, m.p. 68–70 °C, and *1k* according to Ref. 33, m.p. 144 °C. *3* was synthesized by a "double" Skraup synthesis from 2-chloro-4-nitroaniline, m.p. 151 °C. *4a*, *4b*, *5*, and *6* were synthesized from the corresponding oxo-compounds by treatment with $POCl_3$.

General procedure for the carboxylations. The substance (1 g) was electrolyzed in DMF/0.1 M TBAI continuously saturated with CO_2; the electrode potential was held at the peak potential of the substrate in the presence of CO_2. In most cases methyl or ethyl chloride was added during the electrolysis; when methyl iodide was used for alkylation it was added after the electrolysis; the alkylating agent was allowed to react at least for 1 h. The solvent was then removed *in vacuo* and the residue treated five times with hot diethyl ether. The ether extracts were washed three times with a small amount of water and dried (Na_2SO_4). The ether was then removed and the products isolated by column chromatography or preparative TLC. The following compounds were isolated.

8-Methoxy-2-methylquinoline, *1p*, $E=-2.2$ V; the residue was separated by preparative TLC (benzene – ethyl acetate, 3:2). Besides 10 % *1p* were isolated: 4-Ethoxycarbonyl-8-methoxy-2-methylquinoline *7* (25 %), yellow needles, m.p. 116–118 °C, ^{1}H NMR ($CDCl_3$): δ 1.38(3 H, t, J 7 Hz), 2.76 (3 H, s), 4.00 (3 H, s), 4.42 (2 H, q, 7 Hz), 7.00 (1 H, d, 8 Hz), 7.42 (1 H, t, 8 Hz), 7.73 (1 H, s), 816 (1 H, d, 8 Hz). MS (70 eV, *m/e* (%)): 245 (61), 216 (100), 200 (9), 188 (53); 4-ethoxycarbonyl-3-hydroxy-8-methoxy-2-methylquinoline *8* (5 %), m.p. 140–142 °C. ^{1}H NMR ($CDCl_3$): δ 1.34 (3 H, t, 7 Hz), 2.68 (3 H, s), 3.98 (3 H, s), 4.52 (2 H, q, 7 Hz), 6.85 (1 H, d, 8 Hz), 7.38 (1 H, t, 8 Hz), 8.16 (1 H, d, 8 Hz), 12.00 (1 H, br.s). MS (70 eV, *m/e* (%)): 261 (57), 232 (14), 215 (100), 186 (97), 158 (56); 3,4-di(ethoxycarbonyl)-1,2,3,4-tetrahydro-8-methoxy-2-methylquinoline *9* (30 %). ^{1}H NMR (CCl_4): δ 1.02–1.5 (9 H, m), 1.9–2.6 (2 H, m), 3.8 (3 H, s), 3.7–4.3 (5 H, m), 4.7 (1 H, d), 6.8 (3 H, m). The ^{1}H NMR spectrum was not resolved well enough to permit an analysis of the stereochemical relationship of the substituents. MS (70 eV, *m/e* (%)): 321 (7), 248 (52), 174 (100), 159 (23), 131 (6), metastable peaks at *m/e* 191.5 and 122.

2-Methoxyquinoline, *1o*, $E=-2.5$ V. TLC of the residue showed 4 compounds (R_F = 0.43, 0.49, 0.56 and 0.01 using benzene-ethyl acetate 9:1 on silica); column chromatography on silica (dichloromethane – methanol 94:6) gave two compounds *10* and *11* with R_F-values on TLC different from

those in the original product mixture. Isolated were: 3,4-Dihydro-4-methoxycarbonyl-2-quinolinone, *10* (50 %), melted between 145 and 165 °C, ^{1}H NMR ($(CD_3)_2CO$): δ 2,65 (2 H, d, *J* 5.8 Hz), 3.53 (3 H, s), 3.90 (1 H, t, 5.8 Hz), 6.75–7.25 (4 H, m), 9.05 (1 H, br.s.). MS (*m/e* (%)): 205 (60), 146 (100), 128 (64), metastable peak at *m/e* 104. 3,4-Dihydro-3,4-di-(methoxycarbonyl)-2-quinolinone *11* (5 %), ^{1}H NMR ($(CD_3)_2CO$): δ 3.53 (3 H, s), 3.59 (3 H, s), 3.80 (1 H, d, 5.8 Hz), 4.25 (1 H, d, 5.8 Hz), 6.75–7.28 (4 H, m), 9.35 (1 H, br.s). MS (*m/e* (%)): 263 (34), 231 (29), 204 (100), 172 (29), 160 (39), 145 (38).

2-Chloroquinoline, 1a, $E = -2.0$ V; isolated were: *1* (50 %) and 2-ethoxycarbonylquinoline (20 %).

4-Chloro-2,7,8-trimethylquinoline, 1b, $E = -2.35$ V; the residue was separated by preparative TLC (benzene–ethyl acetate, 9:1, silica). Isolated was: 4-Ethoxycarbonyl-2,7,8-trimethylquinoline (25 %), m.p.67 °C. ^{1}H NMR ($CDCl_3$): δ 1.36 (3 H, t, 7 Hz), 2.39 (3 H, s), 2.68 (6 H, s), 4.42 (2 H, q, 7 Hz), 7.30 (1 H, d, 9 Hz), 7.60 (1 H, s), 8.35 (1 H, d, 9 Hz). MS (*m/e* (%)): 243 (100), 215 (92), 171 (36).

3-Bromoquinoline, 1n, $E = -1.95$ V; the residue was separated by preparative TLC (benzene–ethylacetate, 4:1, silica). Besides *1* and an unstable product 3-methoxycarbonylquinoline (*13*) was isolated (32 %), m.p. 70.5–71.5 °C.

6-Chloroquinoline, 1f, $E = -2.0$ V. Besides an unidentified dimer which on storage was transformed to *1f* a mixture of carboxylated isomers was isolated. 6-Chloro-4-methoxycarbonylquinoline, *14* (50 %); ^{1}H NMR ($CDCl_3$): δ 3.75 (3 H, s), 7.0–8.1 (4 H, m), 8.9 (1 H, d, 5 Hz); MS (*m/e* (%)): 223 (35), 221 (100), 165 (15), 163 (40).

6-Chloro-2-methylquinoline, 1g, $E = -2.0$ V. The residue was separated by preparative TLC (benzene–ethyl acetate, 3:2, silica); besides *1g* (33 %) was isolated: 6-Chloro-4-methoxycarbonyl-2-methylquinoline (25 %), it melted between 75 and 93 °C. ^{1}H NMR ($CDCl_3$): δ 1.44 (3 H, t, 7 Hz), 2.74 (3 H, s), 4.46 (2 H, q, 7 Hz), 7.65 (1 H, dd, 9 Hz, 2 Hz), 7.80 (1 H, s), 7.98 (1 H, d, 9 Hz), 8.73 (1 H, d, 2 Hz). MS *m/e* (%)): 251 (38), 249 (100), 223 (10), 221 (32), 206 (16), 204 (45). M^+ 249.0559 ($C_{13}H_{12}ClNO_2$ requires 249.0557).

From *quinoxaline, 2*, $E = -1.7$ V, was isolated: 1,4-Dihydro-1,4-di(methoxycarbonyl)quinoxaline *18*(65 %), m.p. 96 °C (CH_3OH). ^{1}H NMR ($CDCl_3$): δ 3.85 (6 H, s), 6.39 (2 H, s), 7.05–7.35 (2 H, m), 7.6–7.9 (2 H, m). On TLC (dichloromethane, silica) 4 minor components could be detected, but they were not identified.

From *6-chloroquinoxaline, 2b*, $E = -1.7$ V, was isolated: 6(or/and 7)-Chloro-2-methoxycarbonylquinoxaline (60 %), m.p. 153 °C (CH_3OH). ^{1}H NMR ($CDCl_3$): δ 4.10 (3 H, s), 7.6–8.3 (3 H, m), 9.60 (1 H, s). MS (*m/e* (%)): 224 (35), 222 (100), 166 (15), 164 (40). On the ^{1}H NMR spectrum of the crude product a singlet at δ 3.85 suggests the presence of the analogue to *18*.

7-Chloro-4-methoxyquinoline, 1k, $E = -2.0$ V; the residue was a complex mixture, isolated was: 2,2'-Bi(7-chloro-4-methoxyquinolyl), m.p. 322–323 °C, insoluble in most solvents. ^{1}H NMR (CF_3COOD): δ 4.09 (6 H, s), 7.53 (2 H, s), 7.5 (2 H, dd, 9 and 1 Hz), 7.83 (2 H, d, 1 Hz), 8.15 (2 H, d, 9 Hz). MS (12 eV, *m/e* (%)): 388 (4), 387 (19), 386 (77), 385 (37), 384 (100), 355 (53), 339 (22), 192 (14).

1-(4-Quinolyl)ethanol, 1q, $E = -2.85$ V. The residue was separated by preparative TLC (benzene–ethyl acetate, 1:1, silica); isolated were: Ethyl 2-(4-quinolyl)propionate *21* (36 %) and ethyl 2-(2-ethoxycarbonyl-4-quinolyl)propionate *22* (12 %). *21*, ^{1}H NMR (CCl_4): δ 1.10 (3 H, t, 7 Hz), 1.56 (3 H, d, 7 Hz), 4.05 (2 H, q, 7 Hz), 4.36 (1 H, q, 7 Hz), 7.25 (1 H, d, 4 Hz), 7.38–8.25 (4 H, m), 8.70 (1 H, d, 4 Hz). MS (*m/e* (%)): 229 (31), 184 (10), 156 (100). *22*, ^{1}H NMR (CCl_4): δ 1.10 (3 H, t, 7 Hz), 1.43 (3 H, t, 7 Hz), 1.63 (3 H, d, 7 Hz), 4.06 (2 H, q, 7 Hz), 4.38 (1 H, q, 7 Hz), 4.42 (2 H, q, 7 Hz), 7.5–8.0 (2 H, m), 8.1–8.4 (2 H, m), 8.03 (1 H, s).

3,6-Diphenylpyridazine, 4c, $E = -2.0$ V, $n = 3.3$ F mol^{-1}. The residue was dissolved in methanol (5 ml) from which 200 mg *4c* precipitated; the methanol was evaporated and the residue separated on a column of silica using diethyl ether/light petroleum (1:1) as eluent. Isolated were: 1,2,5,6-Tetrahydro-1,2-di(methoxycarbonyl)-3,6-diphenylpyridazine *23a* (150 mg), m.p. 147.2 °C. ^{1}H NMR ($CDCl_3$): δ 2.25 (1 H, dd, *J* 17.6, 6.8 Hz), 3.08 (1 H, ddd, *J* 17.6, 1.8, 1.8 Hz), 3.24 (1 H, ddd, *J* 6.8, 1.8, 2.1 Hz), 3.70 (3 H, s), 3.91 (3 H, s), 6.06 (1 H, dd, *J* 1.8, 2.1 Hz), 7.2–7.5 (8 H, m), 7.7–8.0 (2 H, m); MS 70 eV, *m/e* (%): 352 (20), 293 (100), 233 (80); 1,2,5,6-tetrahydro-1,4-di(methoxycarbonyl)-3,6-diphenylpyridazine *23b* (350 mg), m.p. 171.5 °C. ^{1}H NMR ($CDCl_3$): δ 2.51 (1 H, dd, *J* 13.2, 9.5 Hz), 2.94 (1 H, ddd, *J* 13.2, 7.7, 2.0 Hz), 3.40 (3 H, s), 3.71 (3 H, s), 4.05 (1 H, dd, *J* 9.5, 7.7), 6.9 (1 H, d, 2.0 Hz), 7.2–7.8 (10 H, m). On shaking with D_2O the signal at δ 6.9 disappeared and the signal at δ 2.94 became a double doublet (*J* 13.2, 7.7 Hz). MS (70 eV, *m/e* (%)): 352 (20), 292 (100, 233 (80); besides *23a* and *b* a 3:2 mixture (200 mg) of *23c* and *23b* was isolated but not separated. *23c*, 1,2,5,6-tetrahydro-2,4-di(methoxycarbonyl)-3,6-diphenylpyridazine, ^{1}H NMR ($CDCl_3$): δ 2.7–3.9 (3 H, m), 3.53 (3 H, s), 3.70 (3 H, s), 6.9 (1 H, s), 7.2–7.8 (10 H, m).

3-Chloro-6-phenylpyridazine, 4b, (2 g), $E = 2,0$ V, $n = 1.85$, t = −20 °C, methyl iodide as alkylating agent. The residue was dissolved in a 1:10 mixture of acetone–dichloromethane, from which 4,5-dihydro-4-methoxycarbonyl-6-phenylpyridazine-3(2H)-one (*25*) 55 mg) precipitated. The filtrate was separated on a column of silica with acetone–dichloromethane (1:10) as eluent. *4b* and *25* were

isolated; a fraction containing a mixture of *4b* and *25* was separated by preparative TLC on silica using the same eluent. All together 540 mg of *25* and 420 mg of *4b* were isolated. *25*, m.p. 173 °C, ^{1}H NMR ($CDCl_3$): δ 3.10 (1 H, *J* 16.8 Hz, 6.9 Hz), 3.43 (1 H, *J* 16.8, 8.6 Hz), 3.61 (1 H, *J* 8.6, 6.9 Hz), 3.80 (3 H, s), 7.3–7.5 (3 H, m), 7.6–7.8 (2 H, m), 8.6 (1 H, br.s). IR (KBr, cm^{-1}): 3200 (m), 2900 (m), 1730 (s), 1660 (s). MS (70 eV, *m/e* (%): 232 (11), 173 (100), 115 (10), 103 (12), 77 (14).

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