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# 4-Iminobarbiturates: Tautomerism and Electrochemical Behavior in Relation to N(3) Substitution

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Tautomerism of 4-iminobarbiturates depends upon the presence of a substituent on the N(3) atom. The ultraviolet, infrared, proton nuclear magnetic resonance, $^{13}C$-nuclear magnetic resonance and mass spectrum data show that 3-alkylated compounds present an imido system while 3-unalkylated ones are characterized by an amidinoketone system.

The electrochemical behavior of these two groups was studied by polarography, cyclic voltammetry and controlled potential electrolysis in dipolar aprotic solvents (dimethyl sulfoxide and hexamethyl phosphoric triamide), and was found to be related to the structure: the reduction of 3-substituted compounds is more difficult (about 0.2 V) than the reduction of 3-unalkylated products. The monoelectronic mechanism of this reduction was determined and confirmed by the electrochemically induced formation of an anion which can be alkylated using methyl iodide.

**Keywords**——4-iminobarbiturate; tetrahydroaminopyrimidinedione; tautomerism; structural analysis; reduction; alkylation; aprotic dipolar solvent; structure–electroactivity relationship

Iminobarbiturates, aside from their use as intermediates in barbiturate synthesis, are of interest to medicinal chemists because of the structural analogy with pyrimidine nucleic bases. The lability of hydrogen atoms situated between two electron-attracting groups, as in barbiturates,[1,2] or pyrazolidinediones,[3] can induce tautomerism,[4-6] as well as electrochemical reduction,[1,7] in these heterocycles.

Our purpose is to study in dipolar aprotic media the relation between tautomerism and electrochemical behavior of a series of 4-iminobarbiturates (Fig. 1) (I—V, VIII, and IX) (Table I), represented in the barbiturate-like form in order to allow easy comparison with the drugs. Compounds VI and VII, (Table I), which do not present any labile hydrogen other than that of the imino group are listed here for comparison of their spectral properties.

## Results and Discussion

The compounds which are only monosubstituted at the 5 position are those which present the greatest possibilities of tautomerism. Their structures were previously reported and they were proved to be enamines,[8] in dipolar aprotic solvents (Chart 1). They present no electroactivity under the conditions of our study.

For 5,5-disubstituted derivatives (I—VII), two groups can be distinguished according to the nature of the substituents of the nitrogen atom at the 3 position. 3-Substituted compounds

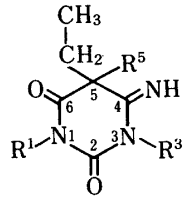


Fig. 1. Representation of 4-Iminobarbiturates in the Barbiturate-like Form

Chart 1

TABLE I. 5,5-Diethyl-4-iminobarbiturates and 5-Ethyl-4-iminobarbiturates

| Compd. | $R^1$ | $R^3$ | $R^5$ | Formula | |
|---|---|---|---|---|---|
| I | H | H | $C_2H_5$ | $C_8H_{13}N_3O_2$ | 5,5-Diethyl-4-iminobarbiturate |
| II | $CH_3$ | H | $C_2H_5$ | $C_9H_{15}N_3O_2$ | 5,5-Diethyl-4-imino-1-methylbarbiturate |
| III | $CH_2C_6H_5$ | H | $C_2H_5$ | $C_{15}H_{19}N_3O_2$ | 1-Benzyl-5,5-diethyl-4-iminobarbiturate |
| IV | H | $CH_3$ | $C_2H_5$ | $C_9H_{15}N_3O_2$ | 5,5-Diethyl-4-imino-3-methylbarbiturate |
| V | H | $CH_2C_6H_5$ | $C_2H_5$ | $C_{15}H_{19}N_3O_2$ | 3-Benzyl-5,5-diethyl-4-iminobarbiturate |
| VI[a)] | $CH_3$ | $CH_3$ | $C_2H_5$ | $C_{10}H_{17}N_3O_2$ | 5,5-Diethyl-1,3-dimethyl-4-iminobarbiturate |
| VII[a)] | $CH_2C_6H_5$ | $CH_2C_6H_5$ | $C_2H_5$ | $C_{22}H_{25}N_3O_2$ | 1,3-Dibenzyl-5,5-diethyl-4-iminobarbiturate |
| VIII | H | H | H | $C_6H_9N_3O_2$ | 5-Ethyl-4-iminobarbiturate |
| IX | $CH_3$ | $CH_3$ | H | $C_8H_{13}N_3O_2$ | 1,3-Dimethyl-5-ethyl-4-iminobarbiturate |

*a*) Included for comparison of the spectral properties.

(IV and V) present the same tautomerism as the corresponding barbiturates, known to exist in a trioxo form in the solid state,[9] as well as in aprotic solvents.[10] On the other hand, the structure of 3-unsubstituted derivatives (alkylated or not at the 1 position) (I—III) present various tautomeric possibilities which can be investigated (Chart 2) by using spectral methods.

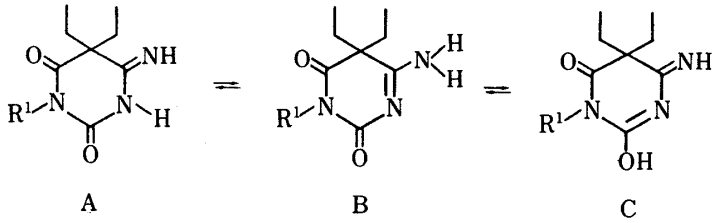
The ultraviolet (UV) study performed in ethanol, in neutral solution, shows that alkylation of N(3) induced a hypsochromic shift (20 nm). In alkaline medium, 3-alkylated derivatives (IV and V) present an important bathochromic effect, analogous to what was observed in barbiturates,[11] while, when the pH is decreased, the compounds which are not alkylated at the 3 position exhibit a large hypsochromic shift (Fig. 2). When dimethyl sulfoxide (DMSO) is used as the solvent, the same behavior is observed in acidic medium.

In the region of 1500—1750 $cm^{-1}$ in the infrared (IR) spectra, stretching vibrations of C=O and C=N groups allow a fast identification of the two classes of compounds according to the number of bands and the wave number values: near 1620 $cm^{-1}$, for 3-alkylated molecules, and near 1560 $cm^{-1}$, for 3-unsubstituted ones.

The proton nuclear magnetic resonance ($^1$H-NMR) spectrum can be used to identify labile hydrogens in dipolar aprotic solvents: 3-unsubstituted compounds (I—III) present two $NH_2$ group signals ($\Delta\delta = 0.4$ ppm, integration 1H each), which collapse when the temperature is raised to 80 °C, while the signal of the corresponding protonated compound is single (integration 3H).

Double-bonded carbon atoms of the ring can be identified by $^{13}$C-nuclear magnetic resonance ($^{13}$C-NMR) spectroscopy. In 3-substituted derivatives, the signals of carbons 2 and 4 appear at higher fields than in 3-unsubstituted ones (about 6 ppm for $C_{(2)}$ and 10 ppm for $C_{(4)}$).

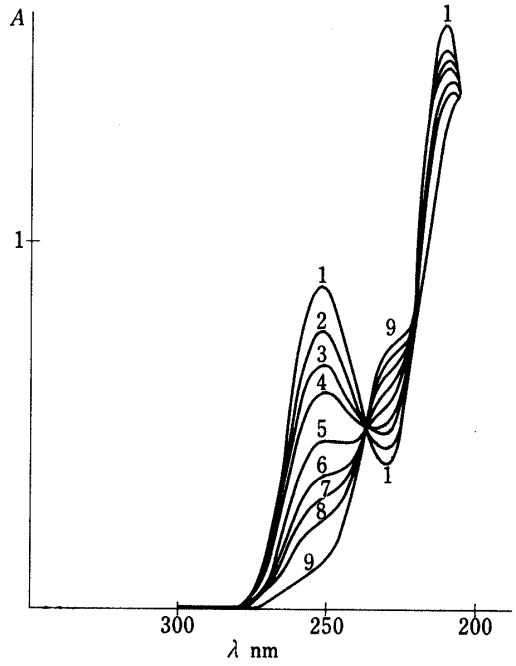
All these data are consistent with a conjugated structure B or C (Chart 2) for 3-unsubstituted compounds and an unconjugated one, as expected, (*vide supra*) for 3-substituted derivatives: in the UV spectrum the hypsochromic shift, in IR the increase of the wave number and in $^{13}$C-NMR the shieldings of the $C_{(2)}$ and $C_{(4)}$ signals reflect a decrease of conjugation.



A B C

$R^1$=H, $CH_3$, $C_6H_5$

Chart 2



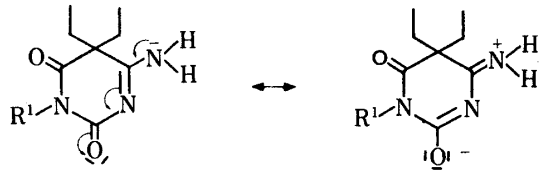



Chart 3

Fig. 2. UV Spectra of II $10^{-4}$ mol $l^{-1}$ in Methanol

1, Without $HClO_4$ addition; 2 to 9, after addition of $HClO_4$ at $2.5\times10^{-5}$, $5\times10^{-5}$, $7.5\times10^{-5}$, $1.25\times10^{-4}$, $1.75\times10^{-4}$, $2.75\times10^{-4}$ and $7.5\times10^{-4}$ mol $l^{-1}$, respectively.

It is then possible to settle the question of which of the two conjugated potential structures B or C actually exists. The assignments of observed wave numbers in the region of double-bonded carbon atoms are only in agreement with form B; 1700 and 1600 $cm^{-1}$ correspond, respectively, to $C=O_{(6)}$ and $C=O_{(2)}$ while 1550 $cm^{-1}$ is assigned to C=N. The 1600 $cm^{-1}$ band cannot be assigned to the second conjugated C=N in form C.

The individual appearance of two signals due to labile hydrogen atoms in the $^1$H-NMR spectrum of these compounds could appear consistent with form C, but these signals are close together and coalesce when the temperature increases, which is evidence of the existence of a restricted rotation at room temperature and of its inhibition at 80 °C. The participation of electrons from extranuclear nitrogen in the mesomerism of the conjugated system in form B can explain the partial double-bond character of the C–N bond and consequently the restricted rotation (Chart 3).

The spectral behavior of protonated compounds is only in agreement with the protonation of exocyclic nitrogen in form B. It causes a conjugation decrease as revealed by the hypsochromic shift observed in the UV spectrum on acidification and destroys the $\pi$ character of the exocyclic C–N bond leading to a single $^1$H-NMR signal for the three equivalent hydrogen atoms.

The observation of a retro Diels–Alder fragmentation in the mass spectrum (MS) of 3-unsubstituted derivatives and the absence of corresponding peaks for 3-substituted compounds can only be explained by the presence of an endocyclic double bond in form B (Chart 4). This conjugated form B, which is characteristic of compounds unsubstituted in the 3

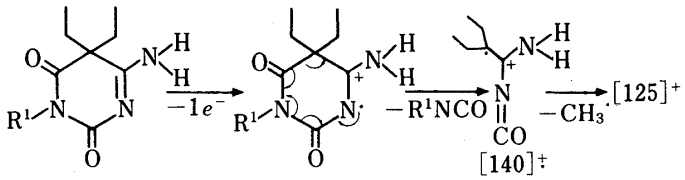


Chart 4

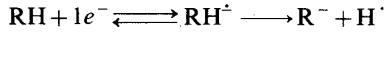


Chart 5

TABLE II. Half-Wave Potentials of Labile Hydrogen of 4-Iminobarbiturates in Aprotic Solvents

| Compd. | Substitution | | Neutral medium | | Alkaline medium | Exhaustive electrolysis |
|---|---|---|---|---|---|---|
| | (1)N | (3)N | $E^{1/2}$,[a] DMSO | $E^{1/2}$ [a] (il),[c] HMPT | $E^{1/2}$,[b] HMPT | $E^{1/2}$,[b] HMPT |
| I | —[d] | —[d] | −2.39 | −2.75 (220) | −0.67 | −0.67 |
| II | +[d] | −[d] | −2.35 | −2.71 (220) | −0.67 | −0.67 |
| III | +[d] | −[d] | −2.35 | −2.71 (210) | −0.67 | −0.67 |
| IV | −[d] | +[d] | −2.55 | −2.89 (200) | −0.65 | −0.65 |
| V | −[d] | +[d] | −2.56 | −2.90 (200) | −0.65 | −0.65 |

*a*) In volts *vs.* SCE. *b*) In volts *vs.* $Ag/Ag^+$. *c*) Limit current in nanoamperes for a concentration of $10^{-3}$ mol $l^{-1}$. *d*) +, N-alkylated; −, N-unalkylated.

position, could affect the electrochemical properties of the corresponding iminobarbiturates.

4-Iminobarbiturates presenting labile hydrogen atoms show, in either DMSO or hexamethylphosphoric triamide (HMPT), a monoelectronic reduction wave at the dropping mercury electrode. For all the tested compounds, the limit currents are slightly different and strictly obey the Ilkovic equation. The anodic wave obtained by exhaustive controlled potential electrolysis presents the same electrochemical characteristics as those observed in alkaline medium.[12] On addition of one acidic equivalent, the anodic waves resulting from either procedures disappear and the initial cathodic wave is observed. Thus the cathodic process seems to lead to a monoanion, as in the cases of barbiturates,[7] and succinimide.[14]

The mechanism is probably an electrochemical-chemical (E.C.) process in which the anion radical formed during the cathodic step would be unstable and yield the iminobarbiturate anion by rapid loss of the hydrogen atom (Chart 5). This last chemical step can also explain the lack of reversibility observed in cyclic voltammetry.

The two groups of iminobarbiturates follow the same reductive pathway in aprotic solvents but the halfwave potentials ($E_{1/2}$) are quite different when N(3) is substituted or not substituted ($\Delta E_{1/2} \simeq 0.2$ V) (Table II). This behavior is consistent with the spectral data and is related to the easier reduction of an amidinoketo conjugated system (Chart 6) than of an imido group.

The electrochemical formations of these anions were confirmed by alkylation. When only one labile hydrogen atom is present at either the 1 or the 3 position (II and IV), the same disubstituted compound (VI) is obtained when methyl iodide is added before or after electrolysis. On the other hand, compound I presents two labile hydrogen atoms as well as the two different groups of functions which can be reduced. It is therefore a good model for studying the formation and the reactivity of the anions. We reported previously the preparation from I of both N(3)-monoalkylated and N(1),N(3)-dialkylated compounds under electrochemical induction, as a probe for N(3) anion formation. The lack of an N(1)-monosubstituted derivative in this experiment was interpreted as being due to easy reduction of this compound into a new anion, which was then alkylated again, yielding the N(1),N(3)-dimethylated compound.[15] In order to test this explanation, it was desirable to avoid the

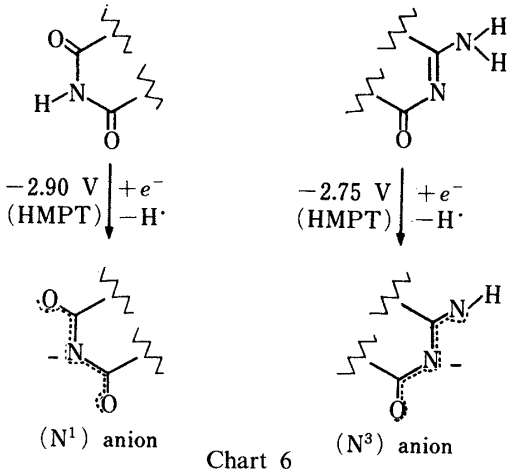



Chart 6

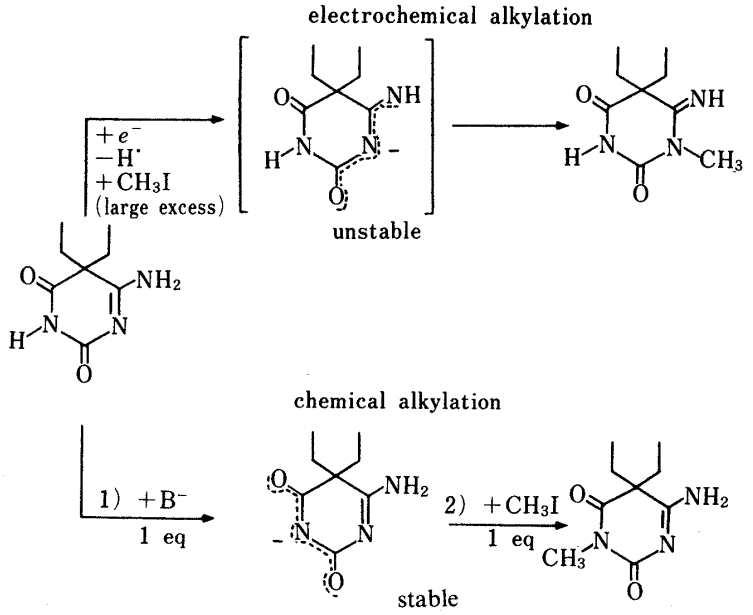



Chart 7

formation of this by-product. The use of a large excess of methyl iodide improved the regioselectivity. The N(3) anion, as soon as it is generated by reduction, udergoes a fast alkylation and does not have enough time to rearrange into the N(1) anion. The N(3)-monosubstituted compound is then obtained alone.

This N(3) regioselectivity can be compared to the N(1) alkylation obtained by classical procedures (Chart 7).

## Conclusion

An interesting relation between tautomerism and electrochemical behavior of 4-iminobarbiturates is described here. When these compounds are alkylated on N(3) their major tautomeric form presents an imido system which can be reduced less easily than the amidinoketone one which is characteristic of 3-unalkylated compounds. It is thus possible to identify the structure of such compounds on the basis of their electrochemical behavior.

### Experimental

**Samples**——I was prepared by condensation of 2,2-diethyl ethylcyanoacetate with urea.[16] The syntheses of N(1)-monoalkylated compounds (II and III) and N(1),N(3)-dialkylated compounds (VI and VII) from I were

described in a previous paper.[8] The N(3)-monoalkylated derivatives cannot be obtained from I in the same manner. Compounds IV and V were obtained by a similar condensation.[16] The purity of all the compounds was carefully checked by elemental analysis and spectroscopic methods (*vide infra*).

**Physicochemical Analysis**

**Apparatus**——All melting points were determined with a Kofler apparatus and are uncorrected. Elemental analyses were carried out using a Perkin Elmer 240 Auto analyzer. UV spectra were taken on a Pye Unicam SP80 spectrophotometer and IR spectra in potassium bromide disks on a Perkin Elmer 39 spectrophotometer. The $^1$H-NMR spectra were recorded by using a Perkin Elmer R 12B spectrometer (60 MHz) and $^{13}$C-NMR spectra by using a Varian CFT 20 apparatus. In both cases, tetramethylsilane (TMS) served as an internal standard. Mass spectra were obtained with a quadrupolar Nermag R10 10 C mass spectrometer (source temperature, 120 °C; electron energy, 70 eV).

**Spectral Data of Iminobarbiturates**——I: mp 265 °C. UV $\lambda_{max}^{ethanol}$ nm ($\varepsilon$): 248 (13000). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1700 (C=O(6)), 1660 (C=O(2)), 1540 (C=N). $^1$H-NMR (10% solution in DMSO-$d_6$) $\delta$: 0.7 (6H, t, C$\underline{H}_3$–CH$_2$), 1.9 (4H, q, CH$_3$–C$\underline{H}_2$), 7.95 (1H, s, 1H of NH$_2$), 8.4 (1H, s, 1H of NH$_2$), 10.8 (1H, s, N(1)-H). $^{13}$C-NMR (10% solution in DMSO-$d_6$) $\delta$: 9.1 (q, $\underline{C}$H$_3$–CH$_2$), 31.6 (t, CH$_3$–$\underline{C}$H$_2$), 52.0 (s, C(5)), 156.9 (s, C(2)), 172.75 (s, C(4 or 6)), 175.75 (s, C(4 or 6)). MS *m/z*: 155 (M−C$_2$H$_4$), 154 (M−C$_2$H$_5$), 140 (M−C$_2$H$_4$–CH$_3$ and M−NHCO), 125 (M−HNCO–CH$_3$), 111, 97, 69, 55, 43, 41. *Anal.* Calcd for C$_8$H$_{13}$N$_3$O$_2$: C, 52.44; H, 7.15; N, 22.94. Found: C, 52.52; H, 7.11; N, 22.77.

II: mp 258 °C (ethanol). UV $\lambda_{max}^{ethanol}$ nm ($\varepsilon$): 252 (9300). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1700 (C=O(6)), 1650 (C=O(2)), 1550 (C=N). $^1$H-NMR (10% solution in DMSO-$d_6$) $\delta$: 0.6 (6H, t, C$\underline{H}_3$–CH$_2$), 1.9 (4H, q, CH$_3$–C$\underline{H}_2$), 3.1 (3H, s, N(1)-CH$_3$), 7.95 (1H, s, 1H of NH$_2$), 8.4 (1H, s, 1H of NH$_2$). $^1$H-NMR (10% solution in DMSO-$d_6$, 80 °C) $\delta$: 0.7 (6H, t, C$\underline{H}_3$–CH$_2$), 2.0 (4H-q, CH$_3$–C$\underline{H}_2$), 3.1 (3H, s, N(1)-CH$_3$), 7.8—8.3 (2H, s, NH$_2$). $^1$H-NMR (perchloric acid salt, 10% solution in DMSO-$d_6$) $\delta$: 0.75 (6H, t, C$\underline{H}_3$–CH$_2$), 2.05 (4H, q, CH$_3$–C$\underline{H}_2$), 3.15 (3H, s, N(1)-CH$_3$), 7.8—8.3 (3H-s, NH$_3^+$). $^{13}$C-NMR (10% solution in DMSO-$d_6$) $\delta$: 9.05 (t, $\underline{C}$H$_3$–CH$_2$), 27.05 (q, N(1)-CH$_3$), 32.1 (t, CH$_3$–$\underline{C}$H$_2$), 52.3 (s, C(5)), 156.2 (s, C(2)), 172.9 (s, C(4 or 6)), 174.35 (s, C(4 or 6)). MS *m/z*: 169 (M−C$_2$H$_4$), 168 (M−C$_2$H$_5$), 154 (M−C$_2$H$_4$–CH$_3$), 140 (M−CH$_3$NCO), 125 (M−CH$_3$NCO–CH$_3$), 111, 97, 69, 55, 43, 42, 41. *Anal.* Calcd for C$_9$H$_{15}$N$_3$O$_2$: C, 54.82; H, 7.61; N, 21.31. Found: C, 54.58; H, 7.83; N, 21.06.

III: mp 239—240 °C (acetone). UV $\lambda_{max}^{ethanol}$ nm ($\varepsilon$): 252 (12200). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1700 (C=O(6)), 1650 (C=O(2)), 1565 (C=N). $^1$H-NMR (10% solution in DMSO-$d_6$) $\delta$: 0.65 (6H, t, C$\underline{H}_3$–CH$_2$), 1.85 (4H, q, CH$_3$–C$\underline{H}_2$), 4.95 (2H, s, N(1)-CH$_2$), 7.3 (5H, m, C$_6$H$_5$), 8.1 (1H of NH$_2$), 8.55 (1H, s, 1H of NH$_2$). $^{13}$C-NMR (10% solution in DMSO-$d_6$) $\delta$: 8.95 (q, $\underline{C}$H$_3$–CH$_2$), 32.35 (t, CH$_3$–$\underline{C}$H$_2$), 43.35 (t, N(1)-CH$_2$), 52.3 (s, C(5)), 127.0, 127.75, 128.2 (3d, C$_6$H$_5$), 138.05 (s, C$_6$H$_5$), 155.8 (s, C(2)), 172.8 (s, C(4 or 6)), 174.35 (s, C(4 or 6)). MS *m/z*: 273 (M),245 (M−C$_2$H$_4$), 244 (M−C$_2$H$_5$), 230 (M−C$_2$H$_4$–CH$_3$), 154 (M−C$_6$H$_5$CH$_2$), 140 (M−C$_6$H$_5$CH$_2$NCO), 132, 125 (M−C$_6$H$_5$CH$_2$NCO–CH$_3$), 111, 106, 97, 65, 55, 44, 42. *Anal.* Calcd for C$_{15}$H$_{19}$N$_3$O$_2$: C, 65.93; H, 6.96; N, 15.38. Found: C, 65.80; H, 6.89; H, 15.26.

IV: mp 137 °C (ethanol). UV $\lambda_{max}^{ethanol}$ nm ($\varepsilon$): 226 (6900). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1690—1710 (C=O(2 and 6)), 1615 (C=N). $^1$H-NMR (10% solution in DMSO-$d_6$) $\delta$: 0.65, (6H, t, C$\underline{H}_3$–CH$_2$), 1.85 (4H, q, CH$_3$–C$\underline{H}_2$), 3.2 (3H, s, N(3)-CH$_3$), 8.4 (1H, s, C=NH), 9.7 (1H, s, N(1)-H). $^{13}$C-NMR (10% solution in DMSO-$d_6$) $\delta$: 9.5 (q, $\underline{C}$H$_3$–CH$_2$), 28.9 (q, N(3)-CH$_3$), 32.7 (t, CH$_3$–$\underline{C}$H$_2$), 55.25 (s, C(5)), 149.8 (s, C(2)), 171.9 (s, C(6)). MS *m/z*: 169 (M−C$_2$H$_4$), 168 (M−C$_2$H$_5$), 154 (M−C$_2$H$_4$–CH$_3$), 125, 111, 69, 57, 55, 41. *Anal.* Calcd for C$_9$H$_{15}$N$_3$O$_2$: C, 54.82; H, 7.61; N, 21.31. Found: C, 54.97; H, 7.51; N, 21.26.

V: mp 110 °C. UV $\lambda_{max}^{ethanol}$ nm ($\varepsilon$): 229 (5900). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1705—1720 (C=O(2 and 6)), 1620 (C=N). $^1$H-NMR (10% solution in DMSO-$d_6$) $\delta$: 0.60 (6H, t, C$\underline{H}_3$–CH$_2$), 1.90 (4H, q, CH$_3$–C$\underline{H}_2$), 5.10 (2H, s, N(3)-CH$_2$), 7.25 (5H, m, C$_6$H$_5$), 9.0 (1H, s, C=NH), 11.2 (1H, s, N(1)-H). $^{13}$C-NMR (10% solution in DMSO-$d_6$) $\delta$: 9.1 (q, $\underline{C}$H$_3$–CH$_2$), 32.75 (t, CH$_3$–$\underline{C}$H$_2$), 44.25 (t, N(3)-CH$_2$), 55.3 (s, C(5)), 126.9, 127.6, 128.15 (3d, C$_6$H$_5$), 138.0 (s, C$_6$H$_5$), 150.35 (s, C(2)), 162.4 (s, C(4)), 172.25 (s, C(6)). MS *m/z*: 273 (M), 272 (M−H), 245 (M−C$_2$H$_4$), 244 (M−C$_2$H$_5$), 230 (M−C$_2$H$_4$–CH$_3$), 201 (M−C$_2$H$_5$–HNCO), 187 (M−C$_2$H$_4$−CH$_3$–HNCO), 169 (M−C$_6$H$_5$CHN), 132, 106, 104, 91 (C$_7$H$_7$), 65, 55. *Anal.* Calcd for C$_{15}$H$_{19}$N$_3$O$_2$: C, 65.93; H, 6.96; N, 15.38. Found: C, 66.08; H, 7.07; N, 15.24.

VI: mp 40 °C (water). UV $\lambda_{max}^{ethanol}$ nm ($\varepsilon$): 234 (7750). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1720 (C=O(6)), 1675 (C=O(2)), 1620 (C=N). $^1$H-NMR (10% solution in DMSO-$d_6$) $\delta$: 0.6 (6H, t, C$\underline{H}_3$–CH$_2$), 1.95 (4H, q, CH$_3$–C$\underline{H}_2$), 3.15 (3H, s, N(1)-CH$_3$), 3.25 (3H, s, N(3)-CH$_3$), 8.6 (1H, s, C=NH). $^{13}$C-NMR (10% solution in DMSO-$d_6$) $\delta$: 9.1 (q, $\underline{C}$H$_3$–CH$_2$), 28.05 (q, N(1)-CH$_3$), 29.7 (q, N(3)-CH$_3$), 33.2 (t, CH$_3$–$\underline{C}$H$_2$), 55.65 (s, C(5)), 150.6 (s, C(2)), 161.6 (s, C(4)), 171.65 (s, C(6)). MS *m/z*: 183 (M−C$_2$H$_4$), 182 (M−C$_2$H$_5$), 168 (M−C$_2$H$_4$–CH$_3$), 125, 111, 57, 55, 42, 41. *Anal.* Calcd for C$_{10}$H$_{17}$N$_3$O$_2$: C, 56.87; H, 8.06; N, 19.9. Found: C, 56.90; H, 7.75; N, 19.63.

VII: mp 107 °C (methanol). UV $\lambda_{max}^{ethanol}$ nm ($\varepsilon$): 235 (7900). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1720 (C=O(6)), 1675 (C=O(2)), 1620 (C=N). $^1$H-NMR (10% solution in DMSO-$d_6$) $\delta$: 0.7 (6H, t, C$\underline{H}_3$–CH$_2$), 1.9 (4H, q, CH$_3$–C$\underline{H}_2$), 5.0 (2H, s, N(1)-CH$_2$), 5.2 (2H, s, N(3)-CH$_2$), 7.30 (10H, m, 2 C$_6$H$_5$), 9.15 (1H, s, C=NH). $^{13}$C-NMR (10% solution in DMSO-$d_6$) $\delta$: 8.95 (q, $\underline{C}$H$_3$–CH$_2$), 33.3 (t, CH$_3$–$\underline{C}$H$_2$), 44.45 (t, N(1)-CH$_2$), 45.35 (t, N(3)-CH$_2$), 55.5 (s, C(5)), 127.0, 127.4, 127.55, 127.7, 128.15, 128.4 (6d, C$_6$H$_5$), 137.2, 137.8 (2s, C$_6$H$_5$), 150.65 (s, C(2)), 161.1 (s, C(4)), 171.55 (s, C(6)). MS *m/z*: 363 (M), 362 (M−H), 320 (M−C$_2$H$_4$–CH$_3$), 272 (M−C$_6$H$_5$CH$_2$), 259 (M−C$_6$H$_5$CHN), 201 (M−C$_2$H$_5$–C$_6$H$_5$CH$_2$NCO), 187 (M−C$_2$H$_4$–CH$_3$–C$_6$H$_5$CH$_2$NCO), 132, 106, 98, 91 (C$_7$H$_7$), 65, 55, 42. *Anal.* Calcd for C$_{22}$H$_{25}$N$_3$O$_2$: C, 72.72; H, 6.88; N, 11.57. Found: C, 72.50; H, 6.89; N, 11.35.

**Electrochemical Procedures**——Solvents, Electrolytes and Reagents: HMPT (99%, OSI) was purified according to Gal and Yvernault.[17] The distillate was kept under a nitrogen atmosphere in the dark at 4 °C. Purification of DMSO (Merck, for spectroscopy) was accomplished according to Kolthoff and Reddy.[18] Purifications of tetrabutylammonium perchlorate (TBAP) and iodide (TBAI) were carried out according to Mann.[19] A 0.1 mol $l^{-1}$ tetrabutylammonium hydroxide (TBAH) in methanol/2-propanol (Merck, for titration) solution was used as the source of hydroxide and reagent-grade perchloric acid (Merck) as the proton donor. Methyl iodide ($CH_3I$) (Merck, for synthesis) was used as the alkylating agent, without further purification.

Apparatus: Polarographic measurements were made on a PRG5 Tacussel potentiostat coupled with a EPL 1 Tacussel recorder. The three electrode jacketed cell used was of conventional design and was thermostated at 25±0.1 °C. The reference electrode and the sample compartment were separated by a TBAP/solvent bridge. Cyclic voltammetric triangular wave forms were obtained from a GSTP 3 Tacussel function generator. Data were recorded on a R 5103M Tektronix oscilloscope. For controlled potential electrolysis, potentials were imposed by a PEM 1000-1 Tacussel potentiostat. The quantity of electricity was measured using a IG 5 Tacussel integrator.

Procedures: For all the electrochemical experiments, the solutions were purged with nitrogen and then kept under a blanket of nitrogen during the recording. For polarography, the working electrode consisted of a MPO Tacussel dropping mercury electrode with an adjustable drop time. A platinum wire served as an auxiliary electrode. The reference electrode was an aqueous saturated calomel electrode (SCE) in DMSO and freshly prepared $Ag/AgClO_4$ (0.1 mol $l^{-1}$ in HMPT).[20] The D.C. polarographic data were obtained at a controlled drop time of 1 s, using a capillary with a mercury flow rate at open circuit of 0.55 mg $s^{-1}$ (in HMPT). Iminobarbiturate solutions, in which the background electrolyte was 0.1 mol $l^{-1}$ TBAP, were about $10^{-3}$ mol $l^{-1}$. Where required, solution of perchloric acid, prepared by dilution of concentrated acid to 0.1 mol $l^{-1}$ in DMSO or HMPT, or the alcoholic TBAH solution were added to the cell. For cyclic voltammetry, a silver button electrode plated with mercury was used as the working electrode while the two other electrodes and solutions were identical to those described above. Cyclic voltammograms were recorded at different potential scan rates (0.1 to 100 V $s^{-1}$). For controlled potential electrolysis, a mercury pool *ca.* 1 cm deep and 12 $cm^2$ area was placed in the cell. A large surface platinum auxiliary electrode was used in the anodic compartment separated by a solvent bridge containing background electrolyte. The reference electrode was the same as described above. Nitrogen was continuously bubbled through the solution during electrolysis and a magnetic stirrer was used. In order to determine the number of electrons ($n$) transferred per mole of iminobarbiturate, the above-mentioned solutions were used. For all the tested iminobarbiturates $n$ was about 1. For preparative electrolysis *vide infra.*

**Synthesis**

**Monomethylated Iminobarbiturates**——HMPT, TBAI, TBAH, $CH_3I$ and the electrochemical apparatus were as described above.

a) Extraction and Purification: Two kinds of chromatographic methods were performed. The first separative step consisted of a liquid chromatography procedure, and preparative high performance liquid chromatography (HPLC) was used for the final purification. A column containing 65 g of active basic aluminium oxide (Merck, for chromatography) was employed. HPLC was performed using a Waters 6000 A liquid chromatograph with a Waters U6K injector, a Cecil CE 2012 variable-wavelength UV spectrophotometer detector (wavelength: 228 nm), a Omniscribe D 5117 recorder and a reversed-phase C 18 column (Lichroprep RP 18 2.0 × 30 cm, particle size 25 : 40 $\mu$m). Reagent-grade solvents were used. Eluents were pure chloroform and a chloroform–ethanol (9 : 1, v/v) mixture in liquid chromatography and a methanol–water–chloroform (45 : 55 : 2, v/v) mixture in HPLC.

b) Electrochemical Synthesis of IV from I: A solution of I (1 g, 5.8 mmol) and TBAI (2 g, 5.4 mmol) in HMPT (25 ml) was electrolyzed at a potential of −2.75 V ($Ag/AgClO_4$ $10^{-1}$ mol $l^{-1}$) for 8 h. This electrochemical reduction was performed in the presence of a twenty-fold excess of methyl iodide which was continuously added in order to avoid artifacts caused by loss of the volatile alkylating agent under these conditions. A 5 ml aliquot of the resulting solution was charged onto the alumina column. The column was washed with 200 ml of chloroform and the eluate containing HMPT was discarded. Then 125 ml of a mixture of chloroform and ethanol was applied to the column. The eluate was collected, and the residue obtained after evaporation, under reduced pressure at room temperature, was purified by preparative HPLC (injected volume, 1 ml; flow rate, 3 ml/min; pressure, 210 bar). The 32—46 min eluate fraction was collected, and evaporation of the solvent gave a white solid. The spectral analysis was performed after recrystallization from ethanol. The synthesized compound was 5,5-diethyl-4-imino-3-methylbarbiturate (IV) the spectral data of which are given above. The residual electrolysis solution was treated in a similar manner. The total yield was about 20%.

c) Chemical Synthesis of II from I: TBAH (5.8 mmol) was added to a solution of I (1 g, 5.8 mmol) in HMPT (10 ml). After addition of methyl iodide (5.8 mmol) the reaction mixture was stirred at room temperature for 15 min. Extraction and purification of the obtained monomethylated compound (II) were the same as described for IV (except for the preparative HPLC step: the 24—38 min eluate fraction was collected). The spectral data are described above. The total yield was about 30%.

**Dimethylated Iminobarbiturate (VI)**——a) Electrochemical Synthesis of VI from II: A solution of II (0.5 g, 2.7 mmol) and TBAI (1 g, 2.7 mmol) in HMPT (25 ml) was electrolyzed at a potential of −2.75 V ($Ag/AgClO_4$

$10^{-1}$ mol $l^{-1}$) for 4 h. This electrochemical reduction was performed in the presence of a twenty-fold excess of methyl iodide. The reaction mixture was poured into 100 ml of water-ice and extracted with chloroform. The extract was washed with water and dried over anhydrous sodium sulfate. The residue obtained by concentrating the solution was purified by successive recrystallization from water. The synthesized compound was VI. The spectral data are given above.

b) Electrochemical Synthesis of VI from IV: The same procedure as for the synthesis of VI from II was performed except that the controlled potential value was $-2.90$ V (Ag/$AgClO_4$ $10^{-1}$ mol $l^{-1}$).

## References and Notes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