Single Electron Transfer Reactions of the Ambident Anion of 2-Cyano-3-ethyl-1-methyl-Δ^3-piperideine[†][1]

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The reaction of the ambident anion (**2**) derived from 2-cyano-3-ethyl-1-methyl-Δ^3-piperideine (**1**) with t-butyl halides and p-$NO_2C_6H_4CH_2X$ led to formation of the C-2 product (**3**) and the C-4 product (**6**) respectively *via* a probable single electron transfer reaction; dimerization of anion (**2**) gave dimers (**8**), (**9**), and (**10**) by electron transfer to *m*-dinitrobenzene, I_2, and 2-methyl-2-nitropropane.

During a recent study[2] of the reactivity of the ambident anion (**2**) derived from the 2-cyano-Δ^3-piperideine (**1**) towards electrophiles it was observed that (**2**) reacted with t-butyl halides (Bu^tX) to give the C-2 substituted product (**3**)[‡] in 40—90% yields[3,4] (Scheme 1). In the light of this unexpected result involving C–C bond formation between two tertiary centres two pertinent questions arose: (i) by what mechanism does the reaction occur since alkylation of carbanions with tertiary-alkyl halides by an S_N2 process is unfavourable (low reaction rate, and competing dehydrohalogenation), and (ii) why was the C-2 product (**3**), and *not* the less sterically crowded and thermodynamically more stable C-4 product (**5**), formed?

The rate of reaction followed the order Bu^tCl (60 °C, 1 h) $\ll$ Br $\leqslant$ I (−78 °C, 1—5 min) which was compatible with S_N2 behaviour. However, the isolation of varying trace quantities of the Δ^2-piperideine (**7**), and in particular the (4–4 linked) dimer (**8**)[‡] suggested the presence of radical species.

A number of investigations provide evidence that reactions of this type can occur by a single electron transfer (SET) mechanism.[3e,5] Transfer of an electron from A^- to RX results in formation of a radical anion–radical pair (RARP) (Scheme 2).[6] Decomposition of this complex can then occur by an inner sphere (recombination of radicals within the solvent cage)[3e] or by an outer sphere ($S_{RN}1$ or radical chain

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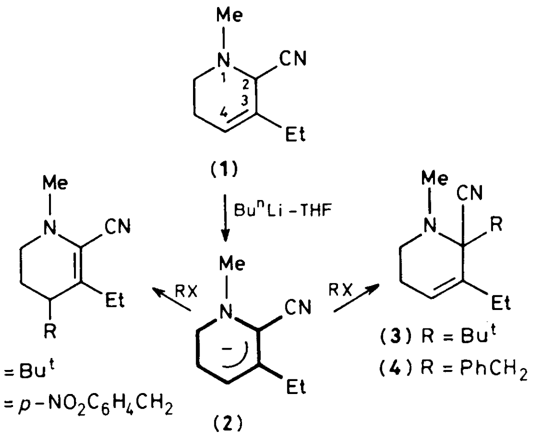
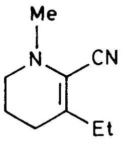
[†] This work was presented at the 8th International Congress of Heterocyclic Chemistry, Graz (Austria) 1981, and is part of the PhD Thesis of M. Urrea, Paris 1980. See also ref. 3f.

[‡] Compound (**3**) (colourless oil) ^{1}H n.m.r. ($CDCl_3$) δ: 1.08 (m, 12H, Me), 2.61 (s, NMe), and 6.00 (br. s, H-4); ^{13}C n.m.r. ($CDCl_3$) δ 51.3 (C-2), 137.8 (C-3), 126.6 (C-4), and 118.3 p.p.m. (CN). Compound (**8**) (colourless oil) (single isomer); i.r. (film): 2220s and 1630 cm^{-1}; ^{1}H n.m.r. ($CDCl_3$) δ: 2.06 (m, 2H, H-4) and 2.76 (s, 6H, NMe); ^{13}C n.m.r. ($CDCl_3$) δ 120.8 (C-2), 132.3 (C-3), 35.35 (C-4), and 114.9 p.p.m. (CN). Compound (**9**) (pale yellow oil) (single isomer); ^{1}H n.m.r. ($CDCl_3$) δ: 0.91, 1.01 (2 × t, 3H each, Me), 2.28 (s, 6H, NMe), and 5.40 (br. s, 2H, H-4). Compound (**10**) (colourless oil) (single isomer); ^{1}H n.m.r. ($CDCl_3$) δ: 1.14 (2 × t, 6H, Me), 2.39, 2.82 (s, NMe), and 5.92 (d, 1H, H-4); ^{13}C n.m.r. ($CDCl_3$) δ 36.7 (C-4), 40.8, 42.8 (NMe), 47.9, 49.7 (C-6), 67.4 (C-2), 114.9, 117.7 (CN), 125.7, 136.4 (C-3,4), 121.3, and 128.0 p.p.m. (C-2,3).



Scheme 1



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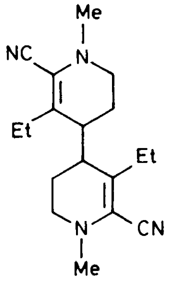

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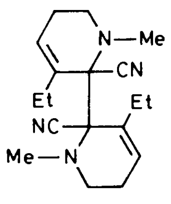

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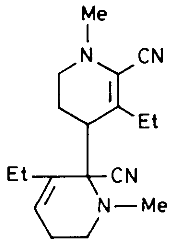
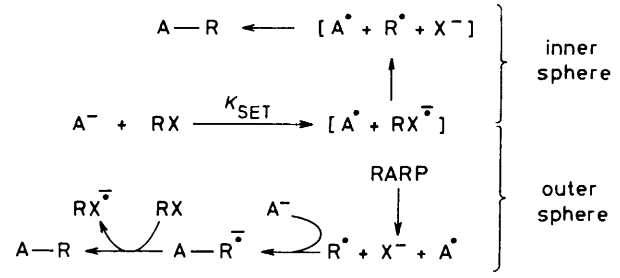


(10)

mechanism)[7] process. The pathway followed depends upon the conditions as well as the stabilities or lifetimes of the RARP components. Arguments have recently been presented which suggest that transfer of an electron from anions such as (2) should be particularly favourable since the resultant radical would be stabilized by the capto-dative substituent effect.[8]

Reaction of (2) with Bu^{t}X in the presence of phenyl-*N*-t-butylnitrone,[9] 2,2′,6,6′-tetramethylpiperidine *N*-oxide, nitrosodurene,[10] *m*-dinitrobenzene[11] (mdb), 12-crown-4,[3b] and oxygen was thus examined to determine the influence of these additives on the outcome of the reaction. In the presence of oxygen, oxidation products were obtained,§ and in the presence of mdb preferential formation of the dimer (8) was observed (see below). However, despite numerous trials in the presence of the other radical traps (0.1—1 equiv.), and 12-crown-4 no significant variations in the yields of compound (3) were observed. Similarly no signals could be detected when the reaction with Bu^{t}Br was followed by e.s.r. The negative results obtained in these latter experiments provide strong evidence against an $S_{RN}1$ mechanism, but do not exclude the possibility of an inner sphere reaction. Such a mechanism is



Scheme 2

not unacceptable since Bu$^{t\bullet}$ is a non-stabilized transient radical, *i.e.* $E_S = 0$.[12]

Positive evidence that (2) can react by transfer of an electron was obtained from the following experiments. From the reaction of (2) with p-NO$_2$C$_6$H$_4$CH$_2$X (an excellent electron acceptor)[7a,c] three products were isolated, the C-4 substituted enaminonitrile (6) (X = Br, 9%; X = Et$_3$N$^+$, 14%), the dimer (8) (6—8%), and *p,p′*-dinitrobibenzyl (15—30%) (remaining polar materials were not characterized). It was clear from the isolation of significant quantities of the two dimers that SET involving the expected $S_{RN}1$ pathway had occurred. The formation of the C-4 alkylation product (6) was in striking contrast with the results of the reaction of (2) with Bu^{t}X (probable SET reaction), and benzyl bromide (S_N2 reaction)[2] where products (3) and (4), respectively, were formed. When this latter experiment was conducted in the presence of mdb formation of the (4—4 linked) dimer (8) was observed. Electron transfer to mdb proved to be very facile where K_{SET} (mdb) > K_{SET} (Bu^{t}X) or K_{SET} (p-NO$_2$C$_6$H$_4$CH$_2$X).

In separate experiments rapid formation of dimeric aminonitriles was observed on reaction of (2) with mdb, I$_2$, and in particular 2-methyl-2-nitropropane in tetrahydrofuran (THF) at −30 °C. Even at −110 °C the reaction with 2-methyl-2-nitropropane was fast (<*ca.* 30 s). By quick chromatographic separation of the crude product mixture three dimers, (9) (2-2 linkage) 10%,‡ (10) (2-4) 30%,‡ and (8) (4-4) 60% were isolated. A key discovery concerning the formation of these products was that on simply heating (*ca.* 40 °C, 3—5 min) a chloroform solution of the dimer mixture the transformation (9) + (10) + (8) → (8) occurred. It was concluded from this experiment that dimerization of (2) initially involves formation of the radical anion of the (2-2) dimer (9),¶ and that this radical anion or dimer (9) itself (as in the above experiment) formed on loss of e$^-$ rearranges by a dissociation–recombination process through the (2-4) dimer (10) to the less crowded and more stable (4-4) dimer (8). The important point to note was the special reactivity of the C-2 position. This may be the result of a higher electron density at this position in the anion (2) and its resultant radical.[13]

Assuming that the formation of (3) involves an inner sphere SET reaction the different regiochemical outcome of the reaction of (2) with Bu^{t}X and p-NO$_2$C$_6$H$_4$CH$_2$X can be rationalized on the basis of this result. Formation of (3) involves the combination of the t-butyl and aminonitrile radicals by reaction at C-2 of the aminonitrile component. As Bu$^{t\bullet}$ is a non-stabilized species there would be little tendency for this initially formed product to dissociate once formed. In contrast, the reaction of p-NO$_2$C$_6$H$_4$CH$_2$X with (2) by an $S_{RN}1$ process would give a radical anion which could dissociate to (2) and the stabilized *p*-nitrobenzyl radical,[7c] and recombine[14]

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§ The results of these experiments will be reported at a later date.

¶ As electron transfer to the oxidizing agent is rapid and the aminonitrile radical is stabilized (ref. 8) the formation of (9) may also involve the coupling of aminonitrile radicals.

to give (**6**) after final loss of an electron. If this latter reaction occurs by an inner sphere process, radical dissociation–recombination of the initial C-2 alkylation product could equally well occur.

In conclusion, the capacity of (**2**) to react as an electron donor in SET reactions was demonstrated. The lack of any significant influence of radical inhibitors on the yields of product (**3**) however suggests that the reaction of (**2**) with Bu^{t}X occurs by an inner sphere SET mechanism.

We thank M. Crozet, L. Stella, and J. M. Surzur for fruitful discussions.

Received, 25th April 1983; Com. 503

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