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Comparison of the Partition Between Polar and SET Pathways in the $S_{RN}1$ Mechanism for the Nitronate and Diethyldithiocarbamate Anions. An Unexpected Result.

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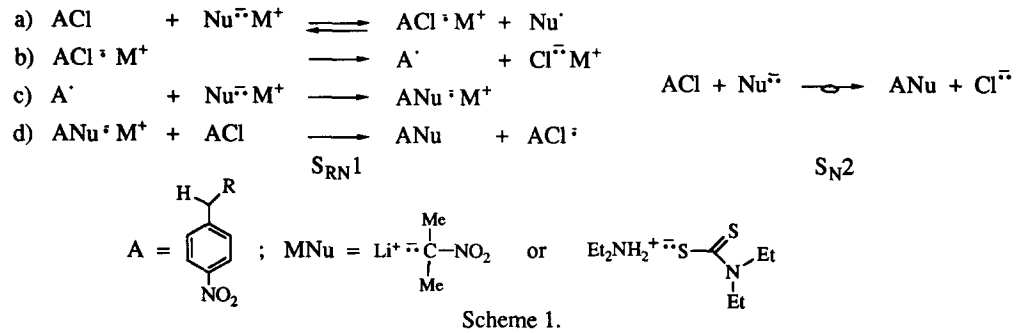
Abstract: Competition between $S_{RN}1$ and S_N2 mechanisms is discussed according to the stereochemical results in the alkylation of two anions by optically active α-chloro*para*nitrophenylethane **1**. In the reaction of **1** with the ambident anion of 2-nitropropane **2**, competing $S_{RN}1$ and S_N2 processes take place, giving C-alkylation **3** with complete racemization and O-alkylation **4** products respectively. On the other hand, S-alkylation of the diethyldithiocarbamate anion **5** by the halide **1** involves also an $S_{RN}1$-S_N2 competition giving the same product **6** with an indication of a less important participation of the $S_{RN}1$ pathway despite the fact that dithiocarbamate is a better reducing agent than nitronate.

Electron transfer induced chain reactions of substitution where discovered for organic substrates[1] on compound, where the substituted group was linked to an sp^3 carbon. This mechanism was then extended to aromatic[2] and heteroaromatic[3] substrates where the substituted group is linked to an sp^2 carbon. Curiously, most of the mechanistic in depth verifications[4] and improvements[5] have been performed in the aromatic series.[6] Nevertheless the potential of using asymetric carbon in sp^3 types of substrates provides an attractive possibility for gaining further insights on this important and general[7] mechanistic pattern of reactivity. This is the aim of the present report. We will show that, in partition of polar versus SET participation to the overall reactivity, the stronger reducing nucleophile is not necessarily the one yielding the highest participation of electron transfer.

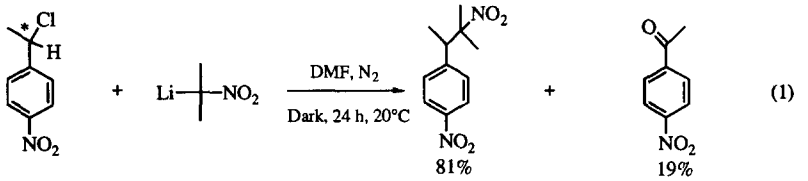
In some alkylation of ambident anions, the S_N2 and the E.T mechanisms compete.[1] Thus, nitronate anion reacting with *p*-nitrobenzylic substrates leads to C-alkylation (E.T) and O-alkylation products (S_N2) as shown in scheme 1 (R = H).

In scheme 1 when R is different from H, the stereochemical course of the $S_{RN}1$ mechanism may be followed. It has been shown to lead to racemization[8] whereas the S_N2 leads to inversion of configuration.[9] It should be noted, however, that for cyclohexyl centered substrates partial retention of configuration has been reported[10] ; this results because of step c) rate constant (scheme 1) was large enough to compete with inversion of the cyclohexyl radical.



Scheme 1.

Treatment of R α-*para*nitrophenylethanol ($[\alpha]_D^{20}$ = +14 ; c = 2, éthanol ; e.e = 48%), obtained by reduction of *para*nitroacetophenone, with thionyl chloride[9] yielded the R enantiomer of **1** (scheme2) ($[\alpha]_{546}^{20}$ = +26 ; c = 6, éthanol ; e.e = 48%). The S enantiomer of α-*para*nitrophenylethanol was obtained in better enantiomeric purity ($[\alpha]_D^{20}$ = -29 ; c = 2, éthanol ; e.e = 95%) through the reduction of *para*nitroacetophenone using (-)-B-chlorodiisopinocampheylborane ((-)-DIP-Cl) according to ref[11,12]. This S-enantiomer by reaction with thionyl chloride provided **S-1** ($[\alpha]_D^{20}$ = -24 ; c = 0.6, éthanol ; e.e = 95%). These enantiomers must be kept in the cold because, at room temperature, they slowly racemize over a period of weeks. Both **R-1** and **S-1**, when reacted with the nitronate anion in a black painted flask, led to a substitution product **3** completly racemized in agreement with Kornblum's[8] and Norris[13] results. The ratio of electron transfer vs S_N2 pathways for this nitronate anion is provided by the ratio of products **[3]/[4]** (scheme 2).



1 Racemic
$R[\alpha]_{546}^{20}$ = + 26 (c = 6, ethanol)
enantiomeric excess = 48%
$S[\alpha]_D^{20}$ = - 24 (c = 0.6, ethanol)
enantiomeric excess = 95%

2

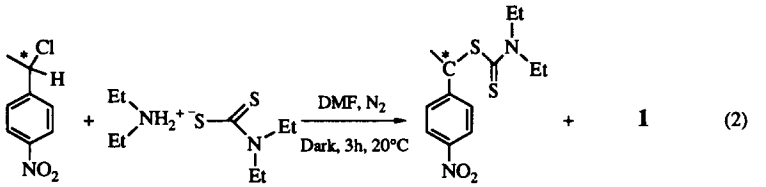
3 Racemic
$[\alpha]_{546}^{20}$ = + 0,00 (c = 6, $CHCl_3$)
$[\alpha]_{546}^{20}$ = + 0,00 (c = 6, $CHCl_3$)

4

Scheme 2.

An intuitive guess for the importance of the electron transfer pathway participation in such a competition would be that nucleophiles of increasing reducing power abilities should increasingly participate to the electron transfer pathway.[14] At the begining of the study of electron transfer induced chain reactions, the emphasis was essentially laid upon the necessity for the electron transfer step to be feasible : $E°_s > E°_p$ ($E°_s$ is the standard reduction potential of the couple $ArX/ArX^{·-}$ and $E°_p$ is the standard potential of the substitution product $ArNu/ArNu^{·-}$)[4a]. The diethyldithiocarbamate anion ($E°$ = - 0.64 V/ECS/25°C/H_2O)[15] is a better reducing agent than the nitronate anion ($E°$ = + 0.04 V/ECS/25°C/acetonitrile).[16] In terms of rate of initiation step (a) in scheme 1, Marcus theory[17] allows an evaluation of the relative rates of electron transfer. Taking values of λ = 50 Kcal/mole for the nitronate[18], 30 Kcal/mole for the diethyldithiocarbamate, 20 Kcal/mole for ACl (scheme 1)[19]

and an approximative value of E° = -0.86 V/ECS for ACl[18] one would expect that the ratio of rates of electron transfer for nitronate with respect to that of diethyldithiocarbamate be approximately 10^{-9}.



1 (2)

1 **5** **6**

Racemic Racemic

$R[\alpha]^{20}_{546}$ = + 26 (e.e = 48%) $S[\alpha]^{20}_{D}$ = - 45 (c = 5, $CHCl_3$; e.e = 18%[(1)])

i.e = 40% of S_N2 and 60% of $S_{RN}1$

$S[\alpha]^{20}_{D}$ = - 24 (e.e = 95%) $R[\alpha]^{20}_{D}$ = + 87 (c = 5, $CHCl_3$; e.e = 38%[(1)])

i.e = 40% of S_N2 and 60% of $S_{RN}1$

(1) = The e.e is determined by HPLC separations on a chiral phase "CHIRALCEL 250 * 4.6 mm"

Scheme 3.

The reaction of **1** with diethyldithiocarbamate anion **5** (scheme 3) is, under the same conditions, more rapid than with the nitronate **2**. It yields only one substitution product and the respective participation of S_N2 and $S_{RN}1$ is measured by the stereochemical outcome shown in scheme 3. This stereochemical outcome was measured by two independent methods. The first one is HPLC separation on a chiral phase (chiralcel 250*4.6 mm) which only provides the percentage of racemization.[20] The second is NMR spectroscopy in nematic liquid crystals.[21] Since compounds of structure type **1** or **2** have been intensively studied by this NMR approach one may unambigously recognise which NMR signal corresponds to a R configuration. Therefore, it clearly appears that a good part of the product **6** (40%) results of configuration inversion S ⟶ R (scheme 3) the remaining being racemized starting substrate. That the racemized part corresponds to an $S_{RN}1$ mechanism is shown by two results : 1) the anion **5** reacts under mild conditions with the *p*-nitrocumyl chloride but not with cumyl chloride. 2) addition of catalytic amounts of $CuCl_2$ to the reactive mixture, quenches almost totally the reaction.

The percentage of **1** being consumed by electron transfer when respectively opposed to the nitronate (19% of S_N2) and to the diethyldithiocarbamte (40% of S_N2) shows that nitronate favours more the $S_{RN}1$ mechanism than diethyldithiocarbamate. This is not what the E° values would have suggested. Several possibilities may explain this unexpected result. The first is that the ratio of S_N2 rates for nitronate and diethyldithiocarbamate on substrate **1** is even smaller than the ratio evaluated precedently (i.e. 10^{-9}). The results shown in scheme 3 do not agree with such an hypothesis. Indeed after 3h of reaction between **1** and **5** still 10% of **1** remain unreacted. If a 10^{-9} value was adopted for the ratio of S_N2 rate constants, reaction (2) should be finished in less than 1 minute. The second possibility could be that the diethyldithiocarbamate liberates small amounts of CS_2[22] which is able to quench the $S_{RN}1$ pathway. We have checked that diethyldithiocarbamate in DMF solution does not show I.R absorption (1500 cm^{-1}) characteristic of CS_2 and ^{13}C NMR confirms this experiment. Therefore we simulated competitions between $S_{RN}1$ and S_N2 using Kinarber[23,a], Simparba[23,b] and Acuchem[23,c] programs. The observed results may be explained if one supposes that the back electron transfer (step a, scheme 1) is faster for **5** than for **2** and that the propagation step d) is faster for **2** than **5** and/or that step c) is reversible for **5**[24].

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