Electron versus Hydride Ion Transfer in the Reduction of β-Halogen-Substituted 1,2-Dioxetanes by 1,4-Dihydronicotinamides

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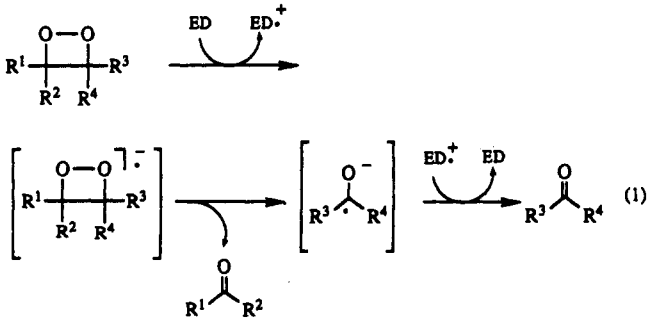
The 3-halo-substituted 1,2-dioxetane **1** was employed as mechanistic probe in the reaction with NADH model compounds, namely, three N-substituted 1,4-dihydronicotinamides and 9,10-dihydro-10-methylacridine ($AcrH_2$), to differentiate between the direct hydride ion transfer and the electron transfer (SET) mechanisms. While $AcrH_2$ led mostly to cleavage into carbonyl products, the nicotinamides reduced the dioxetane **1** to yield the epoxy alcohol **3** as the main product. Additionally, the diol **2**, the cleavage product bromoacetone, and the dehalogenation product acetone were observed. The formation of **3** is interpreted in terms of direct hydride ion transfer from the nicotinamides to the dioxetane with subsequent bromide elimination of the intermediary alkoxide. The dehalogenation product acetone was taken as evidence for initial electron transfer.

In view of the great importance of the 1,4-dihydronicotinamides NADH and NADPH in biochemical oxidation and reduction processes, the mechanism of these reactions is of current interest.[1] Model compounds for NADH, namely, the *N*-alkyl- and *N*-aryl-1,4-dihydronicotinamides (NAH), made it possible to study the reduction mechanism in nonaqueous solution.[1]

Three mechanisms have been suggested for the hydrogen transfer between NADH or its model compounds NAH and organic substrates. These mechanistic alternatives entail the common single-step hydride ion transfer (H^-),[2] single-electron transfer followed by proton transfer and again electron transfer (e^-, H^+, e^-),[2,3] and finally single-electron transfer with subsequent hydrogen atom abstraction from NAH (e^-, $H^\bullet$).[4,5] Recently, 1-benzyl-1,4-dihydronicotinamide (Bn-NAH) was found to reduce a number of functional groups by the electron transfer chain mechanism;[5,6] activated substrates could be initiated thermally[6] and more reluctant ones photochemically.[5]

Although 1,4-dihydropyridines were observed to react with acyl peroxides[7] in a free radical chain process, the reaction of 1,4-dihydronicotinamides with peroxides seems not to have been investigated so far. In this context we showed that tetramethyldioxetane is efficiently reduced by Bn-NAH to yield 1,2-diols.[8] Evidence was presented that the reduction of this four-membered ring cyclic peroxide by Bn-NAH and electron donors like phenothiazines[9] proceeded with single-electron transfer as the first step. Especially the observed dioxetane fragmentation products were thought to arise from fragmentation of the intermediary dioxetane radical anion to give a ketyl radical, which on electron back-transfer yields finally the carbonyl products (eq 1).



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In order to differentiate between the mechanisms of hydride ion transfer and electron transfer, we have investigated the reactions of several 1,4-dihydropyridine derivatives with the β-halo-substituted 1,2-dioxetane **1**. In the case of H^- transfer from the nicotinamide to the dioxetane, intramolecular halide ion displacement by the proximate alkoxide nucleophile should form an epoxide (Scheme I). Electron transfer from the nicotinamide to the dioxetane, on the other hand, would generate a dioxetane radical anion which should fragment into carbonyl compounds faster then it undergoes intramolecular displacement of halogen. The resulting α-halo-substituted ketyl radical should undergo halide elimination,[10] followed by protonation to yield dehalogenated ketone product. Precedents for this have been established in the thermally[6] and photochemically[5e] initiated electron transfer reduction of α-halo ketones by NADH model compounds.

For this study the *N*-alkyl-substituted 1,4-dihydronicotinamides Pr-NAH and Bn-NAH and the *N*-phenyl-substituted Ph-NAH (eq 2) were chosen as electron donors. The low oxidation potentials of these NAH derivatives should be advantageous for redox chemistry (cf. Table I). Additionally, we used 9,10-dihydro-10-methylacridine ($AcrH_2$) as electron donor, which has been reported to be unreactive toward α-haloacetophenones in the dark[5e] but is reactive under irradiation[5e] or acid catalysis.[11]

Results

The reactions of dioxetane **1** with equimolar amounts of 1,4-dihydropyridines were performed in deuterio-

† Undergraduate research participant, Summer 1990.

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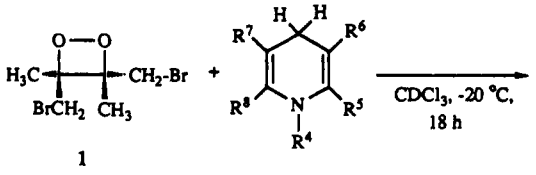

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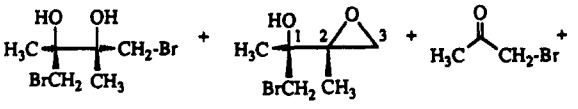
$AcrH_2$: R^4=CH_3; R^5+R^6=R^7+R^8=C_4H_4
Ph-NAH: R^4=Ph; R^5=R^7=R^8=H; R^6=$CONH_2$
Bn-NAH: R^4=$PhCH_2$; R^5=R^7=R^8=H; R^6=$CONH_2$
Pr-NAH: R^4=n-Pr; R^5=R^7=R^8=H; R^6=$CONH_2$



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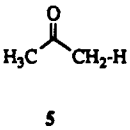

5 (2)

chloroform at −20 °C in the dark. By changing the solvent to acetonitrile-d_3, no substantial changes in the product distributions but lower mass balances were obtained. Within 18 h the dioxetane was completely consumed (^{1}H NMR monitoring) and the products were identified and quantified by ^{1}H NMR spectroscopy (eq 2). The results are collected in Table I.

The epoxy alcohol **3** was formed in variable amounts (0–81%), which depended on the oxidation potential of the 1,4-dihydropyridine (Table I, entries 1, 2, 3, 5). The epoxy alcohol **3** was isolated in 51% yield and was fully characterized when the reaction of dioxetane **1** and Bn-NAH was run on a preparative scale. The Bn-NAH was oxidized to give more than 80% of the pyridinium salt Bn-NA^+Br^-, which was isolated and identified by NMR. The reactions of the two other 1,4-dihydronicotinamides were only run on the NMR scale and the oxidation products were not isolated; but in both cases the expected pyridinium salts were observed and NMR spectrally identified. The base-catalyzed cyclization of diol **2** into epoxy alcohol **3** was ruled out by a control experiment.

In a side reaction, the dioxetane **1** was reduced to the 1,2-diol **2** also in variable yields (1–29%), as displayed in Table I. Except for $AcrH_2$, for which only 1% of **2** was obtained, a regular trend between the amount of reduction product (diol **2**) and the oxidation potentials of the NAH derivatives (Table I, entries 2, 3, 5) was observed. Thus, the amount of diol **2** decreases with decreasing $E_{1/2}$. Diol **2** was not isolated from the reaction mixture but independently synthesized in 43% yield by the reaction of dioxetane **1** with a 2-fold excess of gluthathione.[12]

The dioxetane cleavage product bromoacetone (**4**) was also a side product (5–33%) in the dioxetane/1,4-dihydropyridine reaction (Table I, entries 2, 3, 5), except again $AcrH_2$, for which as much as 96% of **4** was found (Table I, entry 1). Nevertheless, a clear trend is evident in that the amount of cleavage product **4** decreases with decreasing oxidation potential.

It is also significant that the dehalogenation product, namely, acetone (**5**), was observed to some extend in all cases (Table I, entries 1, 2, 3, 5). However, it must be realized that when corrected for stoichiometry, i.e., dehalogenation of 1 mol of dioxetane **1** gives only 1 mol of acetone (**5**) but cleavage gives 2 mol of bromoacetone (cf. Scheme I), the amount of the dehalogenated ketone acetone (**5**) is appreciable. In fact, the ratio of cleavage to halogenation (**4**/**5**) displays a reasonable trend, namely, that with decreasing oxidation potential of the 1,4-dihydropyridine the ratio of **4**/**5** decreases as the result of increased dehalogenation product (Table I). A control experiment showed that the formation of acetone on dehalogenation of bromoacetone by the NAH derivatives was ruled out.

In the presence of about 5 mol % of *m*-dinitrobenzene, the formation of the cleavage product bromoacetone (**4**) and of the dehalogenation product acetone (**5**) was essentially suppressed (Table I, entries 4, 6). Under these conditions the epoxy alcohol **3** was the dominant product. Furthermore, a control experiment (we thank the referee for suggesting it) showed that when dioxetane **1** was allowed to react with $AcrH_2$ in the presence of *m*-DNB even after 7 d at −20 °C only ca. 50% of **1** was consumed to yield exclusively decomposition product **4**. On the other hand, without *m*-DNB and under otherwise identical conditions, dioxetane **1** was completely consumed within 24 h (Table I, entry 1).

The use of the tetrasubstituted dioxetane **1** in the reaction with NAHs was necessary to get defined products and a high mass balance. Thus, when we employed 3,3-disubstituted derivatives, namely, the 3-(bromomethyl)-3-phenyl- and 3-(chloromethyl)-3-phenyl-1,2-dioxetanes,[13] mostly intractable and ill-defined higher-molecular-weight material was obtained. Nevertheless, for the small fraction of definitive products, qualitatively the same types were observed as with the tetrasubstituted dioxetane **1**, i.e., 1,2-diols, epoxy alcohols, and cleavage and dehalogenation products.

Discussion

Our product studies on the reaction of the β-halo-substituted dioxetane **1** with 1,4-dihydropyridine derivatives provide compelling evidence that two different mechanisms are working in competition. On the one hand we have the direct hydride ion transfer pathway and on the other single-electron transfer (SET). Of these, the hydride ion transfer mechanism dominates for the three N-substituted nicotinamides Ph-, Bn-, and Pr-NAH. In view of the electron-rich bis-enamine functionality in the NAH derivatives, the highly reactive 3,3-disubstituted dioxetanes[14a,b] oxidize the NAH substrates to afford exceedingly labile adducts and/or epoxides and the latter are at least in part reasponsible for the observed complexity[14c] compared to the well-behaved tetrasubstituted dioxetane **1**.

Experimental features which are in favor of the hydride ion transfer mechanism include the following:

(1) For dioxetane **1**, the epoxy alcohol **3** was the main reaction product. On the basis of a control experiment, the diol **2** (reduction product of the dioxetane **1**) was excluded as precursor to the epoxy alcohol **3** (of mechanistically trivial origin) because its base-catalyzed cyclization by the nicotinamides was not observed.

(2) The amount of **3** was found to depend on the half-wave potential ($E_{1/2}$) of the NAH derivative. Thus, while $AcrH_2$ (highest $E_{1/2}$ value) does not give any **3**, the nicotinamides afforded the epoxy alcohol **3** in the increasing

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Scheme I

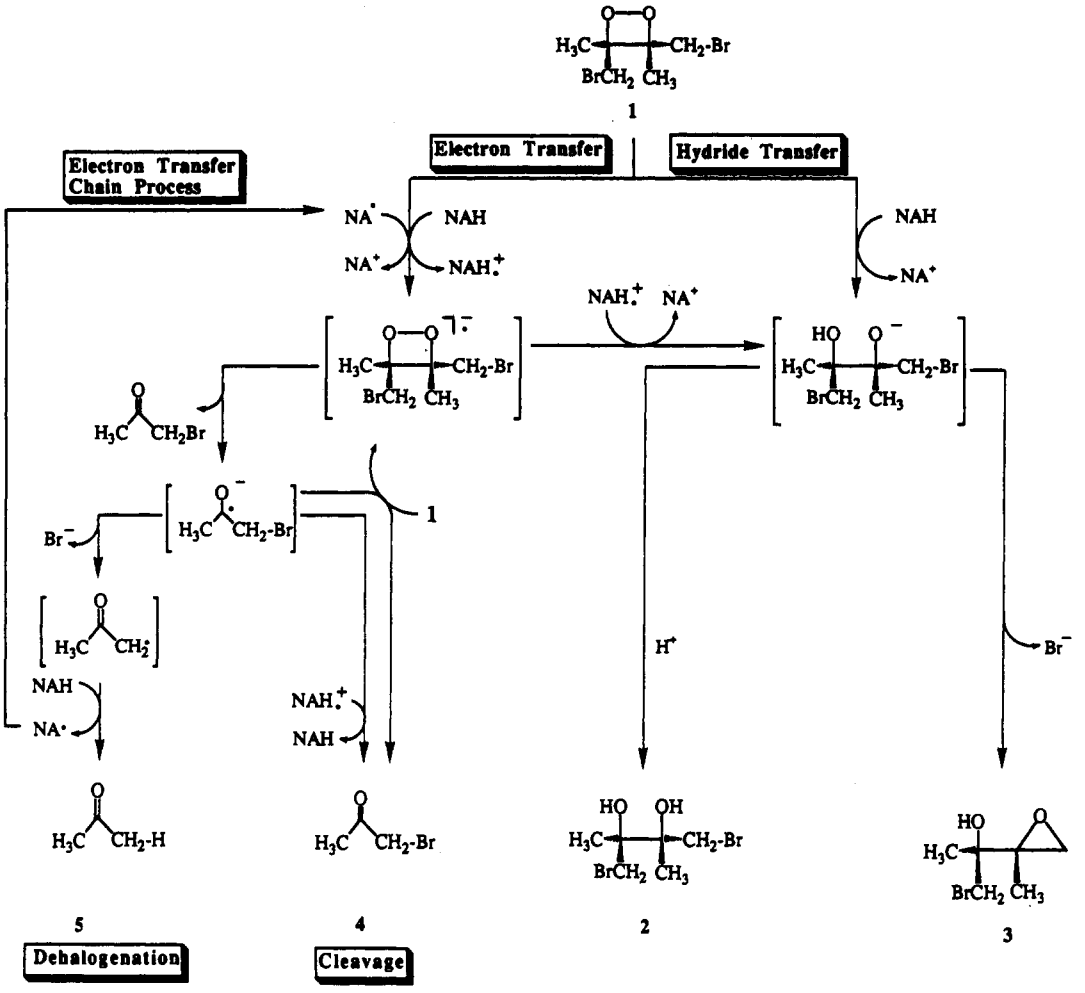

Table I. Reactions of Dioxetane 1 with 1,4-Dihydropyridines in Deuteriochloroform

entry	1,4-dihydropyridine[a] [$E^{1/2}$ (V)]	additive	mass balance[b]	product distribution (%)[b,c] 2	3	4	5	S_N2 vs SET (2+3):(4+5)	cleavage vs dehalogenation[d] 4:5
1	$AcrH_2$ (0.80[e])		90	1	*f*	96	3	1:99	94:6
2	Ph-NAH (0.48[g])		84	29	34	33	4	63:37	78:22
3	Bn-NAH (0.57[e]; 0.39[g])		86	21	46	25	8	67:33	52:48
4	Bn-NAH	*m*-DNB (5 mol %)	94	17	81	1	1	(98:2)	*h*
5	Pr-NAH (0.32[g])		88	12	81	5	2	93:7	43:57
6	Pr-NAH	*m*-DNB (5 mol %)	85	8	90	<1	<1	(>98:2)	*h*

[a] Solutions were ca. 0.1 M in 1 and in 1,4-dihydropyridine. [b] Obtained by quantitative ^1H NMR spectroscopy (250 MHz) with hexamethyldisiloxane as internal standard, based on consumed 1. [c] Normalized to 100%; error ±5%. [d] Cf. experimental part for calculation. [e] vs SCE, taken from ref 2. [f] Not detected. [g] vs $Ag/Ag^+ClO_4^-$, taken from ref 6a. [h] Not calculated because of the low yields.

order Ph < Bn < Pr, i.e., in decreasing order of their $E_{1/2}$ values (Table I). An analogous order of selectivity was previously reported in the bimolecular hydride ion transfer of N-substituted nicotinamides to *N*-methylacridinium iodide.[6b] This was explained in terms of stabilization of the developing positively charged ring nitrogen by electron donors, which facilitates the formation of the pyridinium salt. Since a good correlation exists between the nucleophilicities and one-electron oxidation potentials of a large number of nucleophiles,[15] our observed trend that the yield of epoxy alcohol 3 increases with decreasing oxidation potential of the NAHs and thus with their increasing nucleophilicities is reasonable, provided that the NAHs are regarded as hydride ion-donating nucleophiles. In this context, Verhoeven et al.[16] estimated the rate constants for electron transfer (k_{SET}) of Bn-NAH with a large number of substrates and compared them with the experimental rate constants for hydride transfer (k_{exp}). It was concluded that a SET process may operate only for the strongest one-electron oxidants (ferricinium ion, $Fe(CN)_6^{3-}$), provided that the condition $k_{exp}/k_{SET} \leq 1$ applies. This criterion is only fulfilled when the substrate has a low hydride ion affinity. Since peroxides in general, and dioxetanes particularly, possess a pronounced affinity for hydride ions, the SET process is of subordinate importance in the reaction of NAH derivatives with dioxetanes. In contrast, $AcrH_2$ is a poor H^- donor[16] and consequently electron transfer chemistry prevails for such nucleophiles.

(3) Epoxy alcohol 3 was also the dominating product

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when dioxetane 1 was allowed to react with Bn-NAH or Pr-NAH in the presence of the efficient radical ion scavenger[17] *m*-dinitrobenzene (*m*-DNB), cf. Table I, entries 4, 6. The fact that epoxy alcohol 3 formation was not inhibited by *m*-DNB speaks for a direct hydride ion transfer process.

(4) Like the epoxy alcohol 3, also the diol 2 is a hydride ion transfer product because the amount of 2 was not significantly influenced in the presence of *m*-DNB. Adventitious water, through handling of the dioxetanes at low temperatures, serves as proton source. Thus our previously reported electron transfer mechanism on the reduction of dioxetanes by Bn-NAH must be extended to allow for hydride ion transfer reactivity.

Experimental features which are in favor of the single-electron transfer (SET) mechanism include the following:

(1) The most compelling evidence for SET reactivity is the observation of the dehalogenated ketone 5, of which significant amounts were produced in every reaction of the β-bromo-substituted dioxetane 1 with the 1,4-dihydronicotinamides. A control experiment confirmed that the dehalogenated ketone 5 was not formed by dehalogenation of the cleavage product 4 (bromoacetone) by the NAHs. Thus, despite the low absolute yield of acetone, this dehalogenation product is mechanistically significant in terms of SET chemistry. Moreover, the electron transfer inhibitor *m*-DNB[17] totally supressed the formation of the dehalogenated ketone (Table I, entries 4, 6). A radical chain electron transfer mechanism, as it was reported[6] for the dehalogenation of α-halo ketones, accounts best for the formation of the dehalogenation product (Scheme I).

(2) Also the cleavage ketone 4 is construed to be derived from SET chemistry. In the presence of the NAHs, the dioxetane 1 suffers fragmentation at temperatures much below its thermal cleavage, which speaks for catalyzed decomposition. In this context it is significant to mention that the consumption of the dioxetane 1 ceased after all NAH derivative (less than stoichiometric amounts) was used up. Thus, the cleavage of the dioxetane into ketone 4 was not the result of some undefined catalysis promoted by the reaction products derived from the NAHs and the dioxetanes. We propose that the cleavage product 4 is also generated by electron transfer to give the NAH radical cation and a dioxetane radical anion (Scheme I). The latter cleaves very fast to ketone 4 and a ketyl radical anion; finally, electron back-transfer yields the second mole of ketone 4.

(3) Catalytic amounts of *m*-DNB, an effective scavenger of radical anions,[17] inhibited the formation of the cleavage as well as dehalogenation products 4 and 5. In the reaction of dioxetane 1 with $AcrH_2$ the decomposition of the dioxetane was significantly slower in the presence than in the absence of *m*-DNB, as was shown in a control experiment. These experimental facts imply an electron transfer chain reaction through radical anion intermediates. We propose that the ketyl radical, which is generated from the cleavage of the radical anion of the dioxetane, serves as the chain-carrying species (Scheme I) in this novel electron transfer process. Thus, *m*-DNB not only lowers the rate of decomposition of the dioxetane through scavenging of the ketyl radicals but it also prevents the formation of the dehalogenation products; instead, larger amounts of diol 2 and epoxy alcohol 3 are produced.

As already pointed out, the present results of the reaction of halogen-substituted dioxetane 1 with the NAH derivatives unquestionably reveal both H^- transfer and SET-type character. What remains now to be addressed is their relative importance. The dominant course of action with the NAHs is reduction by hydride ion transfer to afford diol 2 and epoxide 3, while electron transfer (SET) reactivity to give cleavage ketone 4 and dehalogenated ketone 5 is of subsidiary importance. This trend is nicely exhibited in the ratio (2+3):(4+5), a measure of hydride ion transfer versus SET reactivity (Table I). In fact, this ratio is a function of the nucleophilicity of the NAH reaction partners, which in turn depends on their oxidation potentials.[15]

Moreover, as shown in Scheme I, the formation of diol 2 and epoxy alcohol 3 can also be explained in terms of SET chemistry. Thus initial electron transfer followed by H-atom abstraction would yield an alkoxide ion, which on protonation would lead to diol 2 and on dehalogenation to the epoxy alcohol 3. If instead of H-atom abstraction deprotonation of $NAH^{+\bullet}$ would occur, the resulting alkoxy radical could be reduced by $NA^\bullet$ to yield finally the same products (this alternative is not shown in Scheme I).

The $AcrH_2$ partner, the least nucleophilic (highest $E_{1/2}$ value; cf. Table I) and worst hydride ion donor,[16] is a bit special in that it leads almost exclusively to cleavage of the dioxetane 1. At first sight it appears puzzling that the worse electron donor affords more cleavage product 4 (electron transfer reactivity) while the better electron donors give predominantly hydride ion transfer products 2 and 3. Moreover, in view of the lower pK_A value[2] for $AcrH^{+\bullet}$ than $NAH^{+\bullet}$, faster protonation of the dioxetane radical anion would be expected and H^- transfer products 2 and 3 should be formed preferentially; however, the contrary was observed (Table I). As mentioned above, $AcrH_2$ is a poor hydride ion donor compared to the NAHs toward peroxide substrates,[16] so that the former operates mainly through an effective electron transfer chain process, with the ketyl radical as chain carrier (Scheme I).

The fact that for the NAH partners hydride ion transfer dominates over electron transfer must be a quality of the dioxetane 1. Apparently, 1 is more susceptible toward nucleophilic hydride ion attack (S_N2) than single-electron transfer (SET) by the NAH.[16] Thus, by using nucleophiles with low oxidation potentials, but which are incapable of hydride ion transfer, it may be possible to accentuate the SET chemistry of dioxetane 1. Quite generally, such electron transfer chemistry of peroxides is manifested in the chemically initiated electron exchange chemiluminescence (CIEEL) mechanism with arenes and heteroarenes.[18]

The relative importance of the cleavage versus dehalogenation, which both are considered to arise from initial single-electron transfer between 1 and NAH, is reflected in the 4:5 ratio (Table I). Again, this ratio depends on the oxidation potentials of the NAH, i.e., the relative proportion of dehalogenation increases with decreasing E_{ox} values in the order $AcrH_2$ < Ph-NAH < Bn-NAH < Pr-NAH (Table I). This behavior can be reconciled in terms of the stabilization of the intermediary NAH radical cation by the substituent on the nitrogen atom. Thus, a relatively unstable radical cation like $AcrH_2^{+\bullet}$ (highest E_{ox} value, cf. Table I) leads on faster electron back-transfer to the ketyl radical anion preferentially to the cleavage product 4. On the other hand, for the more stable radical cations $NAH^{+\bullet}$ (lower E_{ox} values, cf. Table I), the electron back-transfer is sufficiently slower so that debromination of the ketyl radical anion can compete to afford dehalogenation product 5.

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To summarize, electron transfer chemistry plays only a minor role in the reaction of dioxetanes with 1,4-dihydropyridine derivatives, while hydride ion transfer dominates by far. Thus, although dioxetanes like other peroxides[15a,19] should serve as good single-electron acceptors, they exhibit a more pronounced affinity for hydride ions. Consequently, with substrates such as the nicotinamides, which can both donate hydride ions and/or electrons, the former prevails. In view of this dichotomy, our previously proposed electron transfer mechanism for the reduction of dioxetanes by biological relevant reducing agents must be expanded to include conventional S_N2-type chemistry.

Experimental Section

General Aspects. Melting points were taken on a Reichert Thermovar Kofler apparatus and are uncorrected. ^1H NMR spectra were recorded on Bruker AC 200 (200 MHz) and Bruker AC 250 (250 MHz) instruments, TMS or H_2O as internal standard. ^{13}C NMR spectra were recorded on Bruker AC 200 (50 MHz) and Bruker AC 250 (63 MHz) instruments, with $CDCl_3$ as internal standard. Infrared spectra were recorded on a Perkin Elmer 1420 ratio recording infrared spectrophotometer. Mass spectra (MS) were recorded on a Varian MAT CH 7. Combustion analyses were carried out by the Microanalytical Division of the Institute of Inorganic Chemistry (University of Würzburg). Radial chromatography was carried out in a chromatotron using silica gel 60 PF_{245} (Merck). Dioxetanes **1**[20] was prepared according to the literature procedure by cyclization of the corresponding β-bromo hydroperoxides with silver trifluoroacetate. The 1,4-dihydropyridines $AcrH_2$,[5e] Ph-NAH,[6b] Bn-NAH,[21] and Pr-NAH[22] were available according to literature procedures.

Reaction of Dioxetane 1 with 1,4-Dihydropyridines. Samples of ca. 0.2 M solutions of dioxetane **1** in $CDCl_3$ (5 mol % of *m*-dinitrobenzene in the reactions of entries 4, 6; Table I) were saturated with argon gas in an ultrasound bath and cooled to −20 °C. To these were added ca. 0.2 M solutions of the corresponding 1,4-dihydropyridine (up to 10% excess) and the solutions were kept at −20 °C in the dark for 18 h. The precipitate was removed by filtration over Celite, dissolved in D_2O, and identified by ^1H NMR as the corresponding 3-carbamoylpyridinium salt. After addition of hexamethyldisiloxane as internal standard, the product distributions in the filtrates were determined with the help of ^1H NMR spectroscopy (250 MHz) by integration of appropriate signals (cf. Table I). The ratio cleavage/dehalogenation was determined from [cleavage] = ([4] − [5])/2 and [dehalogenation] = [5].

1-Phenyl-3-carbamoylpyridinium bromide[6a] (Ph-Na$^+$Br$^-$): ^1H NMR (D_2O, 250 MHz) δ 7.73 (m, 5 H, arom H), 8.33 (dd, *J* = 8.2, 6.2 Hz, 1 H), 9.04 (d, *J* = 8.2 Hz, 1 H), 9.25 (d, *J* = 6.2 Hz, 1 H), 9.52 (s, 1 H).

1-Propyl-3-carbamoylpyridinium bromide[6a] (Pr-Na$^+$Br$^-$): ^1H NMR (D_2O, 250 MHz) δ 0.93 (t, *J* = 7.4 Hz, 3 H, CH_3), 2.04 (m, 2 H, CH_2CH_3), 4.62 (t, *J* = 7.3 Hz, 2 H, CH_2N), 8.16 (dd, *J* = 8.1, 6.2 Hz, 1 H) 8.86 (d, *J* = 8.2 Hz, 1 H), 9.00 (d, *J* = 6.2 Hz, 1 H), 9.39 (s, 1 H).

Isolation of Epoxy Alcohol 3. A solution of 276 mg (1.01 mmol) of dioxetane **1** in 10 mL of $CHCl_3$, which contained 25.0 mg (0.150 mmol) of *m*-dinitrobenzene, was cooled to −20 °C (argon gas atmosphere) and 432 mg (2.02 mmol) of Bn-NAH was added in 7 mL of $CHCl_3$. Within 24 h the dioxetane was completely consumed and the reaction mixture was filtered to remove the pyridinium salt Bn-Na$^+$Br$^-$,[6a] which was recrystallized from ethanol to yield 240 mg (82%) of colorless needles, mp 213–214 °C (ref.[6a] not given). The solvent was evaporated (20 °C/15 Torr) and the residue submitted to radial chromatography (5:1 petroleum ether [bp 30–50 °C]/ethyl acetate = 5:1 as eluent) to afford 100 mg (51%) pure epoxy alcohol **3a** as a pale yellow oil.

1-Benzyl-3-carbamoylpyridinium bromide[6a] (Bn-Na$^+$Br$^-$): ^1H NMR (D_2O, 250 MHz) δ 5.58 (s, 2 H, CH_2Ph), 7.40 (m, 5 H, arom H), 8.17 (t, *J* = 7.5 Hz, 1 H), 8.84 (d, *J* = 7.5 Hz, 1 H), 9.05 (d, *J* = 7.5 Hz, 1 H), 9.30 (s, 1 H).

(2*R,3*S**)-(±)-1-Bromo-2,3-dimethyl-3,4-epoxybutan-2-ol (3):** ^1H NMR (250 MHz, $CDCl_3$) δ 1.37 (d, *J* = 0.6 Hz, 3 H, 2-CH_3), 1.43 (s, 3 H, 1-CH_3), 2.45 (d, *J* = 5.1 Hz, 1 H, 3-H), 2.90 (dd, *J* = 5.1 Hz, 0.6 Hz, 1 H, 3-H), AB pattern (δ_A = 3.52, δ_B = 3.63, *J* = 10.8 Hz, 2 H, CH_2Br); ^{13}C NMR (63 MHz, $CDCl_3$) δ 17.5 (q, CH_3-2), 23.1 (q, CH_3-1), 41.2 (t, CH_2Br), 49.3 (t, C-3), 60.2 (s, C-2), 70.4 (s, C-1); IR (CCl_4) 3630, 3110, 3040, 2990, 1470, 1445, 1440, 1380, 1360, 1260, 1215 cm^{-1}; MS (70 eV) *m*/*z* (rel intensity) = 180 (<1) [M^+ − O], 139 (7) 123 (3), 101 (14), 85 (29), 58 (87) [C_3H_6O], 43 (100), 41 (16), 29 (4). Anal. Calcd for $C_6H_{11}BrO_2$: C, 36.96; H, 5.69. Found: C, 36.73; H, 5.78.

Control Experiments. Reaction of Bromoacetone (4) with Bn-NAH. A sample of ca. 150 μmol of ketone **4** and equimolar amounts of Bn-NAH in 0.6 mL of $CDCl_3$ was kept at −20 °C in the dark for 18 h. By ^1H NMR spectroscopy were observed acetone (**5**) and bromoacetone (**4**) in a ratio of ca. 1:99.

Reaction of Diol 2 with Bn-NAH. A sample of 80 μmol of diol **2** was allowed to react with equimolar amounts of Bn-NAH in 0.6 mL of $CDCl_3$ at −20 °C. During a period of 24 h no conversion could be observed by ^1H NMR spectroscopy.

Synthesis of (2*S,3*S**)-(±)-1,4-Dibromo-2,3-dimethylbutane-2,3-diol (2).** Dioxetane **1** (84.0 mg, 0.307 mmol) and gluthathione (188 mg, 0.612 mmol) were stirred in 5 mL of water at 20 °C for 8 h until the dioxetane was completely consumed (negative KI test). The mixture was extracted with methylene chloride (4 × 5 mL) and the combined organic layers were dried over $MgSO_4$. Evaporation of the solvent at 20 °C/15 Torr and recrystallization fom petroleum ether (bp 50–60 °C) afforded 36.0 mg (43%) of colorless needles, mp 90–91 °C: ^1H NMR (250 MHz, $CDCl_3$) δ 1.32 (s, 6 H, CH_3), 2.59 (br s, 2 H, OH), AB pattern (δ_A = 3.60, δ_B = 3.89, *J* = 10.5 Hz, 4 H, CH_2Br); ^{13}C NMR (63 MHz, $CDCl_3$) δ 21.3 (q, CH_3), 42.6 (t, CH_2Br), 74.7 (s); IR (CCl_4) 3600, 2960, 1470, 1380, 1360, 1320, 1220, 1080, 1060 cm^{-1}. Anal. Calcd for $C_6H_{12}BrO_2$: C, 26.11; H, 4.38. Found: C, 26.45; H, 4.19.

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