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THE REACTION OF SUPEROXIDE ANION RADICAL WITH ELECTRON POOR OLEFINS

Aryeh A. Frimer*, Ionel Rosenthal[†] and Shmaryahu Hoz*

*Department of Chemistry, Bar-Ilan University, Ramat-Gan, Israel

[†]Department of Organic Chemistry, The Weizmann Institute of Science, Rehovot, Israel

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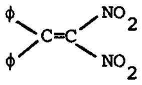
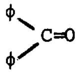
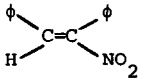
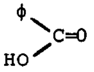
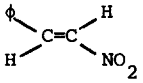
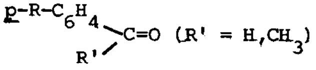
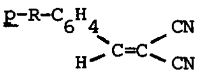
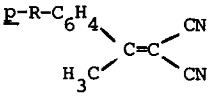
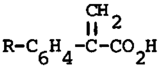
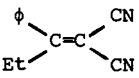
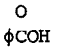
The intermediacy of superoxide anion radical, $O_2^{\dot{-}}$, has been suggested for several different metabolic processes which involve oxidation[1]. Most of the research, however, done to date has been carried out in aqueous and protic media in which it is likely that not O_2^- but rather its conjugate acid $HO_2^{\cdot}$ is the reactive species. Furthermore, organic solvents are more likely to resemble the hydrophobic active sites in many enzymes. The complexation of potassium superoxide with crown ethers[2] permits the unambiguous generation of "naked" O_2^- in aprotic solvents.

Superoxide anion radical does not normally react with olefins.[3] Considering, however, that the redox potentials of O_2-O_2^- and O_2^--H_2O_2 at neutral pH are -0.33 and +0.94V respectively[4], an expected feature of this radical anion is the ability to act as a reductant in the presence of electron acceptors and as an oxidant in the presence of electron donors. Indeed, we have shown that O_2^- oxidatively cleaves chalcones[5] and tetracyclone[3], through a process which probably involves initial electron transfer to the enone moiety. Similarly we reported[6] that O_2^- can react with substituted nitrobenzenes to produce the corresponding nitrophenols. The nucleophilic aromatic substitution also seems to proceed <u>via</u> an electron transfer. We now report the reaction of O_2^- with several electron poor cyano and nitro-olefins.

In a typical experiment, 1 mmol of olefin, 2 mmol of 18-crown-6 and 4 mmol of KO_2 in 20 ml of dry benzene were stirred overnight in the dark. The reaction was followed by TLC and showed in nearly all cases the total disappearance of the starting material. The solution was acidified with conc. HCl and the reaction mixture extracted with saturated $NaHCO_3$ The aqueous extracts were acidified and the acids extracted into ether. The ether layer was dried over $MgSO_4$ and the solvent subsequently removed under vacuum. The residue was weighed and the identity and ratio of the product(s) ascertained by spectral data (MS and NMR). The results are shown in the Table.

As noted above the reactions were followed by TLC and for compounds Va-d the corresponding substituted acetophenones could be clearly observed in each case in the initial stages of the reaction but eventually disappeared. In control experiments the substituted benzaldehydes and acetophenones, corresponding to compounds IV and V respectively, were oxidized by $O_2^{\dot{-}}$ and yielded the corresponding benzoic acids. Atropic acid[9] proved inert to $O_2^{\dot{-}}$. Treatment of IVa and Va with KOH /crown ether gave only small amounts (<10%) of the

Table

	Compound*	Product (yield)**	
I		 (84%)	
II		 (85%)	
III		ϕCO_2H (85%)	
		$R-C_6H_4CO_2H$	
IV		$R-C_6H_4CO_2H$	
a: R = H		70%	
b: R = NO_2		74%	
c: R = Br		90%	
d: R = OCH_3		80%	
V		$R-C_6H_4CO_2H$	 $R-C_6H_4-\overset{\overset{CH_2}{\parallel}}{C}-CO_2H$ VII
a: R = H		81%	10%
b: R = CH_3		50%	25%
c: R = OCH_3		35%	35%
d: R = Br		35% †	- ‡
VI		 $\phi\overset{O}{C}OH$ (87%)	

*The olefins were prepared according to known literature procedures[7]

**For compounds I-III, yields were determined by VPC (10% SE-30 WDMCS) using biphenyl as standard. For IV-VI the total yields are based on the weight of the isolated residue (see text). The ratio of benzoic to atropic acids[8] were determined by NMR integration.

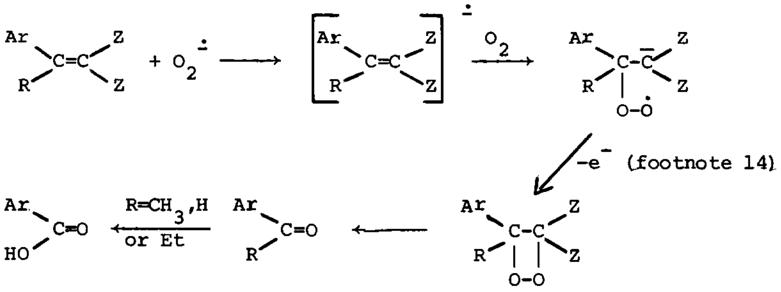
†Substantial amounts of an unidentified polymeric material is formed

‡Presence of this acid in a low yield is indicated by MS.

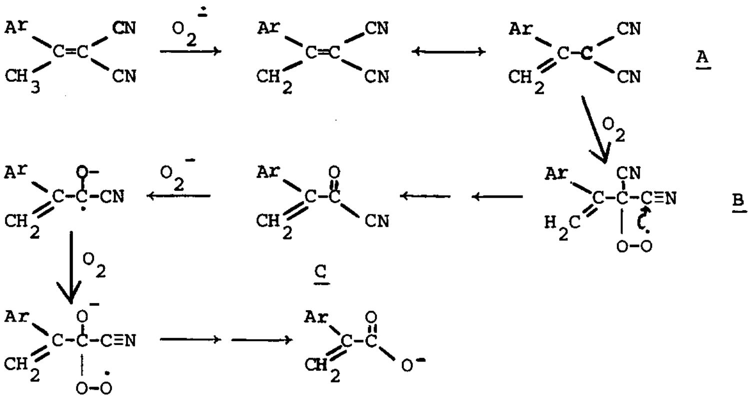
observed products after 24 hours of reaction. Hence base catalyzed autoxidation[10,11] is not involved to any substantial extent. Less than 10% O^{18} - labeled benzophenone was observed in the mass spectrum of the product when KO_2^{18} replaced KO_2^{16} in the oxidative cleavage of I[12]

Attempts were made to detect via ESR, immediately following the mixing of KO_2 and olefin, the paramagnetic specia involved in this reaction. A well resolved spectrum of the corresponding anion radical could be recorded for I (a^N=2.84G, $a_{1(2)}$=2.50G, $a_{2(1)}$=1.05G. a_3=2.80G). The computer simulated spectrum overlapped the experimental one. Paramagnetic specia were also detected for II and IVb but the poor resolution prevented identification.

The data indicates that for olefins I-VI the primary reaction is oxidative cleavage of the double bond. As suggested previously[5,6], it is likely that the reaction proceeds by a preliminary electron transfer from O_2^- to the electron poor double bond. The resulting anion radical reactsin turn with surrounding molecular oxygen as sketched below.



For compounds of Type V there is a second competing pathway which leads to substituted atropic acids. We suggest the following mechanism to rationalize their formation. The first



step involves abstraction of the active allylic hydrogen. One would expect highest radical density in the allylic radical α to the cyano groups. Addition of oxygen to the radical A gives species B. Closure to a dioxetane[16] and cleavage as shown to yield enone C finds precedent in the electrogenerated $O_2^{\dot{-}}$ oxidation of benzyl cyanide to benzoic acid.[13] A second electron transfer, addition of oxygen and oxidative cleavage of the cyano group leads to the desired product.

We have thus demonstrated that superoxide anion radical readily reacts with electron poor olefins yielding products corresponding to oxidative cleavage of the double bond. As noted above, similar products are expected with electron rich olefins such as enol ethers. A report on these systems will be forthcoming shortly.

References and Footnotes

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8. ^{1}H NMR (δ, acetone-d_6):VIIa-7.33(m,5H) 6.30 (d,1H,J=1Hz) 5.94 (d,1H,J=1Hz); VIIb-7.61 (d,2H,J=5Hz) 7.25 (d,2H,J=5Hz) 6.26 (d,1H,J=1Hz) 5.90 (d,1H,J=1Hz) 2.30 (s,3H);VIIc-7.60(d,2H,J=5Hz) 6.89 (d,2H,J=5Hz) 6.22 (d,1H,J=1Hz) 5.88 (d,1H,J=1Hz) 3.83 (s,3H).

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11. No base catalyzed autooxidation was observed in the reaction of KOH/crown with chalcones; cf reference 5.

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