Oxidative Cleavage of Chalcones by Electrochemically Generated Superoxide Ion ($O_2^{\cdot-}$)

Manorama Singh, Krishna Nand Singh, and Ram Achal Misra*
Department of Chemistry, Faculty of Science, Banaras Hindu University, Varanasi 221005, India

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Synopsis. Various chalcones were efficiently cleaved to carboxylic acid(s), in considerably high yield by the reaction with electrochemically generated superoxide ion ($O_2^{\cdot-}$) at mercury cathode and molecular oxygen.

Superoxide ion ($O_2^{\cdot-}$), which is an anion radical and one of the activated oxygen species, plays important roles in biological systems[1—11] and provides impetus to organic chemists to study its chemical reactivity from synthetic considerations.[12—15] It has been recognized that superoxide ion, depending upon the nature of organic substrate, can act as a base, nucleophile, ligand, radical, or an oxidant.[14—22] The electrochemical generation of $O_2^{\cdot-}$ in aprotic medium, in presence of tetraalkylammonium salt by reducing molecular oxygen, is known since 1965[23] and remains a method of choice for preparing and using in situ generated superoxide ion more satisfactorily than using KO_2–crown ether.[24]

The chemistry of superoxide ion with a wide range of simple organic compounds is very little known and needs further investigations. Recently, we have reported the superoxide-initiated oxidation of some secondary alcohols,[25] primary alcohols,[26] and fragmentation of some tosylhydrazones of carbonyl compounds using electrochemically generated superoxide ion.[27] Reactions of electrogenerated $O_2^{\cdot-}$ with chalcones have not been studied so far. A survey of literature reveals that there exists only one report in which Rosenthal and Frimer[28] have studied the reaction of chalcones with KO_2 in 18-crown-6-ether. The reaction of chalcones with electrogenerated superoxide ion has been reinvestigated from following reasons:

a) The best available sample of KO_2 is only 95% pure and is always contaminated with free bases and other impurities.

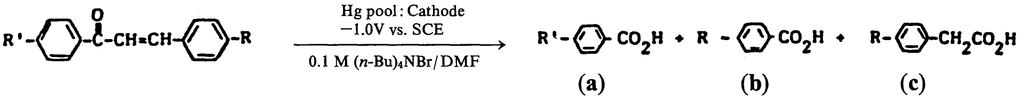
b) The KO_2 in reaction medium easily results in other activated oxygen species such as hydroxyl ($OH^{\cdot}$) and peroxyl ($OOH^{\cdot}$) radicals thereby delimiting the interpretation of results.

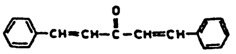
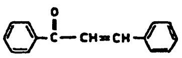
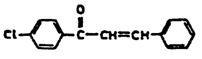
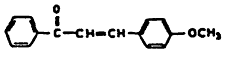
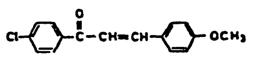
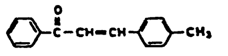
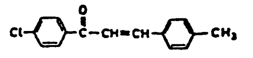
c) The electrogeneration of superoxide ion affords a stable and pure solution of the species in aprotic medium and gives opportunity for in situ reactions with chalcones.

Experimental

Instruments. Melting points were measured with a Buchii melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 783 grating spectrophotometer. ^1H NMR spectra were measured at 90 MHz with

Table 1. Reaction of Electrochemically Generated Superoxide Ion with Chalcones (1—7); Mercury Pool: Cathode, Platinum Disc: Anode. Temp: 25—30 °C



Entry	Chalcone (1—7; 0.5 g)	Current/mA		Electricity passed	Reaction time	Product (Yield/%)		
		Initial	Final	Coulomb[a)]	h	a	b	c
1		100	10	610	10	$C_6H_5CO_2H$ (95)		
2		95	05	686	13	$C_6H_5CO_2H$	$C_6H_5CO_2H$ (75)	$C_6H_5CH_2CO_2H$ (5)
3		100	20	590	18	$ClC_6H_4CO_2H$ (54)	$C_6H_5CO_2H$ (20)	$C_6H_5CH_2CO_2H$ (7)
4		120	10	600	15	$C_6H_5CO_2H$ (65)	$MeOC_6H_4CO_2H$ (14)	$MeOC_6H_4CH_2CO_2H$ (8)
5		75	10	525	10	$ClC_6H_4CO_2H$ (60)	$C_6H_5CO_2H$ (15)	$MeOC_6H_4CH_2CO_2H$ (6)
6		100	15	643	12	$C_6H_5CO_2H$ (64)	$MeC_6H_4CO_2H$ (10)	$MeC_6H_4CH_2CO_2H$ (3)
7		95	15	566	12	$ClC_6H_4CO_2H$ (62)	$C_6H_5CO_2H$ (15)	$MeC_6H_4CH_2CO_2H$ (5)

a) Measured using copper coulometer.

JEOL FT-NMR spectrometer FX-90 Q, chemical shifts are expressed as δ/ppm, downfield from the internal tetramethylsilane reference. Carbon and hydrogen were analyzed using Perkin-Elmer model 240 C elemental analyzer. GLC was carried out on a Shimadzu Gas Chromatograph, GC-9A in conjuction with Shimadzu C-R 6A chromatopac. Cyclic voltammograms were recorded with an X-Y (t) recorder (Servogor type 733). All measurements were carried out at 25 °C by a three electrode system consisting of a counter (stationary platinum disc: 22 mm in diameter), a platinum rod test electrode, 0.1 M (1 M=1 mol dm^{-3}) TBAP (tetrabutylammonium perchlorate) in DMSO (spectroscopic grade) served as supporting electrolyte. The scan rate of the potential was 200 mV s^{-1}.

Chalcones (**1**—**7**; Table 1) were prepared according to the reported method[29] and were characterized by their physico-chemical and spectral studies. These were subjected to the reaction with electrochemically in situ generated superoxide ion. After electrolysis and work-up, all the products isolated were fully characterized by their physico-chemical and spectroscopic data.

Oxidative Cleavage of Chalcones. Typical Procedure for 4-Methoxychalcone (4): Apparatus. Wenking Potentioscan POS 73 (Bank-Electronik, Germany) is used for constant potential macro electrolysis. The electrochemical cell consists of a double walled glass cell (volume 150 ml) in which a medium porosity glass frit separates the anodic and cathodic chambers. The mercury pool (23.76 cm^2) and platinum foil (3.78 cm^2) served as an anode and a cathode respectively. Saturated Calomel Electrode (SCE) served as a reference electrode.

Electrolysis. A solution of tetrabutylammonium bromide (3.22 g; 0.1 M) in DMF (100 ml) was used as supporting electrolyte. The cathodic chamber containing 50 ml of the electrolyte was purged with nitrogen for 15 min. The electrolytic solution was pre-electrolyzed at −1.9 V vs. SCE until the background current drops to about 2 mA. Now 2 ml of cyclohexene was added to anolyte for absorption of liberated bromine. Catholyte was saturated with oxygen for 30 min. Chalcone (**4**; 0.5 g; 2.1×10^{-4} M) was added to the cathodic chamber and reaction was carried out at constant potential of −1.0 V vs. SCE until the loss of starting material as checked by TLC and current falls appreciably (Table 1).

Work-Up. Upon completion of electrolysis, catholyte was taken in 100 ml of cold water and to it was added 25 ml of saturated solution of NaHCO$_3$. The above mixture was extracted with ether (20 ml×3), dried (Na$_2$SO$_4$), filtered and evaporated to yield unreacted chalcone. Now the aqueous layer was acidified with dil aq HCl and extracted with ether (25 ml×4), dried (Na$_2$SO$_4$), filtered and solvent was removed to yield mixture of acids. These acids were separated by column chromatography on 70—230 mesh silica gel (Merck Kieselgel 60 Art. No. 7734) using benzene-MeOH-AcOH (05:04:01) as eluent. Yields were established (after their esterification) by GLC. Products were identified by their physico-chemical and spectral data.

Results and Discussion

During present investigation chalcones (**1**—**7**) are made to react with in situ electrochemically generated superoxide ion at −1.0 V vs. SCE in the atmosphere of molecular oxygen in DMF solution. The chalcones under this reducing conditions, owing to the mediation of $\mathrm{O}_2^{\overline{\cdot}}/\mathrm{O}_2$ are oxidatively cleaved to carboxylic acids (Table 1).

Cyclic Voltammetry. The cyclic voltammogram of superoxide ion formation is shown by dotted line (----) and the CV of oxygen reduction in the presence of chalcone (**2**) by solid line (——) (Fig. 1).

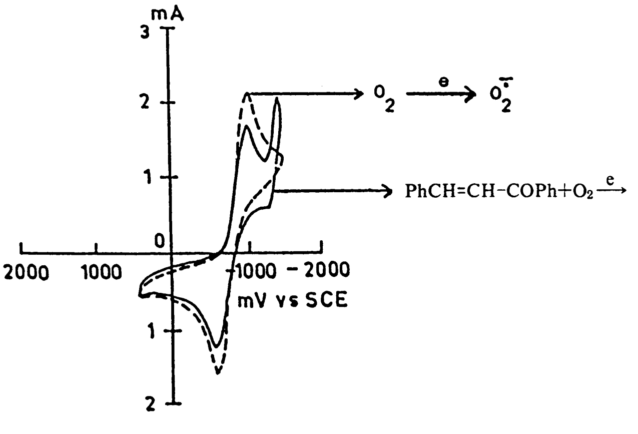
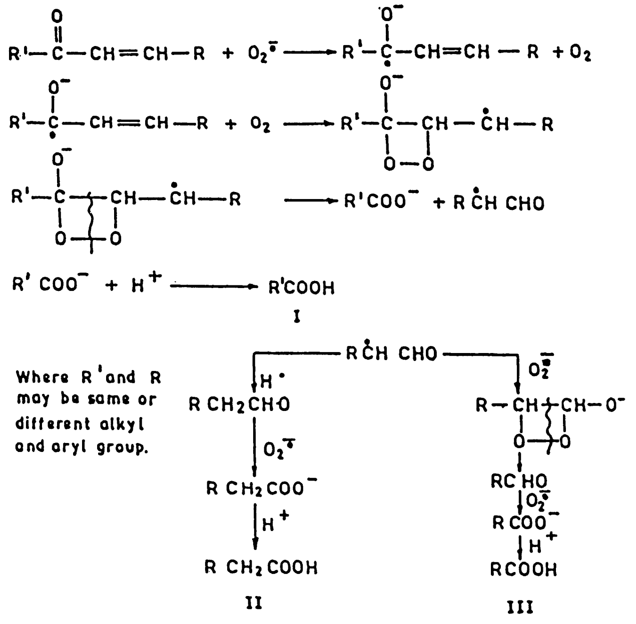


Fig. 1. Cyclic voltammogram for oxygen reduction (----) and in the presence of chalcone (**2**) (——). Solvent: DMSO+0.1 M TBAP; T: 20 °C. Scan rate: 200 mV s^{-1} at Pt.

Examination of Fig. 1 reveals that molecular oxygen is reduced at −0.9 V to $\mathrm{O}_2^{\overline{\cdot}}$, this species is reoxidized in the reverse sweep of potential at −0.60 V. The value of 0.30 V as ΔE_p shows that the electrode process is quasi-reversible.[30] In the CV of superoxide ion in presence of substrate, in addition to CV peak of $\mathrm{O}_2^{\overline{\cdot}}$ (−0.9 V) another peak at −1.45 V is observed, attributable to a possible reduction of substrate. The $\mathrm{O}_2^{\overline{\cdot}}$ oxidation peak at −0.60 V does not disappear as is observed in the CV of superoxide ion reaction with primary alcohols,[26] but its disappearance in the case of tosylhydrazones[27] probably indicates that superoxide ion is destroyed in a fast follow up chemical reaction between the superoxide ion and the substrate. The cathodic peak current (ipc) in absence of chalcone is 2.15 mA and in presence of chalcone is 1.65 mA (decrease 0.5 mA). Similarly the anodic peak current (ipa) in absence and presence of



Scheme 1.

chalcone is 1.6 mA and 1.25 mA respectively (decrease 0.35 mA). Thus the decrease in current ratio is 1.42 (Fig.1).

On the basis of product isolation and CV studies the following mechanism is proposed for the oxidative cleavage of chalcones (Scheme 1).

Thus, superoxide ion reacts with chalcone forming radical anion of the substrate, which reacts with surrounding molecular oxygen to form unstable adduct and is readily cleaved to carboxylate anion ($RCOO^-$) and aldehyde radical ($R\dot{C}HCHO$). The latter, with a sequence of steps involving $O_2^{\bar{\cdot}}$ affords the products.

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