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Reduction of maleate and fumarate by the $CO_2^{\cdot -}$ anion radical

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Abstract—The radical anion $CO_2^{\cdot -}$ reacts with fumarate and maleate at pH 5.3 mainly via electron transfer. The final products are a mixture of $(^-O_2CCH_2\text{–})_2$, *trans*-$(^-O_2CCH\text{=})_2$ and products with higher molecular weight. At higher pHs, the yield of fumarate and succinate decreases. The results suggest that though the radical anions formed by the reduction of fumarate and maleate have different structures, the final products are probably the same.

The reduction of maleate and fumarate in neutral and slightly acidic aqueous solutions by Ni^IL^+ and Co^IL^+ complexes, where L are tetraazamacrocyclic ligands[1,2] has been studied in aqueous solutions containing HCO_2^-. As a blank it was decided to determine the nature of the major final products when maleate and fumarate are reduced by $CO_2^{\cdot -}$. It should be noted that the literature contains conflicting reports on the reaction of $CO_2^{\cdot -}$ with these acids. Neta[3] and Anderson et al.[4] have suggested that the major product is the radical anion $^{\cdot}CH(CO_2^-)CH(CO_2^-)_2$ whereas Hayon and Simic[5] reported that at least at pH ~ 5, the major products are the radical anions formed by an electron transfer process. At higher pHs, the latter reactions were not observed.

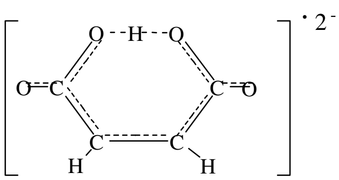
EPR experiments[6] suggest that the reduction of maleate with e_{aq}^- at $pH > 7$ yields the radical anion **I**, which is transformed into the radical anion **II**[6] with a pK_a of 5–6.[5]

The reduction of fumarate with e_{aq}^- was suggested to form the radical anion **III**,[3] which is transformed into the radical anion **IV**.[4]

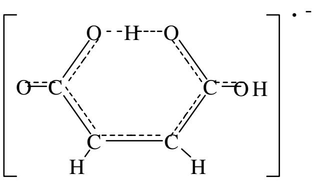
The pK_a of the latter transformation is not clear, Neta[3] observed the radical anion **III** at pH 6.9 whereas Hayon and Simic suggested a pK_a of 10.9 for this anion.[5]

It should be noted that all the EPR spectra indicate that the unpaired electron density in all these radical anions is located mainly on the carbon atoms of the carboxylic groups. It seemed therefore of interest to study the nature of the final products obtained when maleate and fumarate react with e_{aq}^- and with the $CO_2^{\cdot -}$ radical anion.

Maleic or fumaric acid with an initial concentration of 3×10^{-4} M was added to a solution of 0.1 M sodium formate and 0.1 M phosphate buffer at different pH values (5.3; 7.0; 8.0) with He or N_2O saturation. The samples were γ irradiated using a ^{60}Co γ source in sealed



I



II

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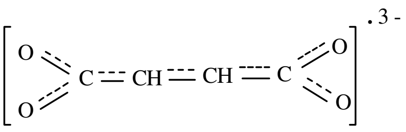
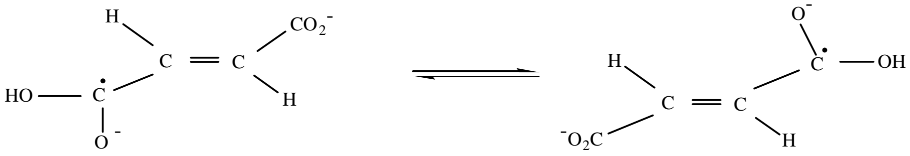


III



IV

bulbs for 20–90 min (66–297 Gy). The results are summarized in Table 1. Product analysis was performed as described in Ref. 7.

$CO_2^{\cdot-}$ radical ion production: When ionizing radiation is absorbed in neutral dilute aqueous solutions, the formation of the primary radicals is summed up in the following equation:[8]

$$H_2O \xrightarrow{\gamma} e^-_{aq}\ (2.65);\quad {}^{\cdot}OH\ (2.65);\quad H^{\cdot}\ (0.60);$$
$$H_2O_2\ (0.75);\quad H_2\ (0.40)$$

The G values are given in parentheses (G values are defined as the number of molecules of each product per 100 eV of radiation absorbed by the solution).[8] When formate is present in the solution, the following reactions take place:[9]

$$HCO_2^- + {}^{\cdot}OH/H^{\cdot} \rightarrow CO_2^{\cdot-} + H_2O/H_2$$
$$k_{\cdot OH} = 2.9 \times 10^9\ M^{-1}\,s^{-1}$$
$$k_{\cdot H} = 2.5 \times 10^8\ M^{-1}\,s^{-1}$$

The $CO_2^{\cdot-}$ radical anion is a very strong reducing agent $E^0 = -1.9$ V[10] versus NHE (normal hydrogen electrode). Thus, in neutral He saturated solutions containing formate, two strong reducing radicals are formed e^-_{aq} (∼45% of the radicals) and $CO_2^{\cdot-}$ (∼55% of the radicals). In N_2O saturated solutions, $[N_2O] = 0.022$ M, the e^-_{aq} react via[9]

$$e^-_{aq} + N_2O \xrightarrow{H+} {}^{\cdot}OH + N_2 \quad k = 9.1 \times 10^9\ M^{-1}\,s^{-1}$$

Thus, in these solutions all the radicals are transformed into the $CO_2^{\cdot-}$ ion radical.

Table 1. Yields of maleate or fumarate after γ-irradiation

Sample	pH	Saturation gas	G^a of maleate	G^a of fumarate
Maleate	5.3	He	$G = -7.6 \pm 0.5$	$G = 2.7 \pm 0.1$
Maleate	7.0	He	$G = -6.9 \pm 1.0$	$G = 1.4 \pm 0.1$
Maleate	8.0	He	$G = -7.0 \pm 0.4$	$G = 1.2^b$
Fumarate	5.3	He	$G = 0.05^c$	$G = -4.7 \pm 0.5$
Fumarate	7.0	He	$G = 0.3^c$	$G = -5.4 \pm 1.0$
Fumarate	8.0	He	$G = 0.7^c$	$G = -7.6 \pm 0.6$
Maleate	5.3	N_2O	$G = -8.9 \pm 0.6$	$G = 3.8 \pm 0.2$
Maleate	7.0	N_2O	$G = -7.7 \pm 0.8$	$G = 1.9 \pm 0.2$
Maleate	8.0	N_2O	$G = -7.2 \pm 0.8$	$G = 0.9 \pm 0.1$
Fumarate	5.3	N_2O	$G = 0.03^b$	$G = -3.4 \pm 0.4$
Fumarate	7.0	N_2O	$G = 0.3^b$	$G = -5.3 \pm 1.0$
Fumarate	8.0	N_2O	$G = 1.0 \pm 0.1$	$G = -6.9 \pm 0.4$

[a] G is defined as the number of molecules of each product per 100 eV of radiation absorbed by the solution.[8]

[b] At 66 Gy, the yield decreases with increasing dose.

[c] At 148 Gy, the yield decreases with increasing dose.

The measured yields, and decrease in concentration or formation of maleate and fumarate were measured. The results are summarized in Table 1.

Succinate was observed as one of the products in all samples. However, accurate yields could not be determined due to the low absorption coefficient in the UV and some overlap with the fumarate peak due to similar retention times. Other products with longer retention times and thus probably with larger molecular weights and/or negative charges, were observed.

The results for the He saturated maleate solutions at pH 5.3 indicate the following conclusions:

(a) Fumarate is a major product of the reaction of radicals **I** or **II**. This is expected to occur via

$$2\mathbf{II} \rightarrow trans\text{-}{}^-O_2CCH{=}CHCO_2^- + {}^-O_2CCH_2CH_2CO_2^- + 2H^+$$

or via

$$2\mathbf{I} \rightarrow trans\text{-}{}^-O_2CCH{=}CHCO_2^- + {}^-O_2CCH_2CH_2CO_2^-$$

(b) As G(-maleate) = 7.6 and G(-fumarate + succinate) = 5.4 clearly other, heavier, products with $G \sim 2.2$ are formed. These might be due to the addition of $CO_2^{\cdot-}$ to the double bond of maleate, which was observed as a major product by EPR spectroscopy.[4]

(c) The fact that G(-maleate) is somewhat larger than $Ge^-_{aq} + G_{\cdot OH} + G_{\cdot H} = 5.9$ in neutral solutions[8] might indicate that the reactions

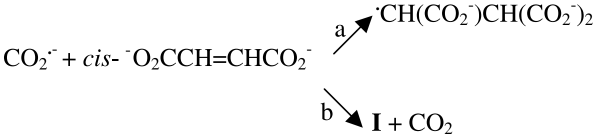
$$\mathbf{I/II} + HCO_2^- \xrightarrow{H+} {}^-O_2CCH_2CH_2CO_2^- + CO_2^{\cdot-}$$

occur. Analogous reactions were recently observed.[2,11] Alternatively, and/or, this increase in yields might be due to $^{\cdot}OH$ scavenging from spurs[12] by formate.

(d) The observation that fumarate is a major product indicates that though the cyclic nature of intermediates **I** and **II** is maintained in their reactions, at least in those of **II**, the unpaired electron is located primarily on the –CH– groups and enables the formation of products which require rotation of the CH–CH bond.

The somewhat larger yields in the N_2O saturated solutions is mainly attributed to the scavenging of e_{aq}^- from spurs by N_2O which is known to increase the radical yields by ca. 0.7.[9] It is of interest to note that UV studies indicate that ca. 65% of the reaction of $CO_2^{\cdot-}$ with maleate results in electron transfer,[5] which is in good agreement with our results in the N_2O saturated solutions at pH 5.3.

The decrease of *G*(-fumarate) with the increase in pH, without a decrease in *G*(-maleate) is probably due to an increase in the yield of $CO_2^{\cdot-}$ addition to maleate and a decrease in the yield of the electron transfer in this reaction.



$$\begin{tikzcd} & {}^{\cdot}CH(CO_2^-)CH(CO_2^-)_2 \\ CO_2^{\cdot-} + cis\text{-}{}^-O_2CCH{=}CHCO_2^- \arrow[ur, "a"] \arrow[dr, "b"'] & \\ & \mathbf{I} + CO_2 \end{tikzcd}$$

This suggestion is in accord with UV studies on the yield of electron transfer in this reaction.[5] Alternatively, it is plausible that radical anion **I** tends to dimerise, or add to maleate to a greater degree than the radical anion **II**.

Looking at the results for the fumarate system it is obvious that *G*(-fumarate) increases with the increase in pH. This result seems surprising as *G*(-maleate) is pH independent. A plausible explanation of this observation is that the yield of the reactions:

$$CO_2^{\cdot-} + \text{maleate} \rightarrow (\mathbf{I/II} + CO_2)/{}^{\cdot}CH(CO_2^-)CH(CO_2^-)_2$$

$$CO_2^{\cdot-} + \text{fumarate} \rightarrow (\mathbf{III/IV} + CO_2)/{}^{\cdot}CH(CO_2^-)CH(CO_2^-)_2$$

is similar, if not identical. Then the difference between *G*(-fumarate) and *G*(-maleate) observed at each pH is attributed to the reaction:

$$2\mathbf{III}/2\mathbf{IV}/(\mathbf{III} + \mathbf{IV}) \xrightarrow{H_2O} \text{fumarate} + \text{succinate}$$

As fumarate is thermodynamically more stable than maleate,[13] the yield of maleate is expected to be small as observed. (We have no explanation for the slight, though significant, increase in *G*(-maleate) with the increase in pH.) According to this assumption, the *G* yields of fumarate in the latter reaction are 2.9 ± 0.5 and 1.5 ± 1.0 at pH 5.3 and 7.0, respectively, in the He saturated solutions. Surprisingly, these *G* yields are identical with the yields of fumarate in the maleate system at these pHs. This observation was unexpected as it suggests that

(a) The yields of electron transfer in the reactions of $CO_2^{\cdot-}$ with maleate and fumarate are similar. This conclusion contradicts earlier suggestions based on the UV absorptions of the radicals formed.[5]

(b) The chemical properties of the radical anions **I/II** are similar to those of the radical anions **III/IV**.

Thus, it is tempting to suggest that though the radical anions **I/II** and **III/IV** are clearly different, as the EPR spectra point out, they decompose via

$$\mathbf{I/II} \text{ or } \mathbf{III/IV} \xrightarrow{H_2O} {}^{\cdot}CH(CO_2^-)CH_2CO_2^-$$

and the radicals ${}^{\cdot}CH(CO_2^-)CH(CO_2^-)_2$ then decompose mainly via

$$2{}^{\cdot}CH(CO_2^-)CH_2CO_2^- \rightarrow trans\text{-}{}^-O_2CCH{=}CHCO_2^- + {}^-O_2CCH_2CH_2CO_2^-$$

and to some degree via

$$2{}^{\cdot}CH(CO_2^-)CH_2CO_2^- \rightarrow ({}^-O_2CCH_2CH(CO_2^-)^-)_2$$

and via

$${}^{\cdot}CH(CO_2^-)CH_2CO_2^- + {}^-O_2CCH{=}CH(CO_2^-) \rightarrow {}^{\cdot}CH(CO_2^-)CH(CO_2^-)CH(CO_2^-)CH_2CO_2^-$$

Thus, the results suggest that the mechanism of reaction of the radical anions in the two systems are similar though the structures of the initial radical anions formed are different.

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7. Product analysis was performed by HPLC (Waters, Delta 600 model) with a Waters 996 photodiode array detector capable of measuring in the 190–800 nm range. Analysis was carried out with an Ultrasphere RP-18 Beckman column (250 mm × 4.6 mm × 5 μm) using a mobile phase consisting of 99% water (pH 2.8 with phosphoric acid) and

1% methanol. The flow rate was 0.8 ml/min and the injection volume was 20 μl. The samples were acidified prior to injection into the HPLC with phosphoric acid to pH 2.0. Detection was performed at 210 nm and the samples were identified from spectra and retention times.

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