

KINETIC DECAY OF $H\cdot$ IN THE RADIOLYSIS OF TETRACYCLINE HYDROCHLORIDE IN POWDER FORM AT 77 K*

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Kinetic decay of paramagnetic species formed in the radiolysis of tetracycline hydrochloride in powder form, at 77 K, shows that most of the $H\cdot$ is not able to migrate. Geminate recombination between $H\cdot$ and its partner is the main reaction: $H\cdot + TC\cdot \rightarrow TCH$, although a few $H\cdot$ succeed in diffusing slowly. But when $H\cdot$ acquires enough kinetic energy to migrate, it reacts preferentially with species different from its partner. The e^- is not observed by ESR, at 77 K, although tetracycline hydrochloride is a chemical trap for e^- in methanol, benzyl alcohol and alkaline aqueous solutions. In the radiolysis of tetracycline hydrochloride in powder form, the dimethylammonium group blocks $H\cdot$ abstraction reaction at 77 K.

Introduction

Crystalline solvent plays an important role in migration and in reactivity of species formed in radiolysis of solvent at 77 K. The study of selective hydrogen atom abstraction reaction has shown that the existence of channels in crystalline solvent renders possible migration of $H\cdot$ and reaction with solute selectively at 77 K.¹⁻⁴ Thermal decay of species formed in the radiolysis of solvent in frozen medium takes place in the vicinity of phase transition temperatures.⁵

The e^- is not observed by ESR when hydroxides of alkaline-earth elements in polycrystalline state are gamma-irradiated at 77 K, although these hydroxides in aqueous solutions behave as physical traps for e^- .⁶

DZIEGIELEWSKI and co-workers¹⁰ studied the radiolysis of four tetracyclines compounds in powder form by NMR and they proposed reaction mechanisms. They also studied the kinetic decay of paramagnetic species and they did not observe e^-

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by ESR, although these compounds behave as chemical traps¹¹⁻¹³ when they are dissolved in aqueous solutions or in organic compounds.¹⁴⁻¹⁶

In this paper we have studied reactions which are responsible for the kinetic decay of H• formed in the radiolysis of tetracycline hydrochloride (TC) in powder form by ESR at 77 K.

Experimental

The SF₆ and propene from Merck Co, and TC and desdimethylaminoxytetracycline from "Indústria Farmacéutica Bristol Laborerápica S. A." of São Paulo are CP grade. Four samples containing the same mass of TC in powder form (0.4 g) were prepared in the presence of H• and e⁻ scavengers and in the absence of air. Only one sample of desdimethylaminoxytetracycline was prepared in the absence of air. All samples were gamma-irradiated with the same dose of 3 kGy in the ⁶⁰Co-Gammacell 220 source from Atomic Energy of Canada Limited. The ESR spectra were recorded on a JEOL JES-ME-3 spectrometer at 77 K.

Results and discussion

ESR spectrum of TC in powder form (Fig. 1) shows the presence of chlorotetracycline as a paramagnetic impurity in small concentration.¹⁷ When TC in powder form is gamma-irradiated at 77 K, H• is observed and another paramagnetic species whose unpaired electron does not receive nuclear magnetic influence from neighbouring atoms (Fig. 2). This paramagnetic species corresponding to a singlet in the ESR spectrum will be represented by TC•. When this sample is warmed up at room temperature during 30 seconds, H• disappears completely while H₂Ċ-C₆ radical (triplet, a_H = 20 Oe) is observed in the ESR spectrum (Fig. 2). The H• abstracts another H• from H₃C-C₆ group of TC molecule. When desdimethylaminoxytetracycline in powder form is gamma-irradiated at 77 K, H•, TC• and H₂Ċ-C₆ were formed (Fig. 2). In some way, dimethylammonium group of TC blocks H• abstraction reaction in the radiolysis of TC at 77 K, but this group does not block this reaction when H• has enough kinetic energy to migrate.

In the radiolysis of alkaline solutions, methanol and benzyl alcohol containing TC at 77 K, the e⁻ is stabilized by solutes because they behave as physical or chemical traps.^{10,15,16} The formation of TC• can take place as a consequence of R-H bond scission of TC molecule or capture of e⁻ by TC molecule. Both possibilities were investigated with H• and e⁻ scavengers, respectively (Fig. 3).

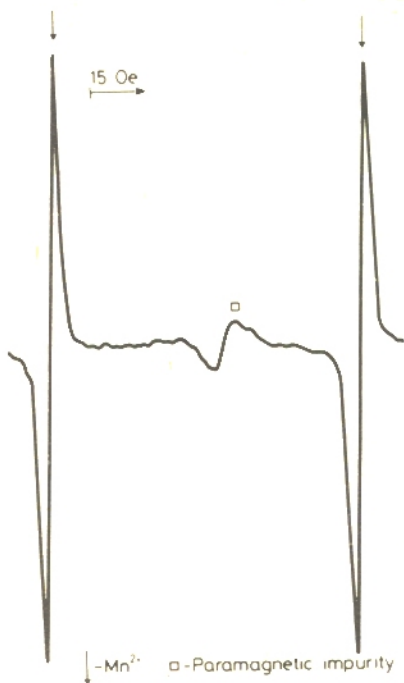


Fig. 1. ESR spectrum of TC in powder form at 77 K, without gamma-irradiation

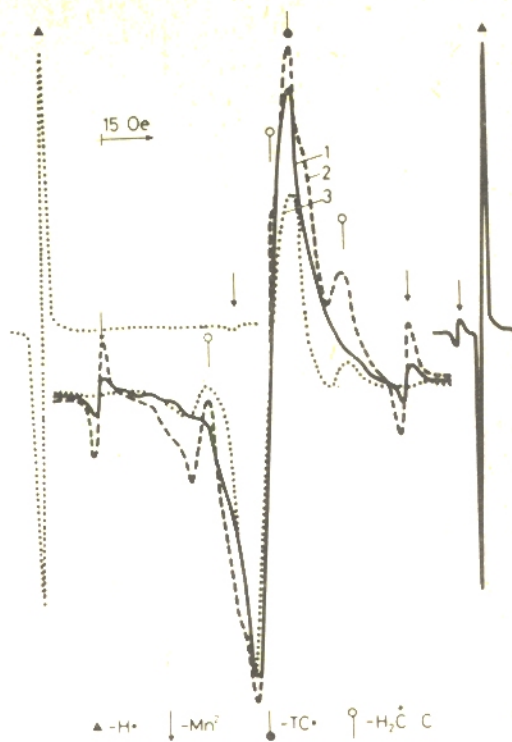


Fig. 2. Radiolysis of TC and desdimethylaminoxytetracycline in powder form at 77 K, TC (curve 1), TC gamma-irradiated at 77 K and warmed at room temperature during 30 seconds (curve 2), desdimethylaminoxytetracycline (curve 3)

The presence of air and SF_6 in the radiolysis of TC in powder form does not change the relative yield (RY) of $H\cdot$ or $TC\cdot$, indicating that e^- is not the precursor of these species. But addition of $H\cdot$ scavengers decreases both RY. Propene competes with TC in $H\cdot$ abstraction reaction. Therefore the formation of $TC\cdot$ is a consequence of R-H bond scission of TC molecule. It is an interesting fact, because TC in alkaline solutions or organic compounds capture e^- formed in the radiolysis of solvent at 77 K. The e^- is not stabilized by TC in powder form at 77 K. The C-OH bond scission takes place only with doses greater than 55 kGy^{10} and $OH\cdot$ is not observed by ESR while $H\cdot$ is observed by ESR at 77 K. The C-H bond scission is responsible for the formation of $TC\cdot$ in the radiolysis of TC in powder form at 77 K.

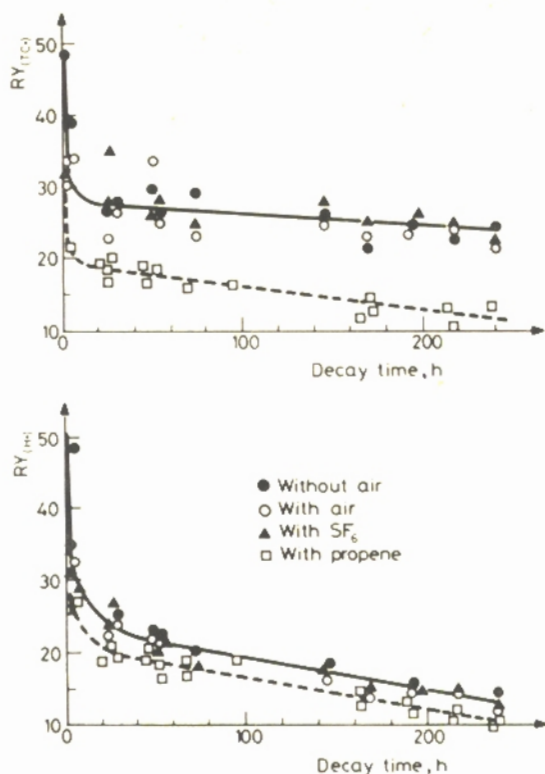


Fig. 3. The effect of H· and e⁻ scavengers addition on the kinetic decay of H· and TC· formed in the radiolysis of TC in powder form at 77 K

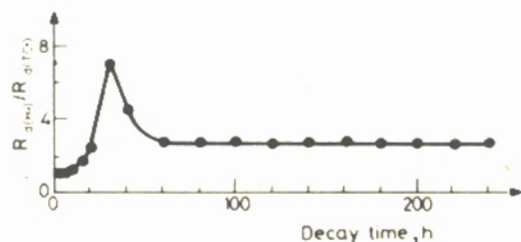


Fig. 4. ($R_{gh}(H\cdot)/R_{gh}(TC\cdot)$) during decay time after radiolysis ending

Figure 3 shows the slow kinetic decay of H· and TC· in the radiolysis of TC in powder form at 77 K. Considering the following facts relating to TC molecules: (a) interdependence among atoms;¹⁰ (b) the aromatic ring is an excitation scavenger;¹⁸ (c) it is quite resistant to chemical or biological change in activity when it is gamma-

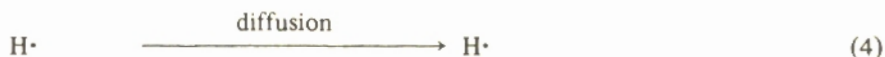
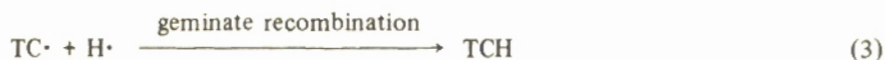
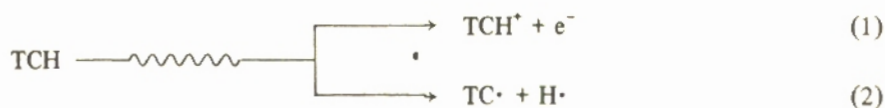
irradiated in powder form (10 kGy);¹⁷ it is possible to think that most of the energy from gamma-radiation is distributed among all TC molecules causing excitation.

A small amount of this energy is responsible for C-H bond scission so that H• has not enough energy to migrate. On the other side slow kinetic decay can be caused by difficult migration of H• by TC in powder form.

Figure 4 shows the relation between instantaneous rate of decay [$R_{id} = -(dRY/dt)$] for H• and TC• during decay time, t , after the end of radiolysis. Although R_{id} for both species decreases, it is interesting to note that

$$(R_{id}(H\cdot)_{0-5h} = R_{id}(TC\cdot)_{0-5h}).$$

Therefore, geminate recombination reaction between H• and TC• takes place:



TCH is another symbol of the TC molecule. The direct interaction of gamma-radiation with TC in powder form produces TC• and H• when C-H bond scission occurs [Reaction (2)], besides e⁻ [Reaction (1)]. Most part of the H• recombines with TC• partner [Reaction (3)] and a few H• diffuse slowly [Reaction (4)]. Reaction (3) is responsible for the decay of most of these species at 77 K.

On the other side, Reaction (5) prevails during an interval from 5 hours to 60 hours after end of radiolysis and $1 \leq (R_{id}(H\cdot)/R_{id}(TC\cdot)) \leq 7$. Not all H• formed in reaction recombine with TC• partner but some H• succeed in diffusing slowly and react with another H• preferentially or react with TC• in some cases [Reaction (6)]



It is interesting to note that R_{id} for both species are small and $R_{id}(H\cdot) = 3R_{id}(TC\cdot)$ after 60 hours from end of radiolysis. Reactions (5) and (6) are slow and the proba-

bilities of H \cdot reacting with TC \cdot or another H \cdot are small because concentration of H \cdot which are able to migrate is small.

When TC in powder form is gamma-irradiated at 77 K and warmed up to room temperature for some seconds (Fig. 5), the following facts are observed: (a) geminate recombination reaction between H \cdot and TC \cdot does not take place; (b) TC \cdot decays independently of H \cdot ; (c) H \cdot acquires enough energy to migrate and it reacts preferably

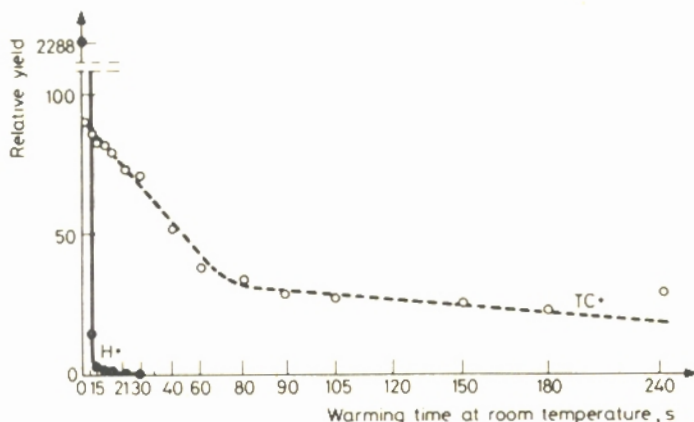


Fig. 5. Decay of H \cdot and TC \cdot formed in the radiolysis of TC in powder form at 77 K when the sample is warmed for different times at room temperature

with species different from its partner; (d) H \cdot is able to abstract another H \cdot from the H $_3$ C-C $_6$ group of TC molecule.

Most of the H \cdot formed in the radiolysis of TC in powder form, at 77 K, is not able to migrate because it has not enough kinetic energy. Therefore, geminate recombination reaction between H \cdot and TC \cdot is responsible for the decay of most of H \cdot .

In the radiolysis of TC in powder form at 77 K, e $^-$ is not observed by ESR although TC is a chemical trap for e $^-$ in methanol, benzyl alcohol and alkaline aqueous solutions.

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