Electron spin resonance study of the reaction of $SO_4^{\bullet-}$ with azolinones

M. Câmdida B. L. Shohoji, Horácio M. Novais and Abel J. S. C. Vieira
Instituto Superior Técnico, Química Orgânica, Av. Rovisco Pais, P-1096 Lisboa codex, Portugal

The reactions of photolytically generated sulfate radical-anion, $SO_4^{\bullet-}$, with several nitrogen-containing heterocycles of the azolinone type in aqueous solutions were studied by ESR spectroscopy. $SO_4^{\bullet-}$ reacts by formal hydrogen abstraction from an NH group to yield neutral radicals in acidic and neutral solutions and the respective radical-anions at basic pH. The pK_a-values of radicals derived from 2,3-dihydroimidazol-2(1*H*)-one, 2-oxo-2,3-dihydro-1*H*-imidazole-4-carboxylic acid and 2,3-dihydroindazol-3(1*H*)-one were determined to be in the range 8.5–10.4. In the cases of 2,3-dihydroimidazol-2(1*H*)-one and 2,3-dihydropyrazol-3(1*H*)-one secondary radicals were detected at basic pH. These radicals resulted from the disproportionation of the primary radicals followed by addition of OH^- and oxidation of the OH-adduct.

Introduction

Photolytically generated sulfate radical-anion, $SO_4^{\bullet-}$, reacts with several pyrimidines to yield radicals which are derived from the parent compound by one-electron oxidation followed by deprotonation[1] or by addition followed by hydrolysis of the sulfate adducts.[2]

The reaction of $SO_4^{\bullet-}$ with five-membered heterocyclic compounds, such as oxazole, imidazole, pyrrole and pyrazole derivatives, has also been investigated. With oxygen-containing heterocycles $SO_4^{\bullet-}$ adducts were formed, whereas with nitrogen-containing heterocycles, radicals derived from the parent compounds by one-electron oxidation followed by deprotonation were detected.[3]

In a previous work[4] we found that radicals formed by the reaction of $SO_4^{\bullet-}$ with six-membered heterocycles such as hydrazides resulted from formal hydrogen abstraction from the NH group. In order to obtain more information about the mechanisms involved, these studies have now been extended to five-membered nitrogen heterocycles of the azolinone type.

Experimental

Commercial 2,3-dihydrobenzimidazol-2(1*H*)-one (benzimidazolinone) (Aldrich) was used without further purification. 2,3-Dihydropyrazol-3(1*H*)-one (pyrazolin-3-one),[5] 2,3-dihydroimidazol-2(1*H*)-one (imidazolin-2-one),[6] 2-oxo-2,3-dihydro-1*H*-imidazole-4-carboxylic acid ('imidazolin-2-one-4-carboxylic acid')[6] and 2,3-dihydroindazol-3(1*H*)-one (indazolinone)[7] were prepared as described. All the inorganic chemicals were of analytical grade. Disodium hydrogen phosphate, potassium dihydrogen phosphate and trisodium borate were used as buffers.

ESR spectra were recorded by using a Bruker 200D spectrometer. The measurements were carried out at ~8 °C with argon-saturated solutions containing 1–2 mmol dm^{-3} of the compound and 30 mmol dm^{-3} $K_2S_2O_8$. In some cases 1% acetone was used as a sensitizer. The standard flow rate was ~0.1 cm^3 s^{-1}. In order to assign the NH proton coupling constants, some radicals were generated in D_2O. The experimental details for the *in situ* photolysis have been previously described.[4]

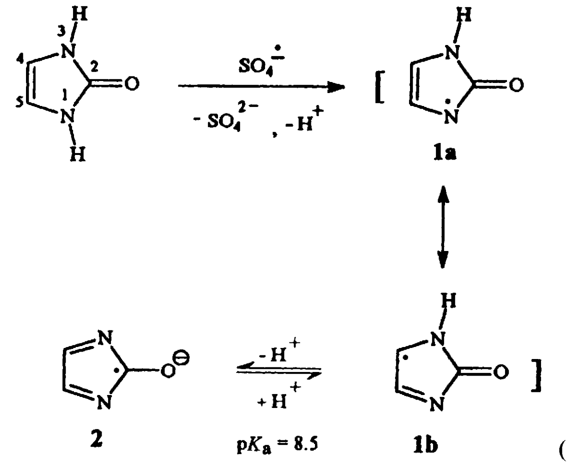
The *g*-factors of the radicals were determined with reference to the radical cation of perylene in conc. H_2SO_4 (g = 2.002 578).[8]

The relative concentrations of the radicals involved in the pK_a determinations were estimated from computer simulations of the overlapping spectra of the corresponding acidic and basic forms.

Results and discussion

2,3-Dihydroimidazol-2(1*H*)-one

The reaction of imidazolin-2-one at pH 5.5–8 yielded a radical whose ESR spectrum showed two different nitrogen splittings (0.017 and 0.16 mT) and three different hydrogen splittings (0.185, 0.494 and 1.008 mT). A similar spectrum was obtained in the absence of persulfate and presence of acetone. Since imidazolin-2-one exists predominantly in the tautomeric oxo form,[9] the ESR pattern was assigned to radical **1** formed by hydrogen abstraction by $SO_4^{\bullet-}$ (or by the acetone triplet, in the absence of persulfate) from N-1 or N-3 [eqn. (1)]. Hydrogen abstraction probably results from one-electron oxidation followed by deprotonation.

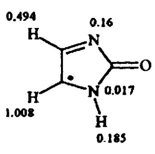


(1)

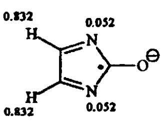
The 0.185 mT splitting (Table 1) was assigned to the acidic proton based on its exchange by D in D_2O and the largest splitting (1.008 mT) to hydrogen on position 4 due to the contribution of structure **1b**. The largest nitrogen splitting was assigned to N-1 considering the contribution of structure **1a**. The tautomeric oxo form of radical **1** is more in accordance with the relatively high hyperfine splitting constant observed for the acidic hydrogen (0.185 mT).

In the pH range 8.0–9.8 radical **1** existed together with its basic form **2**, whose spectrum consisted of a triplet (0.832 mT)

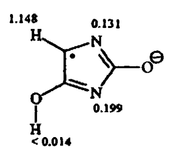
Table 1 ESR parameters of the radicals obtained on the reaction of $SO_4^{\bullet -}$ with azolinones[a]



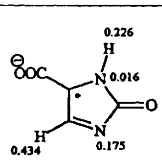
$g = 2.00364$
1



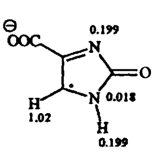
$g = 2.00359$
2



$g = 2.00385$
3



$g = 2.00396$
4



$g = 2.00409$
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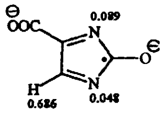

$g = 2.00404$
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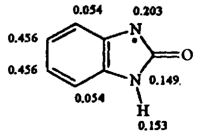
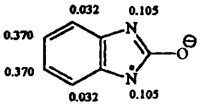


$g = 2.00378$
7



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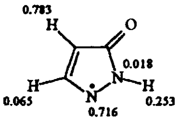
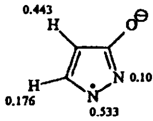


$g = 2.00431$
9



$g = 2.00425$
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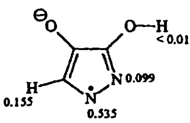
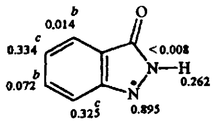
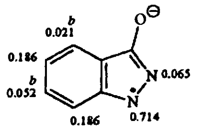


$g = 2.00426$
11



$g = 2.00338$
12



$g = 2.00405$
13

[a] The hyperfine splitting constants are in mT. [b,c] The assignments may be reversed.

of nitrogen quintets (0.052 mT). The same radical has been observed by Samuni and Neta[10] on the reaction of OH$^\bullet$ with imidazole at pH 13 and by Dogan *et al.*[3] on the oxidation, by OH$^\bullet$, of a species which resulted from the disproportionation of the imidazolidin-2-one radical.

The pK_a of **1** was estimated as 8.5 from the dependence of the concentrations of radicals **1** and **2** on the pH.

The pK-curves may be distorted by the effect of the different lifetimes of radicals **1** and **2**. Since **1** is a neutral radical and **2** a radical-anion, the lifetime of the former is expected to be shorter than that of the charged radical, due to decay processes such as dimerization. Therefore, the pK_a-values estimated for all the radicals in this work represent the lowest possible values.

Radical **2** was the only species observed in the pH range 9.8–11.5. Above pH 8.5 the reaction of $SO_4^{\bullet -}$ with the substrate may be in competition with OH^- to generate OH$^\bullet$[11] which can react with the azolinones. However, we found that OH$^\bullet$ (generated by photolysis in the presence of H_2O_2) adds to the C=C double bond of some compounds studied in this work (imidazolin-2-one and 'imidazolin-2-one-4-carboxylic acid') to yield OH-adducts which were not detected when $SO_4^{\bullet -}$ was used as an oxidant at basic pH values.[12] Above pH 11.5, a third radical coexisted with radical **2**, becoming predominant at low flow rates of the solution. Its ESR spectrum was characterized by a doublet (1.148 mT) of two nitrogen triplets (0.131 and 0.199 mT). This spectrum was assigned to the secondary radical **3** (Table 1) which was identical with the one obtained by Taniguchi and Kirino[13] on the reaction of OH$^\bullet$ with hydantoin at basic pH. Although the splitting of the acidic proton could not be observed, we believe that structure **3** is correct since the pK_a of the radical was found to be 13.5.[13] Radical **3** can be formed by disproportionation of radical **2** followed by nucleophilic addition of OH^- and subsequent oxidation of the adduct [eqn. (2)].

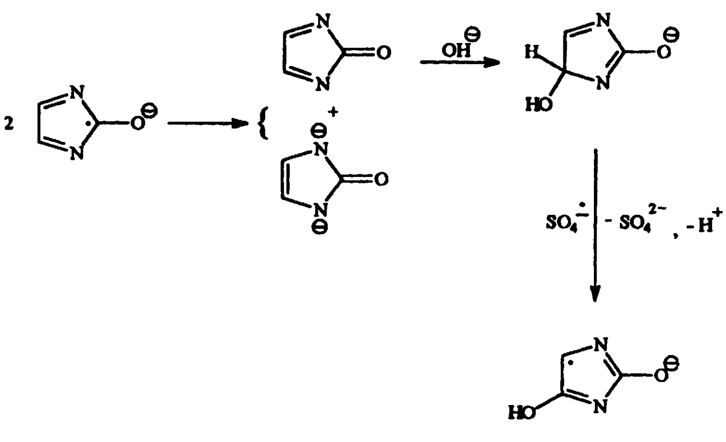
A mechanism of this type was previously proposed to explain the formation of secondary radicals on the reaction of OH$^\bullet$ with hydroxypyrimidines.[1] Another mechanism proposed for hydroxypyrimidines, involving disproportionation of OH-adducts, was ruled out since these species were only detected in the photolysis in the presence of H_2O_2 and not in the presence of persulfate.

2-Oxo-2,3-dihydro-1*H*-imidazol-4-carboxylic acid

The ESR spectrum obtained in the pH range 5.0–7.8 showed the existence of two radicals with slightly different *g*-values and relative concentrations ~2:1 [Fig. 1(*a*)]. The most abundant radical has two non-equivalent nitrogens (0.016 and 0.175 mT) and two non-equivalent hydrogens (0.226 and 0.434 mT). The other radical is characterized by two non-equivalent nitrogens and two non-equivalent hydrogens, as well, but with coupling constants different from those of the first radical (a_N = 0.018 and 0.199; a_H = 0.199 and 1.02 mT). These two radicals were identified as having the structures **4** and **5**, which are produced by formal H-abstraction by $SO_4^{\bullet -}$ from N-1 or N-3, respectively [eqn. (3)].

Radical **4** is expected to be less acidic than radical **5** due to the location of the carboxylate group near the NH. On this basis, structure **4** was assigned to the most abundant (and less acidic) radical and structure **5** to the less abundant radical. This assignment is confirmed by the splitting constant of the hydrogen on position 5, which is expected to be larger in radical **5**. The smallest nitrogen splitting was assigned to the nitrogen of the NH group by comparison with radical **1**.

In the pH range 7.7–11.0 a third overlapping spectrum appeared which showed two different nitrogen splittings (0.048 and 0.089 mT) and one hydrogen splitting (0.686 mT). This spectrum was due to radical-dianion **6** which is the basic form of both radical-anions **4** and **5**. The largest nitrogen splitting (0.089 mT) was assigned to N-3 by comparison with radicals derived from pyrroles[10] where it was found that the nitrogen



3 (2)

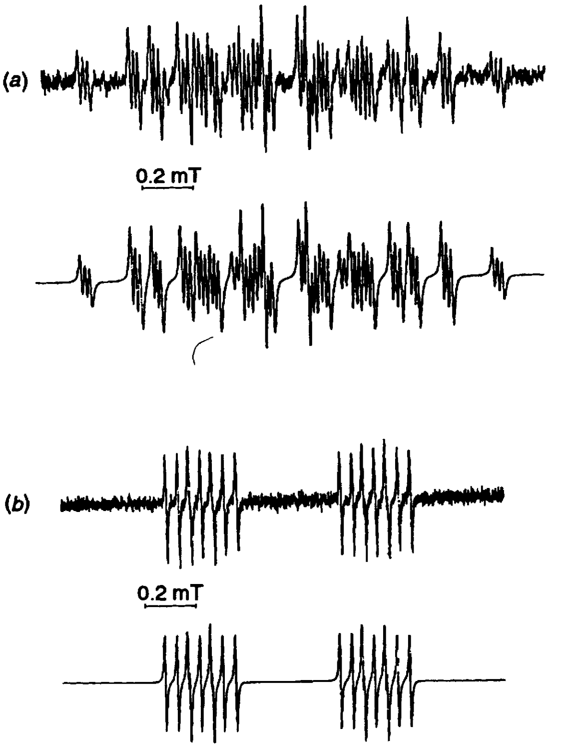


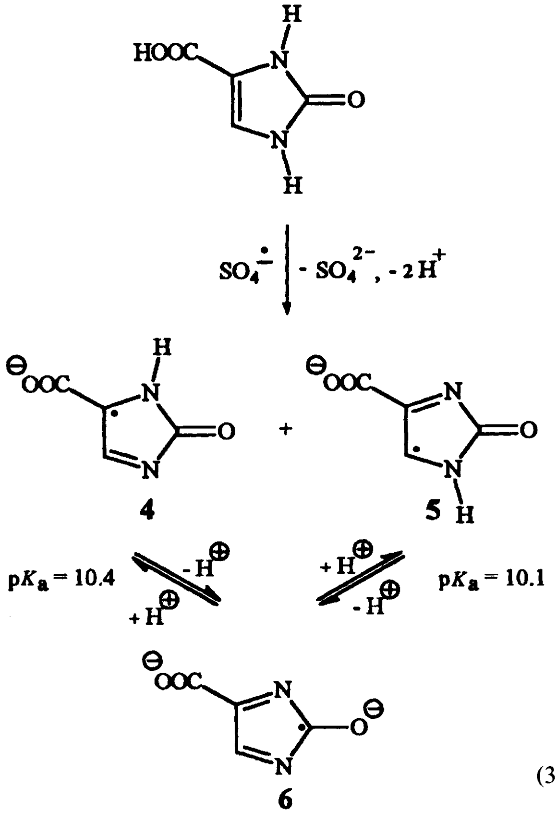
Fig. 1 ESR spectra of radicals obtained in the reaction of $SO_4^{\bullet -}$ with 2-oxo-2,3-dihydro-1*H*-imidazole-4-carboxylic acid. The computer-simulated spectra are shown below the experimental ones. (*a*) pH 7.7, radicals **4** (67%) and **5** (33%). (*b*) pH 11.4, radical **6**.

splitting constant increased when one hydrogen was replaced by a carboxylate group.

The pK_a-values of radicals **4** and **5** were determined as 10.4 and 10.1, respectively, from the dependence of the concentrations of species **4**, **5** and **6** on pH. Above pH 11 only radical **6** was present [Fig. 1(*b*)].

2,3-Dihydrobenzimidazol-2(1*H*)-one

A very weak ESR spectrum was obtained in the pH range 5.0–7.0. This spectrum consisted of lines due to two pairs of equivalent hydrogens (0.054 and 0.456 mT), one hydrogen (0.153 mT) and two non-equivalent nitrogens (0.149 and 0.203 mT). Accepting that benzimidazolinone exists predominantly in the tautomeric oxo form,[14] the radical responsible for this spectrum was identified as having structure **7**, which results from formal hydrogen abstraction from an NH group [eqn. (4)].



(3)

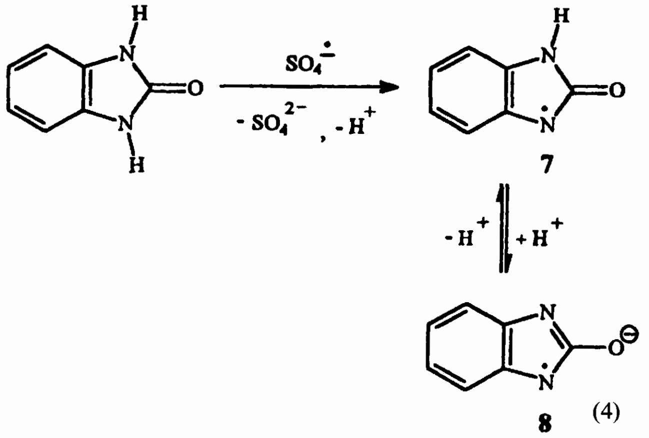
Above pH 10.0 a strong ESR spectrum was recorded which showed two pairs of equivalent hydrogens (0.032 and 0.370 mT) and two equivalent nitrogens (0.105 mT). The radical **8** (basic form of **7**) satisfies this pattern. The pK_a of radical **7** could not be estimated due to its poorly resolved ESR spectrum.

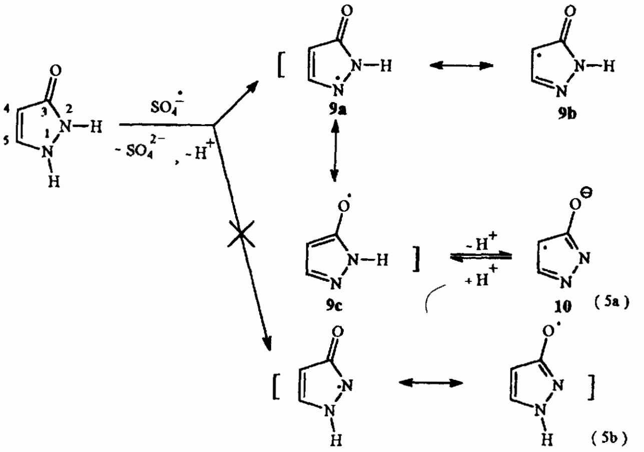
2,3-Dihydropyrazol-3(1*H*)-one

On the reaction of $SO_4^{\bullet -}$ with pyrazolin-3-one, at pH 4–9, only one radical was detected. Its ESR spectrum [Fig. 2(*a*)] was characterized by two different nitrogen splittings (0.018 and 0.716 mT) and three different hydrogen splittings (0.065, 0.253 and 0.783 mT). On the basis of these constants and taking into account that pyrazolin-3-one in aqueous solution exists mainly in the tautomeric oxo form,[15] the spectrum was assigned to a radical with the structure **9** formed by formal hydrogen abstraction by $SO_4^{\bullet -}$ from N-1 [eqn. (5a)].

A radical formed by hydrogen abstraction from N-2 [eqn. (5b)] was ruled out, since such a radical is expected not only to be less stable than radical **9** but also to have a smaller splitting for hydrogen on position 4 and a larger splitting for N-2. The 0.253 mT splitting was assigned to the NH proton based on its exchange by D in D_2O, the largest splitting (0.783 mT) being assigned to hydrogen on position 4 on the basis of structure **9b**, and the largest nitrogen splitting to N-1 taking into account structure **9a**.

Above pH 9 two overlapping spectra were obtained. The concentration ratio of the two radicals was dependent on the flow rate of the solution. At standard flow rates (~ 0.1 cm^3 s^{-1}), the most abundant radical, **10**, exhibited a spectrum [Fig. 2(*b*)] with a pattern resulting from two non-equivalent nitrogens (0.108 and 0.533 mT) and two non-equivalent hydrogens (0.176 and 0.443 mT). This radical was formed by deprotonation of radical **9**. The radical which became predominant at low flow rates of the solution was characterized by a spectrum [Fig. 2(*c*)] which consisted of a hydrogen doublet (0.155 mT) and two nitrogen triplets (0.099 and 0.535 mT). Radical **11** (Table 1) formed by disproportionation of radical-anion **10** following a mechanism similar to the one depicted for imidazolin-2-one [eqn. (2)] accounts for that spectrum.





In order to ensure that the attack by OH^- had not occurred on the pyrazolin-3-one itself, a sample of the compound in basic solution was analysed by HPLC with photodiode array detection. The resulting chromatogram showed neither any peak besides that of pyrazolin-3-one nor the consumption of this compound.

The pK_a of radical **9** was not determined due to the impossibility of maintaining a constant pH of the solutions (even with the addition of buffers). This is possibly a result of the slow hydrolysis of the compound.

2,3-Dihydroindazol-3(1*H*)-one

In the range of pH 4.0–8.1 we detected a radical whose spectrum exhibited lines resulting from the interaction of the unpaired electron with one nitrogen (0.895 mT) and five different hydrogens (0.014, 0.072, 0.262, 0.325 and 0.334 mT). In contrast to the other azolinones studied in this work, indazolinone exists in solution mainly in the tautomeric hydroxy form, 1*H*-indazol-3-ol.[16] However, the radical which was detected in the pH range 4.0–8.1 exhibited an ESR spectrum [Fig. 3(*a*)] characterized by one nitrogen and one hydrogen coupling constants similar to those of radical **9**. Therefore, radical **12**, formed by hydrogen abstraction from N-1 by $SO_4^{\bullet-}$ [eqn. (6)], has a structure similar to that of radical **9**.

The 0.262 mT splitting constant was assigned to the NH proton on the basis of its exchange by D in D_2O. The two smallest hydrogen splittings were assigned to positions 7 and 5, whereas the two largest were assigned to positions 6 and 8.

In the range of pH 8.1–9.6 a second spectrum overlapped the

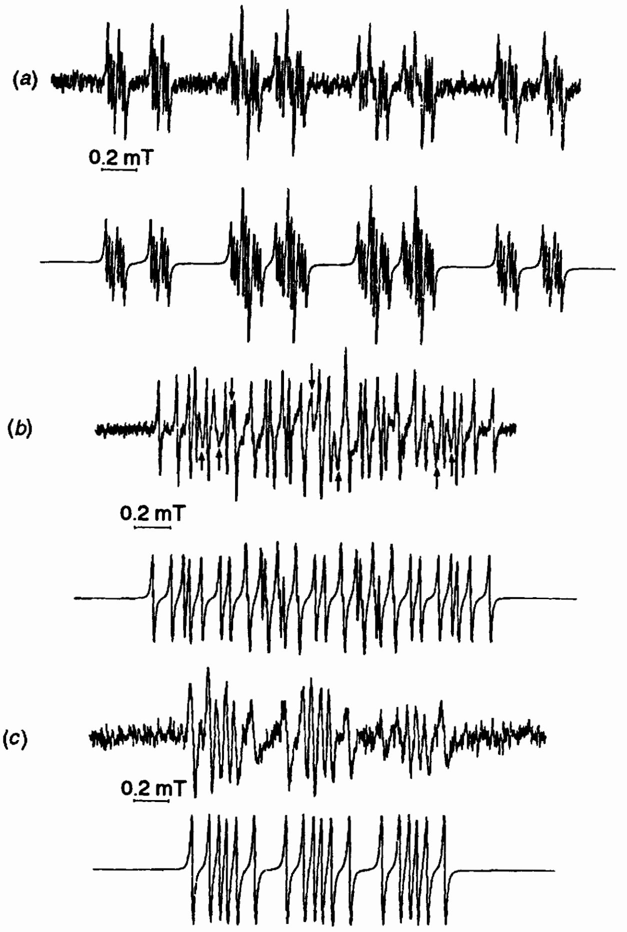


Fig. 2 ESR spectra of radicals obtained on the reaction of $SO_4^{\bullet-}$ with 2,3-dihydropyrazol-3(1*H*)-one. The computer-simulated spectra are shown below the experimental ones. (*a*) pH 6.3, radical **9**. (*b*) pH 12.8, radical **10** (arrows indicate lines from radical **11**). (*c*) pH 11.9, radical **11**.

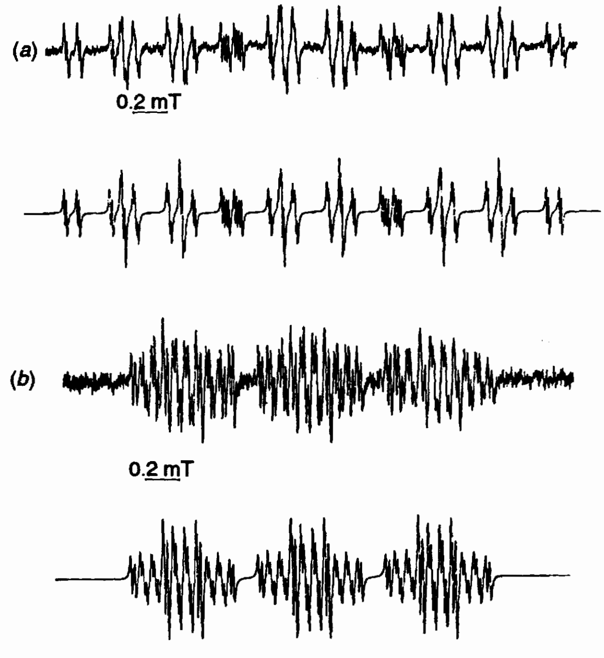
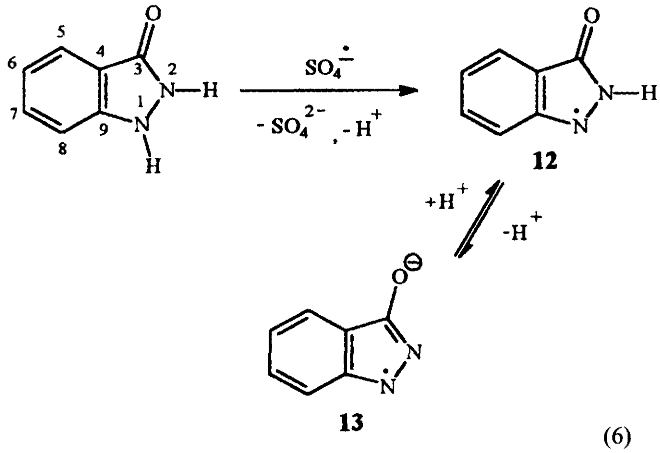


Fig. 3 ESR spectra of radicals obtained on the reaction of $SO_4^{\bullet-}$ with 2,3-dihydroindazol-3(1*H*)-one. (*a*) pH 5.0, radical **12**. (*b*) pH 11.5, radical **13**.



(6)

first one. Radical-anion **13**, which is the basic form of radical **12**, was responsible for the second spectrum consisting of lines from two different nitrogens (0.065 and 0.714 mT), one pair of equivalent hydrogens (0.186 mT) and two non-equivalent hydrogens (0.021 and 0.052 mT). Assignments were made by comparison with radical **12**.

In contrast to pyrazolin-3-one, the hydrolysis of indazolinone was found to be very slow during the time of the experiment, allowing the determination of a pK_a value = 9.0 for radical **12**.

Above pH 9.6 only radical **13** was observed [Fig. 3(*b*)].

Conclusions

Photolytically generated sulfate radical-anion, $SO_4^{\bullet-}$, reacts with azolinones such as imidazolin-2-one, pyrazolin-3-one and related compounds by hydrogen abstraction from an NH group, possibly *via* one-electron oxidation followed by deprotonation.

Radicals resulting from addition of $SO_4^{\bullet-}$ to double bonds were not observed.

At basic pH and low flow rates of the solutions, secondary radicals derived from imidazolin-2-one and pyrazolin-3-one were formed. These radicals resulted from the disproportionation of the primary radicals followed by addition of OH^- and oxidation of the OH-adduct.

Acknowledgements

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