Photochemical Substitution of Amino- and Hydroxy-anthraquinones

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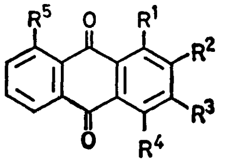
Irradiation of 1-aminoanthraquinone with visible light in the presence of an excess of either sodium sulphite or sulphide in 50% aqueous pyridine gives exclusively sodium 1-aminoanthraquinone-2-sulphonate and -2-thiolate, respectively, in good yield. Under similar conditions with sodium sulphite, 1-methylamino-, 1-amino-4-chloro-, and 1-amino-5-chloro-anthraquinone give the respective sodium 2-sulphonate only, while 2-aminoanthraquinone gives the sodium 3-sulphonate. In contrast, 1-hydroxyanthraquinone gives a mixture of the sodium 2- and 4-sulphonates and disodium 2,4-disulphonates. The different substitution pattern observed for 1-amino- and 1-hydroxy-anthraquinone has been rationalised by application of semi-empirical molecular orbital theory.

One of us has shown that irradiation of 1-aminoanthraquinone (Ia) and sodium sulphite in aqueous pyridine with visible light at 22 °C gives sodium 1-aminoanthraquinone-2-sulphonate (Ib) in high yield.[1] Similar irradiation of sodium 8-hydroxyanthraquinone-1-sulphonate (Ic) and sodium sulphite in aqueous ammonia at 25 °C gives a mixture of disodium 8-hydroxyanthraquinone-1,7-disulphonate (Id) and trisodium 4-hydroxyanthraquinone-1,3,5-trisulphonate (Ie).[2]

The related thermal dark reactions of both the amino- and hydroxy-derivatives (Ia and c) give similar products of substitution.[2,3] Because it is known [4-6] that radical anions are present in this type of system at 150 °C, one step in the reaction probably involves electron transfer from the reagent to the substrate (A) [equation (1)] akin to the behaviour of the more powerful reductant, sodium dithionite [7] [equation (2)].

$$A + SO_3^{2-} \longrightarrow {}^{\cdot\,-} + SO^{\cdot\,-} \qquad (1)$$

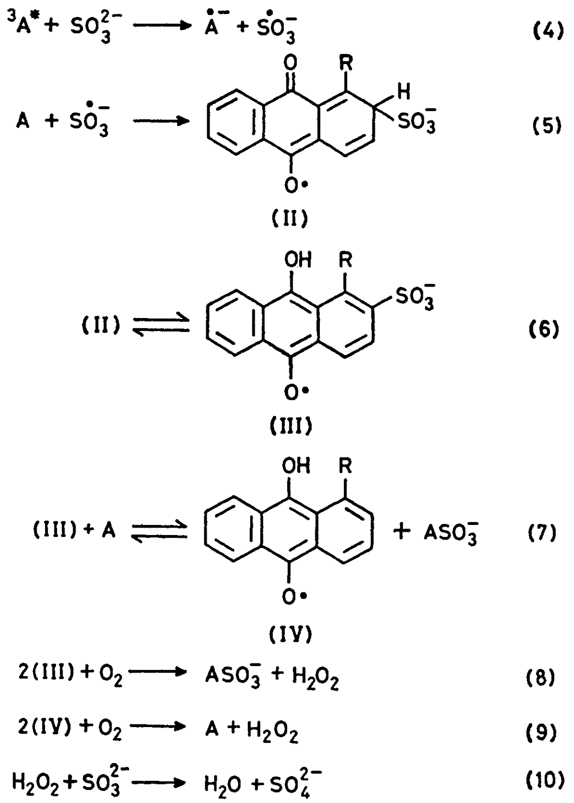
$$A + S_2O_4^{2-} + 4\,OH^- \longrightarrow A^{2-} + 2SO_3^{2-} + 2H_2O \qquad (2)$$



(I)

a; $R^1 = NH_2, R^2 = R^3 = R^4 = R^5 = H$
b; $R^1 = NH_2, R^2 = SO_3Na, R^3 = R^4 = R^5 = H$
c; $R^1 = OH, R^5 = SO_3Na, R^2 = R^3 = R^4 = H$
d; $R^1 = OH, R^2 = R^5 = SO_3Na, R^3 = R^4 = H$
e; $R^1 = OH, R^2 = R^4 = R^5 = SO_3Na, R^3 = H$
f; $R^1 = NH_2, R^4 = Cl, R^2 = R^3 = R^5 = H$
g; $R^4 = NH_2, R^5 = Cl, R^1 = R^2 = R^3 = H$
h; $R^1 = NH_2, R^4 = Cl, R^2 = SO_3Na, R^3 = R^5 = H$
i; $R^4 = NH_2, R^5 = Cl, R^3 = SO_3Na, R^1 = R^2 = H$
j; $R^1 = NH_2, R^2 = CH_3, R^3 = R^4 = R^5 = H$
k; $R^2 = NH_2, R^1 = R^3 = R^4 = R^5 = H$
l; $R^2 = NH_2, R^3 = SO_3Na, R^1 = R^4 = R^5 = H$
m; $R^1 = NHMe, R^2 = R^3 = R^4 = R^5 = H$
n; $R^1 = NHMe, R^2 = SO_3Na, R^3 = R^6 = R^5 = H$
o; $R^1 = NMe_2, R^2 = R^3 = R^4 = R^5 = H$
p; $R^1 = NH_2, R^2 = SNa, R^3 = R^4 = R^5 = H$
q; $R^1 = OH, R^2 = R^3 = R^4 = R^5 = H$
r; $R^1 = OH, R^2 = SO_3Na, R^3 = R^4 = R^5 = H$
s; $R^1 = OH, R^4 = SO_3Na, R^2 = R^3 = R^5 = H$
t; $R^1 = OH, R^2 = R^4 = SO_3Na, R^3 = R^5 = H$
u; $R^1 = O^-, R^2 = R^3 = R^4 = R^5 = H$

Treatment of the hydroxy-derivative (Ic) with the sulphite radical anion (generated from Fenton's reagent and sodium sulphite [8]) also results in the formation of the same products (Id and e) [2] as those observed in the photochemical and thermal dark reactions. The mechanism shown in the Scheme has been proposed for the photosubstitution reactions of (Ia and c) with sodium sulphite (A = anthraquinone: R = NH_2,OH).



Scheme

The aim of the present work was to assess the preparative scope of such reactions and adduce evidence regarding the mechanism.

Aminoanthraquinones.—Irradiation of 3.75mM-1-

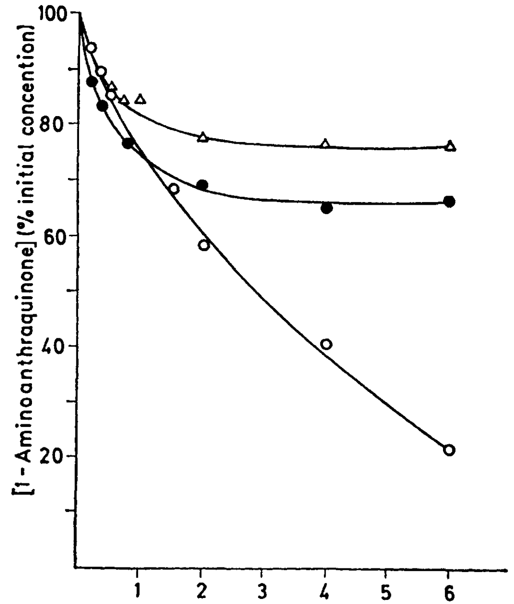
aminoanthraquinone (Ia) with 37.5mM-sodium sulphite in aerated 50% aqueous pyridine during 6 h at 22 °C with a medium pressure mercury arc lamp fitted with a Pyrex filter results in a 95% conversion of the substrate into sodium 1-aminoanthraquinone-2-sulphonate (Ib) (93%) with no dark reaction. A similar irradiation with 1.75mM-(Ia) and a tenfold excess of reagent gives a 77% conversion into (Ib) under the same conditions (Table 1). However, the reaction stops after 33% conversion under pure oxygen (Figure), either because of quenching (which suggests triplet participation in the reaction) or more likely, because the competing oxidation of sulphite to sulphate is more rapid than that which occurs under air {though the initial rate is faster due to oxidation of the semiquinone [equation (8)]}. Under nitrogen, however, the reaction stops after 22% conversion because of the attainment of an equilibrium between the semiquinone of the substrate and that of the product [equation (7)]. At 52 °C, with 35mM-sodium sulphite both substrate conversion and product yield are quantitative but a dark reaction also occurs to give the 2-sulphonate in 5% conversion.

TABLE 1

Photosubstitution of amino- and hydroxy-anthraquinones in aqueous pyridine (200 ml) [a]

Anthraquinone substrate (mmol)	Reagent (mmol) [b]	Reaction temp. (°C), time (h)	Substrate recovered (%)	Anthraquinone product(s), yield (%)
1-NH_2 (0.75)	Na_2SO_3 (7.5)	22, 6	5	(Ib), 93
1-NH_2 (0.35)	Na_2SO_3 (3.5)	22, 6	23	(Ib), 100
1-NH_2 (0.35)	Na_2SO_3 (3.5)	52 ± 1,6	0	(Ib), 100
1-NH_2 (0.35)	Na_2S (7.0)	22, 6	82	(Ip), 70 [c]
1-NHMe (0.35)	Na_2SO_3 (3.5)	22, 6	77	(In), 36
2-NH_2 (0.35)	Na_2SO_3 (7.0)	22, 6	82	(Il), 100
1-OH (0.35)	Na_2SO_3 (7.0)	22, 6	0	(Ir), 30.5 (Is), 15.7 (It), 24.0
1-OH (0.35)	Na_2S (7.0)	22, 6	31	(Ir), 45.4 [c] (Is), 19.4 [c] (It), trace
1-NH_2-4-Cl (0.75)	Na_2SO_3 (7.5)	22, 12	18	(Ih), 94
1-NH_2-2-Me (0.75)	Na_2SO_3 (7.5)	22, 12	97	None detected
1-NH_2-5-Cl (0.75)	Na_2SO_3 (75)	22, 12	13	(Ii), 97

[a] See text for general procedure. [b] Na_2SO_3 and Na_2S were hepta- and nona-hydrates respectively. [c] Determined as the respective sodium sulphonates by H_2O_2 oxidation (see text).



Reduction of substrate concentration with time during the photolysis of 1-aminoanthraquinone (1.7mM) and sodium sulphite (17.5mM) in 80% aqueous pyridine at 22 °C under: air (○), nitrogen (△), and oxygen (●)

Attempts to implicate the intramolecular charge transfer triplet state of 1-aminoanthraquinone,[9] which lies between 176 and 197 kJ mol^{-1}, as the reactive species in the photosubstitution were carried out by adding triplet quenchers such as anthracene and its derivatives to the system. Because anthracenes absorb strongly at λ 370—380 nm an additional filter consisting of a 25% solution of nitrobenzene in ethanol was employed.* However, neither anthracene nor 9,10-dibromoanthracene (E_T 176 and 166 kJ mol^{-1}, respectively) [10] were found to be sufficiently soluble in 50% aqueous pyridine to warrant investigation.†

The reported absence of conjugation between the sulphonic acid group and the aromatic nucleus in anthracene-1-sulphonic acid [11] suggests that the triplet excitation energy of the molecule is comparable in magnitude to that of anthracene itself. Quenching experiments were carried out, therefore, using either sodium anthracene-1-sulphonate or disodium anthracene-1,5-disulphonate.

Irradiation of 1.75mM-1-aminoanthraquinone with 17.5mM-sodium sulphite gives only a 45% conversion into the 2-sulphonate at 30 °C under control conditions using the nitrobenzene filter. However, the conversions observed when similar irradiation is carried out with the

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* This was placed in the cooling jacket of the lamp and was found to remove 100% of light at < λ 420 nm and transmit >90% at >λ 460 nm.

† Other strengths of aqueous pyridine were equally ineffective: as the solubility of the anthracenes improves with increasing concentrations of pyridine in the solvent the corresponding solubility of sodium sulphite falls rapidly.

filter in the presence of 7.18mM either of sodium anthracene-1-sulphonate or disodium anthracene-1,5-disulphonate, show that only a relatively small quenching effect occurs in either case (Table 2). Since both bromide and iodide ions are reported to induce intersystem crossing from the excited singlet manifold to the corresponding triplet manifold during irradiation of potassium anthraquinone-2-sulphonate in aqueous ammonia,[12] the irradiation of 1-aminoanthraquinone was repeated in the presence of an excess of both anions in the expectation that if the reactive state is singlet in character the reaction would be at least partially quenched (Table 2). However, no quenching effect is observed and the improved conversions obtained *versus* the control may either reflect the participation of the triplet state of the amine in these reactions * or may be due simply to an increase in the polarity of the medium. The multiplicity of the excited state responsible for reaction, therefore, remains unresolved.

TABLE 2

Irradiation of 1-aminoanthraquinone (1.75mM) and sodium sulphite (17.5mM) in the presence of certain additives in 50% aqueous pyridine

Additive	Reaction temp. (°C) and time (h)	Substrate recovery (%)	Yield of (Ib) (%) [a]	Filter
None	30, 6	55	92	Pyrex–nitrobenzene
Sodium anthracene-1-sulphonate (7.18mM) [b]	30, 6	65	94	Pyrex–nitrobenzene
Disodium anthracene-1,5-disulphonate (7.18mM) [d]	30, 6	66	97	Pyrex–nitrobenzene
Sodium bromide [c] (52.5mM)	22, 6	8	98	Pyrex
Sodium iodide [c] (52.5mM)	22, 6	9	99	Pyrex
None [c]	22, 6	20	100	Pyrex

[a] Based on consumed substrate. [b] Maximum solubility in 50% aqueous pyridine in the presence of sodium sulphite. [c] 33mM-Sodium sulphite used in these experiments.

The photochemical reaction of the amine (Ia) with sodium sulphite can be extended also to derivatives such as 1-amino-4- and 5-chloroanthraquinones (If and g) to give similar products of substitution (Ih and i) in high yield, but not to 1-amino-2-methylanthraquinone (Ij) in which the potential site of substitution is blocked (Table 1).

A related photolysis of 1.75mM-2-aminoanthraquinone (Ik) with sodium sulphite during 6 h at 22 °C gives only an 18% conversion into sodium 2-aminoanthraquinone-3-sulphonate (Il) with no dark reaction. Similar irradiation of 1-methylaminoanthraquinone (Im) gives a 13% conversion into sodium 1-methylaminoanthraquinone-2-sulphonate (In), but no sulphonated products are observed in the corresponding photolysis of 1-demethylaminoanthraquinone (Io) although some demethylation occurs to 1-methylaminoanthraquinone (Im) [84% yield based on 12% conversion of (Io)].

In contrast to the reactions with sodium sulphite, little or no reaction is observed on irradiation of 1.75mM-1-aminoanthraquinone in aqueous pyridine alone or with 35mM-sodium chloride, iodide, hydroxide, nitrite, or thiosulphate during 6 h at 22 °C. The possibility that the photosubstitutions described with sodium sulphite proceed *via* an intermediate hydroxyl radical which then reacts with the sulphite anion can be discounted because of the absence of hydroxylated products in the reaction with aqueous pyridine (py) alone [equations (11)—(13)]. However, both sodium dithionite

$$\mathrm{py} + \mathrm{H_2O} \rightleftharpoons \mathrm{p\overset{+}{y}H} + \mathrm{OH^-} \qquad (11)$$

$$^3\mathrm{A}^* + \mathrm{OH^-} \longrightarrow \mathrm{A}^{\cdot -} + \dot{\mathrm{O}}\mathrm{H} \qquad (12)$$

$$\mathrm{SO_3}^{2-} + \dot{\mathrm{O}}\mathrm{H} \longrightarrow \mathrm{SO_3}^{\cdot -} + \mathrm{OH^-} \qquad (13)$$

and sulphide react to give a 51 and 18% conversion, respectively, of the amine into sodium 1-aminoanthraquinone-2-sulphonate (Ib) and sodium 1-aminoanthraquinone-2-thiolate (Ip) (estimated also as the 2-sulphonate by oxidation of the reaction product with an excess of hydrogen peroxide). The formation of the 2-sulphonate in the former case probably arises by reaction of the amine (Ia) with the sulphite anion which is generated in turn from dithionite by electron transfer [see equation (2)]. The thiolate (formed in the latter reaction) probably arises by a related electron transfer mechanism to that proposed for the anthraquinone sulphonates (see Scheme). Neither 1-methylamino- nor 2-amino-anthraquinone (Im and k) react with sodium sulphide under these conditions of irradiation.

Other Substituted Anthraquinones.—Irradiation of 1-hydroxyanthraquinone (Iq) with sodium sulphite under conditions similar to those described for 1-aminoanthraquinone gives a 100% conversion of the substrate into sodium 1-hydroxyanthraquinone-2-sulphonate (Ir) (31%), the 4-sulphonate (Is) (18%), and the disodium 2,4-disulphonate (It) (24%) with no dark reaction (Table 1). A related reaction with sodium sulphide results in a 69% conversion into a mixture of anthraquinone-thiolates and -sulphonates which on oxidation with aqueous hydrogen peroxide gives the 2-sulphonate (Ir) (45%) and the 4-sulphonate (Is) (19%) with a trace only of the 2,4-disulphonate (It). No dark reaction is observed.

Molecular Orbital Studies.—There are strong similarities between the selectivities of the hydroxyl radical and the sulphite radical anion in their reactions with

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* A referee has suggested that because aminoanthraquinones tend to fluoresce rather than phosphoresce, little triplet participation would be expected.

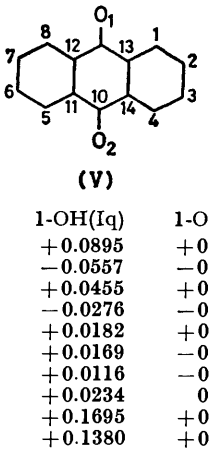
1,8-dihydroxyanthraquinone.[2] However, because the former displays only a low substrate and positional selectivity [13,14] by comparison with electrophilic reagents it follows by inference that the transition state for each substitution occurs early along the reaction coordinate and probably bears a structural resemblance to the aromatic substrate. A picture of the charge distribution calculated by molecular orbital methods in the quinones studied here would be expected, therefore, to show a correlation with the reactivities observed experimentally.

π-Charge densities were obtained for 1- and 2-amino- and 1-hydroxy-anthraquinone (Ia, k, and q) and its oxyanion (Iu) by application of the CNDO/2 method [15] using the same geometries for the anthraquinone molecule (V) as those described previously but with 25 iterations of the computer program.[2,16]

Both 1-amino- and 1-hydroxy-anthraquinone show similar π-charge densities with most negative charge concentrated at the 2-position of each molecule with smaller charge at the 4-position (Table 3). Electrophilic attack would be expected to occur, therefore, mainly if not exclusively at the 2-position of each molecule and this is indeed observed with 1-aminoanthraquinone. That the observed substitution in the hydroxy-compound contrasts markedly with the MO predictions is almost certainly attributable to ionisation of the hydroxy-group in aqueous pyridine. Thus while 1-hydroxyanthraquinone shows a single long wave absorption at 402 nm (log ε 3.74 in MeOH),[17] its oxyanion is different and absorbs at 493 nm (log ε 3.70 in MeOH) with no absorption in the 400 nm region.[17] However, in 50% aqueous pyridine the hydroxy-compound shows two absorptions, one at 407 (log ε 3.63) and the other at 493 nm (3.19) which demonstrates the presence of both the hydroxy-compound and its oxyanion.

TABLE 3

Calculated CNDO/2 π-charge densities for substituted anthraquinones



(V)

Atom	1-NH_2(Ia)	1-OH(Iq)	1-O^-(Iu)	2-NH_2(Ik)
C(1)	+0.1028	+0.0895	+0.1926	−0.0702
C(2)	−0.0779	−0.0557	−0.0998	+0.0895
C(3)	+0.0513	+0.0455	+0.0325	−0.0770
C(4)	−0.0430	−0.0276	−0.1316	+0.0562
C(5)	+0.0185	+0.0182	+0.0120	+0.0188
C(6)	+0.0140	+0.0169	−0.0196	+0.0131
C(7)	+0.0115	+0.0116	−0.0022	+0.0109
C(8)	+0.0208	+0.0234	0.0000	+0.0191
C(9)	+0.1628	+0.1695	+0.1433	+0.1404
C(10)	+0.1390	+0.1380	+0.1640	+0.1475
C(11)	+0.0017	+0.0031	+0.0057	+0.0025
C(12)	−0.0019	+0.0061	+0.0409	−0.0020
C(13)	−0.0979	−0,0807	−0.1522	+0.0336
C(14)	+0.0329	+0.0278	+0.0168	−0.0623
O(1)	−0.2521	−0.2585	−0.2482	−0.1998
O(2)	−0.1974	−0.1957	−0.2410	−0.2230
N [a]	−0.8852			−0.8971
O [a]		−0.4753	−0.7177	

[a] Heteroatom of the respective substituent.

The corresponding π charge densities of the oxyanion (Iu) show considerable differences from the 1-hydroxy-compound (Iq) since most negative charge is now concentrated at the 4-position in contrast to the 2-position of the latter (Table 3). Electrophilic attack would be expected to occur, therefore, at the 4-position in the oxyanion. There is a very good correlation, therefore, between the observed substitution of 1-hydroxyanthraquinone in aqueous pyridine and the charge distribution of (Iu and q): the preponderance of 2-substitution probably reflects the proportion of un-ionised material in solution.

The charge distribution of 2-aminoanthraquinone (Table 3) is also consistent with the experimental results since most charge is concentrated at the 3-position of the molecule, though the correlation is less satisfactory because of the relatively high charge observed at the 1-position.

EXPERIMENTAL

AnalaR grade reagents were used throughout. Authentic samples of the anthraquinones described here were either provided or synthesised by I.C.I. Ltd. using known methods [18] and purified by recrystallisation from dimethylformamide. Products from the photolyses were identified by comparison with authentic samples using t.l.c. and visible absorption spectroscopy and/or by ^1H n.m.r. spectroscopy with a Perkin-Elmer R 32 instrument operating at 90 MHz. In the latter case, pyridine and any unchanged starting material were removed from the irradiated solutions by steam distillation and filtration respectively. The aqueous extracts were evaporated to dryness and the residue was then dissolved in [$^2H_6$]dimethyl sulphoxide. In this way, the spectrum of the product from irradiation of 1-aminoanthraquinone (Ia) was shown to be identical with that obtained from an authentic sample of sodium 1-aminoanthraquinone-2-sulphonate (Ib) with two characteristic doublets (J 8 Hz) at δ 7.94 and 7.38 relative to tetramethylsilane (internal standard) assigned to the 3- and 4-protons of the anthraquinone ring. Other products were identified in a similar way.

Photolyses were carried out using a conventional photochemical reactor with a medium pressure mercury arc lamp (200 ml capacity; Baird and Tatlock 360/129; 100 V–125 W) fitted with a Pyrex glass filter (to eliminate light below 370 nm) and cooled by an external water jacket. Quenching experiments were carried out by passing a 25% nitrobenzene–ethanol mixture through the water jacket (2—3 mm thickness) using a peristaltic pump connected to a heat exchanger. Photolyses were monitored by t.l.c. on Merck DC–Alufolien Kieselgel $60F_{254}$ eluted with dioxan–n-butanol–ammonia (d 0.880)–water (4 : 2 : 2 : 1) for sulphonates and thiolates (eluant A) and toluene–acetone (95 : 5) [eluant B] for non-polar compounds.

Photosubstitution of Amino- and Hydroxy-anthraquinones in Aqueous Pyridine. General Procedure.—The anthraquinone derivative in pyridine (100 ml) at 0—5 °C was added to aqueous sodium sulphite heptahydrate or sodium sulphide nonahydrate (100 ml) held at 0—5 °C during the addition. Air, saturated with 50% aqueous pyridine, was passed through the irradiated solution at *ca.* 15 ml min^{-1}. 1-Aminoanthraquinone (Ia) and its 2-sulphonate (Ib) were separated by column chromatography [Kieselgel 60; water eluant for (Ib) and ethanol for (Ia)], and estimated spectrophotometrically by reference to their absorption maxima at 486 and 474 nm, respectively. A similar procedure was used to determine the concentration of the products (Ih, i, e, and n) from photolysis of (If, g, j, k, and m), respectively. Products (Ir, s, and t), were separated (Kieselgel H) with eluant A [for (It and s)] and 2% aqueous ammonia [for (It)] and determined by absorption spectroscopy as before.

[0/131 . *Received*, *24th January*, 1980]

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