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On the mechanism of the Elbs peroxydisulfate oxidation and a new peroxide rearrangement

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Abstract—Semiempirical calculations show that the intermediate formed by reaction between peroxydisulfate anion and the phenolate ion (the Elbs oxidation) is the species resulting from reaction of the tautomeric carbanion rather than the one resulting from attack by the oxyanion. This is confirmed by synthesis of the latter intermediate by reaction between Caro's acid dianion (peroxymonosulfate) and some nitro-substituted fluorobenzenes. This intermediate rearranges preferentially to give the phenol *ortho*-sulfate rather than the *para*-sulfate characteristic of the Elbs oxidation. This reaction of an arylperoxysulfate to give a phenol *ortho*-sulfate is a new rearrangement. © 2002 Elsevier Science Ltd. All rights reserved.

The Elbs peroxydisulfate oxidation is the reaction of phenolate anions with peroxydisulfate ions to form a mixture of the *ortho*- and *para*-sulfates of the parent phenol.[1] The *para* product predominates in contrast to the situation in the related Boyland–Sims oxidation of aromatic amines in which the *ortho* product is favored. A mechanistic point which has been in doubt for some time is whether initial attack is at carbon or at oxygen followed by rearrangement[2] (Fig. 1). In the case of the Boyland–Sims oxidation, the evidence favors attack at nitrogen followed by rearrangement to the *ortho* product.[3]

We have approached this problem in two ways: the first is by calculation of the energies of both possible species and the second by synthesis of one of these intermediates.

We carried out calculations at the semi-empirical level (MOPAC, AM1) of the heats of formation of the two possible intermediates, **I** and **II**, resulting from attack at oxygen or carbon. We find a difference of about 65 kcal mol^{-1} in favor of **II**. These are gas phase calculations, but the estimated solvation energies (5–10 kcal mol^{-1}) are not likely to alter this preference. This appears to

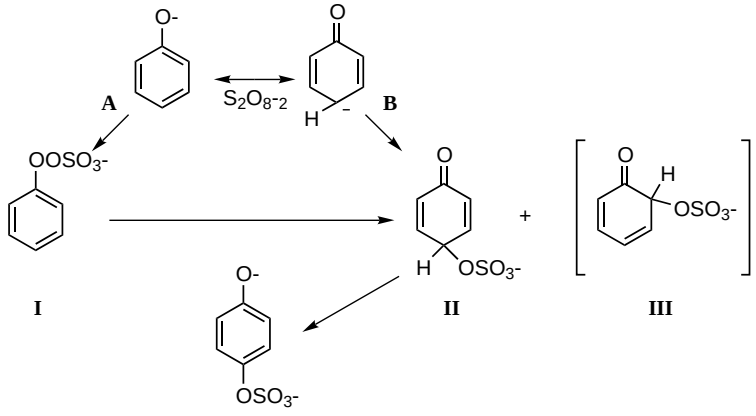

Figure 1.

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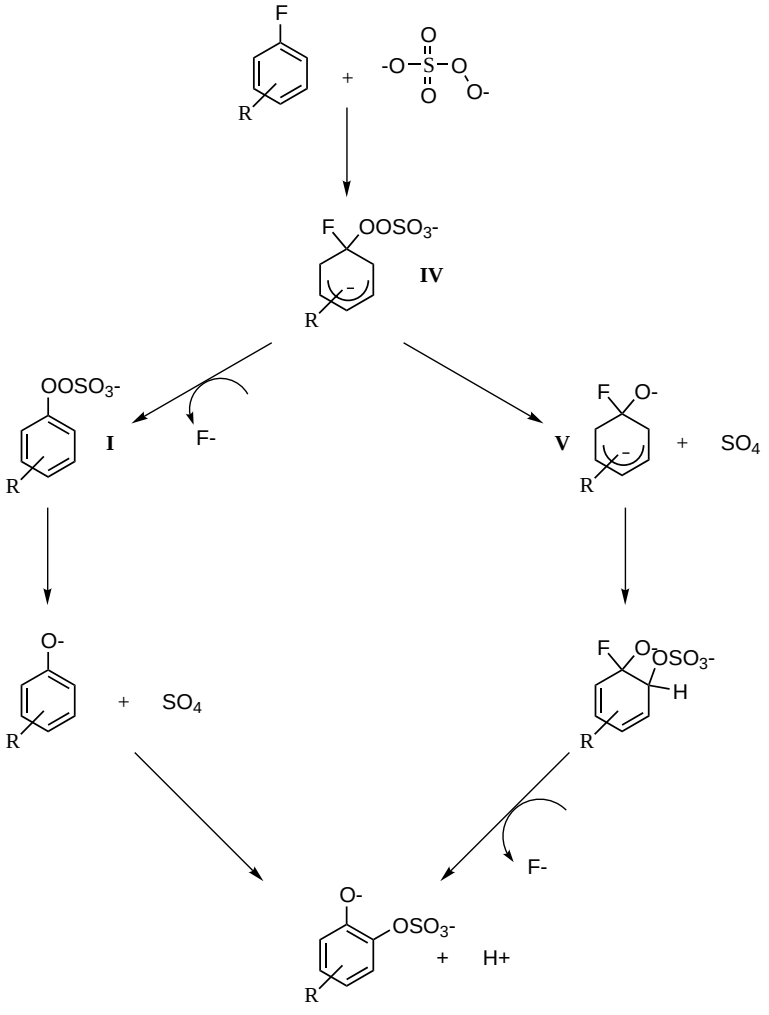
establish the route as direct attack at carbon rather than at oxygen followed by rearrangement, i.e. pathway B. Further calculations give a comparison between the *para* and *ortho* intermediates (i.e. between **II** and **III**). Following a bulk correction for solvation, we find that the *para*-isomer is favored by about 3 kcal mol^{-1} in reasonable agreement with the observed *para–ortho* ratio of about 10 (1.5 kcal mol^{-1}).[1]

The synthetic route relies on previous work[4] which suggested that Caro's acid dianion, an alpha nucleophile, ought to react with an appropriately substituted fluorobenzene to form an intermediate of type **I**, pathway A (Fig. 1). A direct synthesis of an intermediate of type **I** was carried out according to Scheme 1. The expectation was that **IV** would rapidly expel a fluoride ion leading to a type **I** intermediate. Analysis would then reveal if **I** gave rise to the normal products of the Elbs oxidation or not.

We examined the reaction of Caro's acid with three dinitrofluorobenzenes (2,4; 2,5; 2,6) since we expected to find rearrangement products *ortho* and *para* to the fluoro substituent. These isomers offer, respectively, an *ortho*, both an *ortho* and a *para*, and a *para* position for substitution. 2,6-Dinitrofluorobenzene reacted with Caro's acid at pH 7 to give 2,6-dinitrohydroquinone-4-sulfate in about 25% yield (Fig. 2). Its identity was established using ^{1}H NMR by comparison with known material prepared by Elbs oxidation of 2,6-dinitrophenol at pH 7 and confirmed by hydrolysis to 2,6-dinitrohydroquinone. However, when given a choice between the *ortho* and *para* positions, the *ortho* product is formed exclusively as shown by the case of 2,5-dinitrofluorobenzene. Reaction of 2,5-dinitrofluorobenzene with Caro's acid at pH 8 gave the *ortho* sulfate (3,6-dinitropyrocatechol monosulfate) as the major product in about 20% yield with no trace of the *para* sulfate (Fig. 2).[†]

Since about 70% of the starting material was recovered, the conversion was about 65%. The *ortho* sulfate was identified by its characteristic pair of doublets, $\delta = 7.60$ and 6.45, $J = 9$ Hz, in the proton NMR spectrum of



Scheme 1.

[†] A referee raised the question of why any product is formed in the 2,6-dinitro case. One possibility is that intermediate **IV** can undergo intramolecular rearrangement to either the *ortho*- or *para*-position but that the *ortho*-rearrangement is much faster.

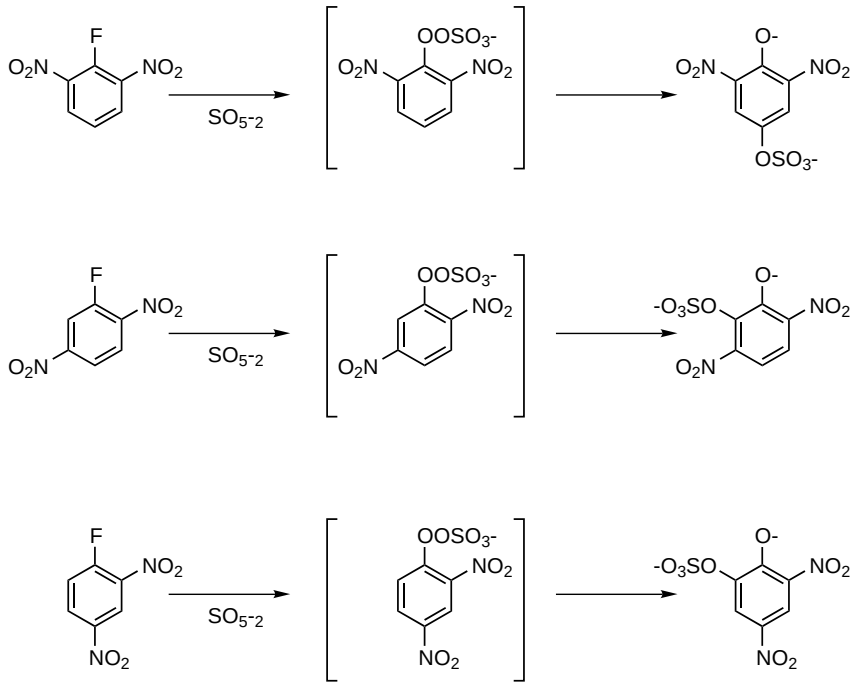


Figure 2.

reaction mixtures. These were identical to those seen in controlled reactions of chlorosulfonic acid with 3,6-dinitropyrocatechol and also identical to those found in small amounts in reaction mixtures of peroxydisulfate with 2,5-dinitrophenol. Hydrolysis of the *ortho* sulfate gave 3,6-dinitropyrocatechol. This material showed a singlet within 0.1 ppm of the resonance of 2,5-dinitrohydroquinone (the *para* isomer), but was easily distinguished by TLC on silica. The pyrocatechol gives a reddish spot with $R_f = 0.1$ using dichloromethane: methanol, 10:1; the hydroquinone gives a yellow spot with $R_f = 0.95$. The reaction of peroxydisulfate in an Elbs oxidation of 2,5-dinitrophenol at pH 7 gives, by contrast, a mixture in which the hydroquinone sulfate predominates; the ratio of the hydroquinone to the pyrocatechol sulfate is about 90 (NMR integration).

2,4-Dinitrofluorobenzene (Sanger's reagent) reacted with Caro's acid to give, following hydrolysis, 3,5-dinitropyrocatechol with melting point and IR spectrum identical to material prepared via nitration of pyrocatechol diacetate.[5]

Our assumption that intermediates of type **IV** necessarily decompose by expulsion of the fluoride ion to form intermediates of type **I** could be challenged since we realized that intermediates of type **IV** have at least two pathways open to them for formation of the observed products. Scheme 1 shows these possibilities. It is a question of whether fluoride ion expulsion is faster than cleavage of the peroxide bond followed by rearrangement or vice versa. We therefore calculated the heats of formation for the two intermediates, **I** and **V**. Intermediate **I** is about 158 kcal mol^{-1} (R = H) and 74 kcal mol^{-1} (R = 2,5-dinitro) more stable than intermediate **V**. Application of the Hammond principle to this situation suggests that decomposition of **IV** proceeds first by expulsion of the fluoride ion and then rearrangement of the peroxide.

We tested our calculational approach using an analogous case from the literature[6] in which *t*-butylhydroperoxide anion is known to react with 4-methyl-6-chloropyrimidine to yield a stable pyrimidinyl peroxide that undergoes a slow rearrangement to a *t*-butoxypyrimidone (Fig. 3). Calculation of the energies of the two possible intermediates in this process involving either expulsion of the halide first (this is what occurs) or peroxide cleavage first gives a result in

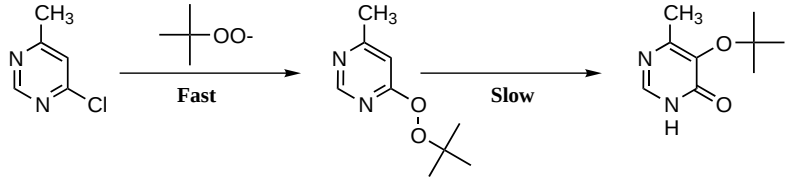


Figure 3.

agreement with experiment: halide cleavage is favored by about 16 kcal mol^{-1}. This result lends confidence to the calculational conclusions.

There are some additional analogous cases in the literature involving other peroxides, but why a particular reaction leads to rearrangement[6] or simply to cleavage of the peroxide[7] is unclear at this time. It is particularly notable that cumyl hydroperoxide sometimes shows rearrangement,[6] but gives rise only to 2,4-dinitrophenol in the reaction with Sanger's reagent.[8]

Experimental

NMR was at 600 MHz. 2,6-Dinitrofluorobenzene was prepared by a modification of the method of Parker and Read.[9] 2,5-Dinitrofluorobenzene, a new compound, was prepared by dimethyldioxirane oxidation of 2-fluoro-4-nitroaniline.[10] Crystals from hexane, mp 74–75°C, calcd for $C_6H_3FN_2O_4$: C, 38.72; H, 1.62; N, 15.05. Found: C, 39.07; H, 1.70; N, 14.69. 3,6-Dinitropyrocatechol was prepared from the dinitroguaiacol[11] by treatment with HBr.[12] Elbs oxidation of 2,5-dinitrophenol was carried out under standard conditions using the ammonium salts of the reactants. Acid hydrolysis and cooling gave crystals of 2,5-dinitrohydroquinone, mp 203–205°C (lit.[13] 201–203°C).

Reaction of Caro's acid (12 mg Oxone, 8 mg $NaDCO_3$) with 2,6-dinitrofluorobenzene (3 mg) was carried out in D_2O, 0.2 M phosphate pD7 (1 ml), with stirring for 3 h at rt. The reaction of Caro's acid (12 mg Oxone) with 2,5-dinitrofluorobenzene (6 mg) was carried out in a 7:3 mixture of 0.2 M phosphate, D_2O, pD 8: CD_3OD (5 ml). A trace of EDTA·$2D_2O$ was added to both reactions to decrease the autodecomposition of Caro's acid. Solid K_2CO_3 was added as needed to maintain the pH.

3,5-Dinitropyrocatechol and 3,5-dinitropyrocatechol-1-*O*-sulfonate, sodium salt

2,4-Dinitrofluorobenzene (1.86 g, 0.01 mol), Caro's acid (6 g, 0.02 mol, Oxone), and disodium EDTA (10 mg) were added all at once to 150 ml 0.5 M sodium phosphate buffer, pH 7 and 50 ml methanol. The mixture was stirred for 2–3 h at rt and then allowed to stand for 3 days. It was then cooled on ice and acidified with 10 ml acetic acid. Byproducts and unreacted starting material were extracted with dichloromethane. Conc. HCl was then added to the aqueous phase and the solution was boiled until the volume was about 100 ml. Glistening yellow crystals formed at 5°C after a few days, 0.96–1.04 g, 53–56%, mp 168–170°C (lit.[5] 166–166.5°C). IR (Nujol): 3585, 3513, 1600, 1552, 1514, 1342, 1259, 1212, 1151, 1080, 994, 938, 888, 823, 811, 792, 77 737, 680, 656 cm^{-1}. ^1H NMR: (DMSO-d_6) δ 8.22, 7.77 (d, $J=2.8$ Hz).

The intermediate sulfate ester was isolated in about 50% yield by allowing the reaction mixture of Caro's acid and Sanger's reagent to stand at 5°C for 2 days following the rt reaction (see above). Orange crystals of the product were filtered, dried, washed with dichloromethane, and recrystallized from isopropanol/water (2:1). Fine yellow needles, mp 209–211°C, calcd for $C_6H_2N_2Na_2O_9S{\cdot}H_2O$: C, 21.05; H, 1.17; N, 8.19. Found: C, 20.8; H, 0.79; N, 7.87. IR (Nujol): 3625, 3441, 3105, 3056, 1668, 1618, 1598, 1573, 1548, 1482, 1433, 1363, 1339, 1321, 1283, 1260, 1237, 1200, 1169, 1080, 1052, 979, 933, 917, 834, 811, 799, 750, 728, 711, 685, 642, 588, 542 cm^{-1}. ^1H NMR (D_2O): δ 8.80, 8.18 (d, $J=3.1$ Hz).

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