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Rearrangements in the Cerium(IV) and Manganese(III) Oxidations of Substituted Naphthalenes and the NIH Shift Mechanism

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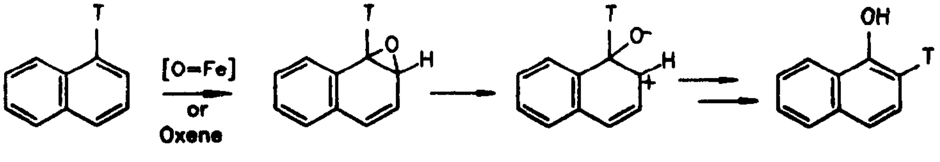
Abstract: Ceric ammonium sulphate oxidation of 1- and 1,4- disubstituted naphthalenes gives 2- and/or 2,3- disubstituted 1,4- naphthoquinones through migration of substituents (D, Br, Ph). Similar rearrangements are also observed in the manganese(III) oxidation and also in the anodic oxidation of these substrates. The results are consistent with the proposal that these oxidations go through the formation of radical cation followed by reaction with H_2O and further oxidation of the radical to the carbocationic intermediate on the way to the corresponding 1,4-naphthoquinone. Oxidation of 1,4-diphenylnaphthalene gives 2,3-diphenyl-1,4-naphthoquinone or 4-hydroxy- 2,4- diphenyl - 1(4)H - naphthalenone. The results are in accordance with the conclusion that such rearrangements do not require prior formation of arene oxide intermediates, originally proposed for the NIH shift mechanism.

Introduction

The NIH shift of substituents (CH_3, D, Cl) was first observed in aromatic hydroxylations with certain oxygenases. Such 1,2- shifts were initially understood in terms of arene oxide intermediates formed through the oxygenation of the aromatic rings by the oxidant behaving like an oxene or an oxenoid.[1-6]

Scheme 1



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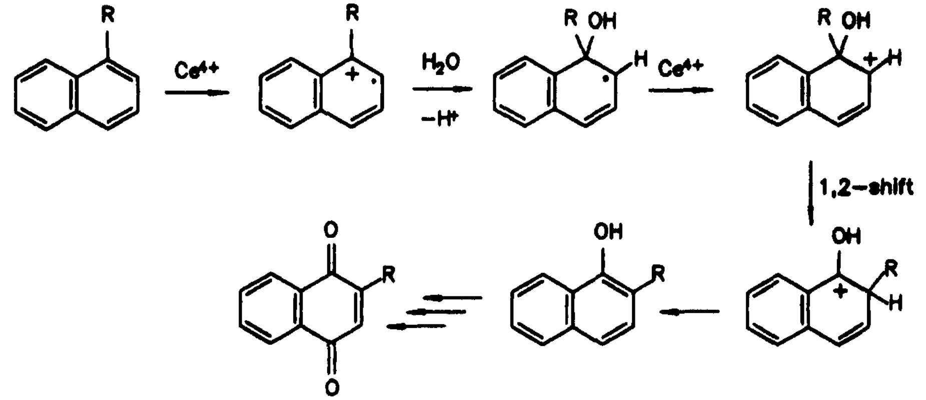
We have first reported 1,2- shifts in the oxidation of 1-substituted naphthalenes to 2-substituted 1,4-naphthoquinones by cerium(IV) which functions as a single electron transfer oxidant.[7] We have suggested the mechanism outlined in Scheme 2 in order to rationalize these 1,2-shifts of substituents.[7]

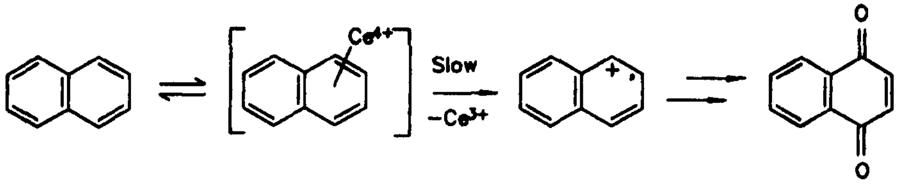
Scheme 2



We have referred to this as a new 1,2- shift since this oxidation does not involve the oxene or oxenoid species then reported to be involved in the celebrated NIH shift mechanism (Scheme 1). In recent years, there is renewed interest in the NIH shift mechanism.[8-10] Unfortunately, these reports do not include our preliminary results in their discussion. We describe here our results of further investigations on the CAS oxidation of some 1,4- disubstituted naphthalenes and also the results of the manganese(III) oxidation of the 1- and 1,4- disubstituted naphthalenes.

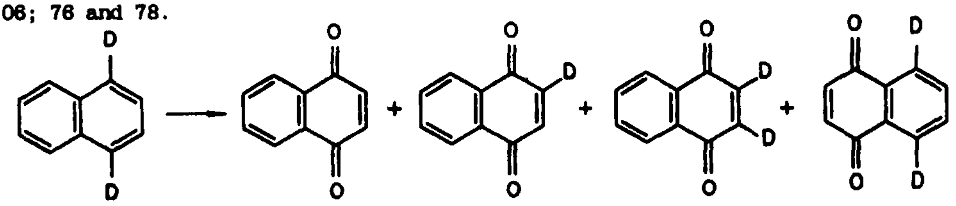
Results and Discussion

CAS oxidation of 1- and 1,4- disubstituted naphthalenes: Kinetic results of the CAS oxidation of naphthalene are consistent with a mechanism involving initial 1:1 complex formation followed by decomposition of the complex to the radical cation in the rate limiting step.[11]



However, stoichiometric studies indicated that six moles cerium(IV) are required for the oxidation of one mole of naphthalene to 1,4- naphthoquinone[11] and hence kinetic results do not help in the understanding of the mechanism of further conversion of the radical cation to 1,4-naphthoquinone.

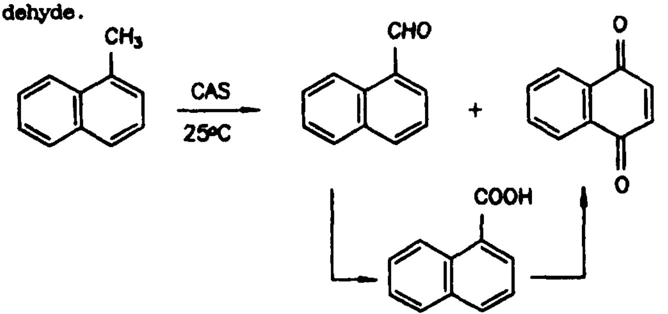
The isolation of naphthalene-1,2-oxide and the observation of the NIH shift in the hydroxylation of 1-substituted naphthalenes shed light on the mechanism of biological oxidation of naphthalene.[2] It was thought that CAS oxidation of 1-and 1,4-disubstituted naphthalene derivatives would throw light on this single electron transfer oxidation. Therefore, we have examined the CAS oxidation of several of these derivatives. We have observed that CAS oxidation of the readily accessible 1,4-dideuterionaphthalene gives 1,4-naphthoquinone, containing deuterium in the quinonoid moiety as revealed by the 1.5:2 ratio observed for the 2,3-quinonoid and 6,7- aromatic protons in the ^{1}H-NMR spectrum. The mass spectrum of the product showed M^+ peaks at m/e: 158, 159 and 160 ; fragments at 130, 131, and 132; 104, 105, and 106; 76 and 78.



1 2 3 4

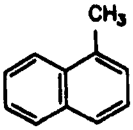
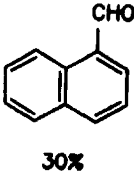
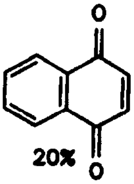
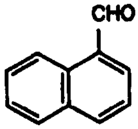
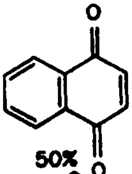
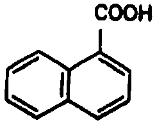
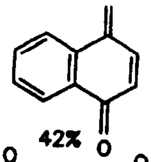
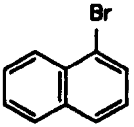
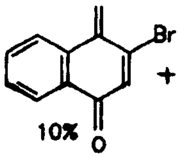
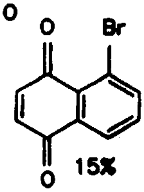
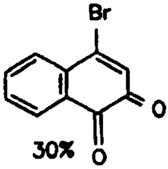
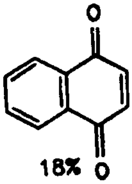
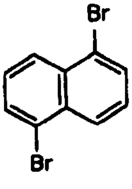
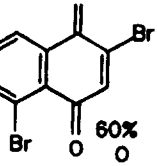
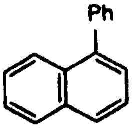
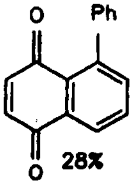
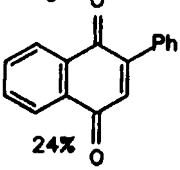
However, presence of the compound 3 in the product mixture cannot be ascertained.

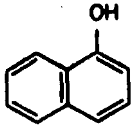
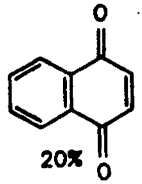
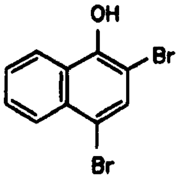
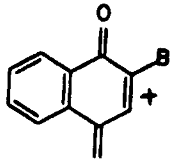
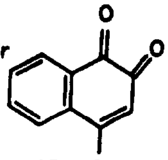
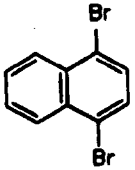
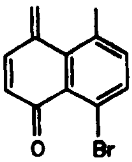
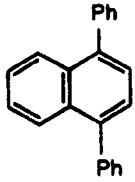
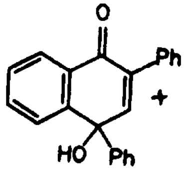
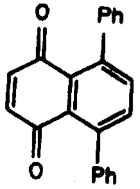
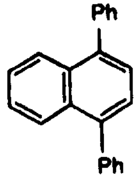
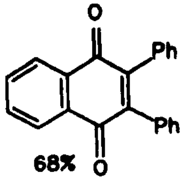
Oxidation of 1-methylnaphthalene (Table 1) yields 1-naphthaldehyde (30%) and 1,4-naphthoquinone(20%) and the 2-methyl-1,4-naphthoquinone and 5-methyl-1,4-naphthoquinone were not formed. Interestingly, CAS oxidation of 2-methyl naphthalene gives 2-methyl-1,4-naphthoquinone(60%) and 6-methyl-1,4- naphthoquinone(15%) and 2-naphthaldehyde was not formed. Further, it has been observed that the CAS oxidation of 1-naphthaldehyde and 1-napthoic acid gives 1,4-naphthoquinone in 50% and 42% yields, respectively (Table 1). Probably, the 1,4-naphthoquinone is formed in the oxidation of 1-methylnaphthalene through further oxidation-decarboxylation of 1-naphthaldehyde.



Whereas the CAS oxidation of 1-bromonaphthalene at 50^{0}C (Table 1) gives 5-bromo-1,4-naphthoquinone (15%), 4-bromo-1,2-naphthoquinone (30%) and 1,4-naphthoquinone (18%) beside 2-bromo-1,4-naphthoquinone (10%), oxidation of 1,5-dibromonaphthalene

Table 1. CAS oxidation of 1- and 1,4- disubstituted naphthalenes

S.No	Substrate	Reaction conditions Temp(°C)	Time(h)	Products[b] Yield [%][c]
1.		25	24	 30% +  20%
2.		25	24	 50%
3.		25	2	 42%
4.		50	5	 10% +  15% +  30% +  18%
5.		60	5	 60%
6.		50	4	 28% +  24%

7.		25	2[d]	 20%
8.		25	2[e]	 +  60% 15%
9.		50	4	 60%
10.		50	3[f]	 +  52% 20%
11.		50	4[g]	 68%

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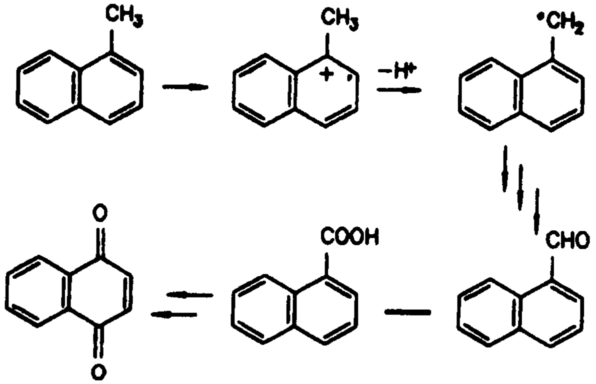
a) Oxidations were carried out in CH_3CN/2M H_2SO_4 mixture using 1 mmol of organic substrate and 6 mmol of CAS. b) Products were identified by IR and ^1H NMR spectral data and comparison of physical constant data with data reported in the literature. Products in entries 5 (m.p. 68-70°C) and 10 (hydroxy diphenyl naphthalenone (m.p.152-153°C) are new compounds. Expected M^+ in the mass spectra and satisfactory analytical data (C± 0.3 and H± 0.3%) were obtained for these compounds. c) Yields are of products isolated by preparative TLC [silicagel/benzene benzene/chloroform (1:1)]. d) 4 mmol of CAS was used. The 1-naphthol(1 mmol) in CH_3CN(30 ml) was added drop wise to a solution of CAS(4 mmol) in 2M H_2SO_4(50 ml)/CH_3CN(10 ml) mixture. e) 4 mmol of CAS was used. f) 0.5M H_2SO_4 was utilized. g) 6M H_2SO_4 was utilized.

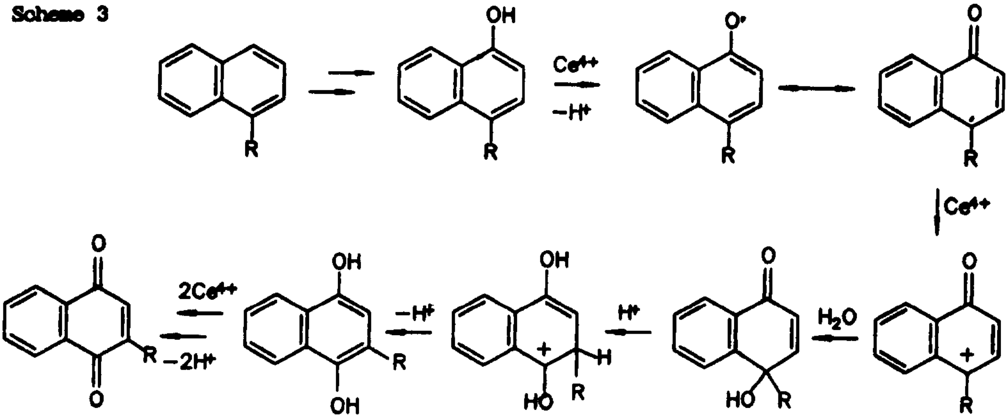
results in the formation of 2,5-dibromo- 1,4-naphthoquinone. Similarly, oxidation of 1-phenylnaphthalene at 50°C yields 5-phenyl-1,4-naphthoquinone(28%) through reaction of the unsubstituted ring and 2-phenyl-1,4-naphthoquinone(24%) via oxidation induced 1,2-shift of the phenyl group.

The 1,2-shift observed in these cases could be visualized by the mechanism in Scheme 1. In the case of 1-methylnaphthalene, the reaction takes a different course leading to deprotonation of the methyl group.



We have also found that slow addition of 1-naphthol to the CAS in CH_3CN -2M H_2SO_4 mixture gives 1,4-naphthoquinone in 20% yield, the main products being polymeric, oxidatively coupled materials. This is not surprising since oxidation of phenols with single electron transfer oxidants usually leads to oxidatively coupled products due to the formation of radicals in relatively large concentrations.[12] However, formation of 1,4- napthoquinone in the CAS oxidation of 1-naphthol does indicate that it is reasonable to expect the intermediacy of 1-naphthol in the oxidation of naphthalene to 1,4- naphthoquinone as visualized in Scheme 2.

Scheme 3



In the mechanism outlined in Scheme 2, it is implied that the migration of substituents takes place before the formation of 1-naphthol intermediate. However, migration of substituents after the 1-naphthol intermediate also (Scheme 3) cannot be ruled out. Further, there is also an interesting possibility of two migrations in the oxidation of 1,4-disubstituted naphthalenes. In order to examine these possibilities, we have carried out the CAS oxidation of some 1,4-disubstituted naphthalenes.

As discussed previously, formation of 2,3-dideuterio-1,4-naphthoquinone in the CAS oxidation of 1,4-dideuterionaphthalene cannot be supported or ruled out on the basis of available data. We have observed that the CAS oxidation of 4-deuterio-1-bromonaphthalene gives 2-bromo-1,4-naphthoquinone (10%) which does not contain deuterium in the quinonoid moiety, indicating the loss of deuterium during this transformation. Unfortunately, CAS oxidation of 1,4-dibromonaphthalene gives only the 5,8-dibromo-1,4-naphthoquinone (Table 1) through oxidation of the unsubstituted ring.

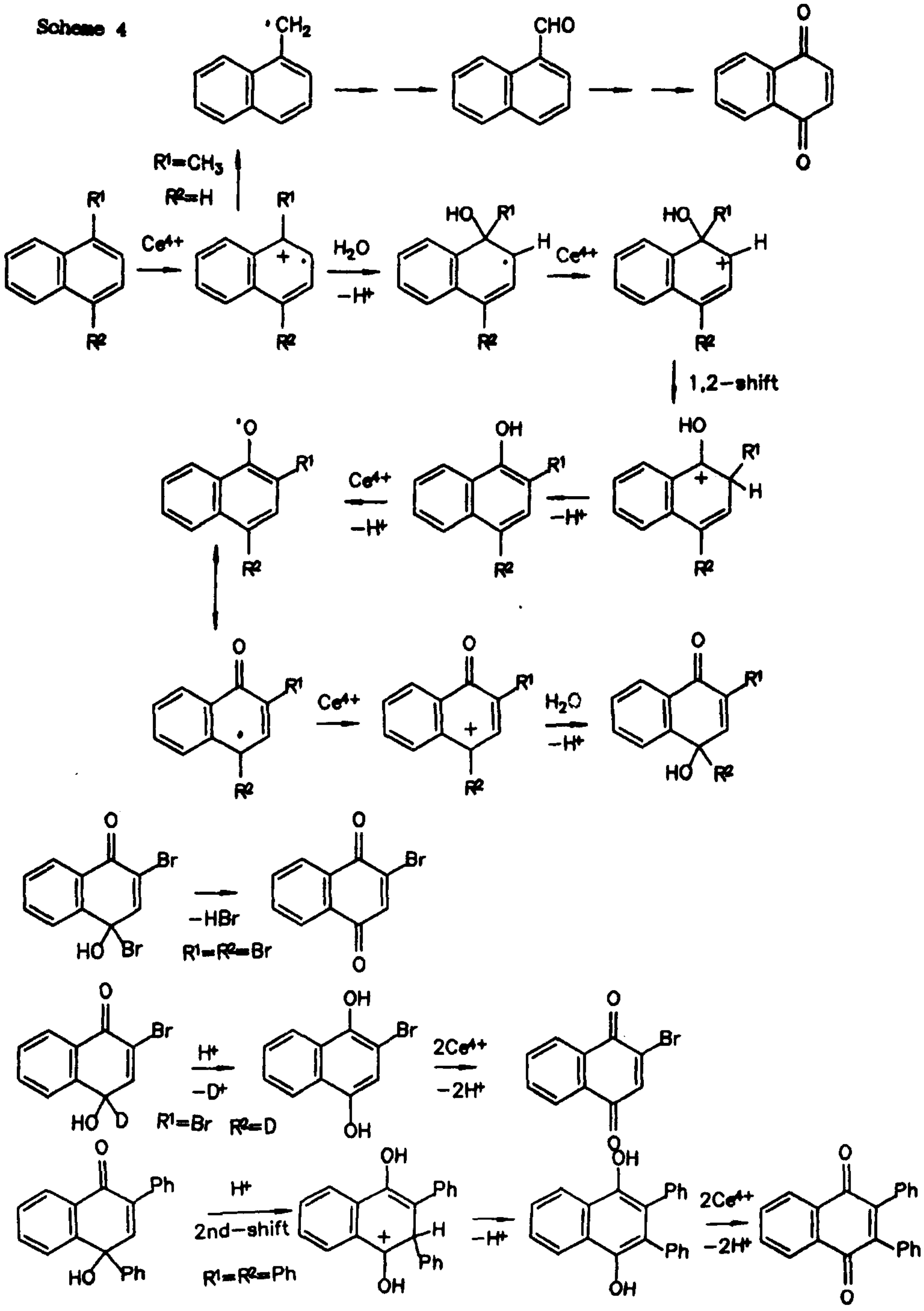
In the mechanism of CAS oxidation of 1-bromonaphthalene(Scheme 2), the intermediacy of 2-bromo-1-naphthol is suggested. So, it was thought that the CAS oxidation of the readily accessible 2,4-dibromo-1-naphthol would throw light on the further conversion. In this case, only 4-bromo-1,2-naphthoquinone and 2-bromo-1,4-naphthoquinone were obtained and 2,3-dibromo-1,4-naphthoquinone was not formed. It is clear that the loss of one of the bromine atoms is the preferred pathway in this case. Further, it can be inferred that in the CAS oxidation of 1-bromonaphthalene to 2-bromo-1,4-naphthoquinone, the latter could not have been formed from 4-bromo-1-naphthol intermediate resulting from possible initial hydroxylation on the position para to the bromine (Scheme 3). It is therefore most plausible that the 2-bromo-1,4-naphthoquinone and 2,5-dibromo 1,4-naphthoquinone obtained in the oxidation of 1-bromonaphthalene and 1,5-dibromonaphthalene, respectively, (Table 1) are formed through the mechanism outlined in Scheme 2.

The CAS oxidation of 1,4-diphenylnaphthalene gives different products, depending on the acidity of the medium. Whereas in 6M H_2SO_4 - CH_3CN mixture the oxidation gives 2,3-diphenyl-1,4-naphthoquinone, in 0.5M H_2SO_4 - CH_3CN mixture, the 5,8-diphenyl-1,4-naphthoquinone(20%) and 4-hydroxy-2,4-diphenyl-1(4H)-naphthalenone are formed. Clearly, in the oxidation of 1,4-diphenylnaphthalene to 2,3-diphenyl-1,4-naphthoquinone two migrations take place, one before and another after the formation of the 4-hydroxy-2,4-diphenyl-1(4H)-naphthalenone intermediate (Schemes 2 and 3).

All the results obtained in the CAS oxidation of 1-substituted and 1,4-disubstituted naphthalene derivatives are consistent with the mechanism outlined in Scheme 4.

Manganese(III) oxidation of 1- and 1,4-disubstituted naphthalenes: The manganese(III) sulphate can be readily prepared by titrating $KMnO_4$ against $MnSO_4$ in dil.H_2SO_4 medium at 0°C.[13] It is a powerful one electron oxidant (E_0 = 1.51V in 7.5M

Scheme 4


•CH₂
CHO
R¹=CH₃
R²=H
R¹
R²
Ce⁴⁺
H₂O
−H⁺
HO
H
1,2-shift
•O
OH
O
Br
−HBr
R¹=R²=Br
H⁺
−D⁺
D
R¹=Br R²=D
2Ce⁴⁺
−2H⁺
Ph
2nd−shift
R¹=R²=Ph

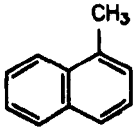
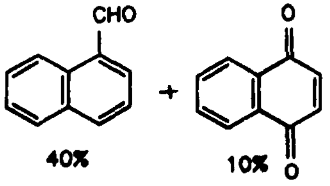
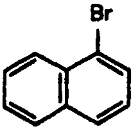
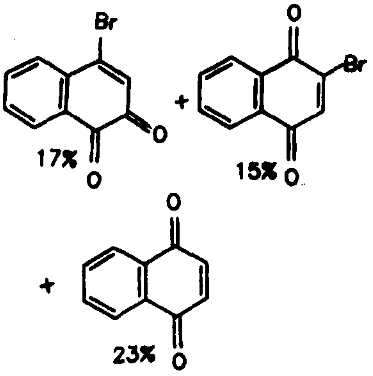
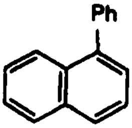
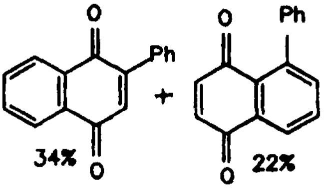
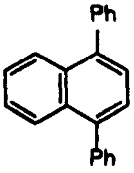
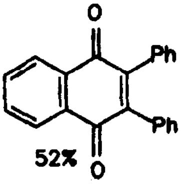
H_2SO_4).[14] It was observed that manganese(III) sulphate in 6M H_2SO_4 - CH_3CN mixture oxidizes polycyclic aromatic hydrocarbons to the corresponding quinones in 50 - 80% yields.[15] Manganese(III) oxidation of 1,4-dideuterionaphthalene gives 1,4-naphthoquinone containing deuterium in the quinonoid moiety similar to the observation in the CAS oxidation (ie. 1.5:2 ratio for quinonoid and 6,7-aromatic protons in the ^{1}H-NMR spectrum). Mn(III) oxidation of other 1-substituted and 1,4-disubstituted naphthalene derivative also gives similar results (Table 2).

The 1,2-shifts observed in the reactions using these single electron transfer oxidants have been also observed in the anodic oxidation of these derivatives in DMF - dil.H_2SO_4 mixture.[16] Accordingly, the mechanism outlined in Scheme 4 is consistent with the products obtained in all these single electron transfer oxidations.

Relationship to the NIH shift mechanism. The NIH shift observed in the hydroxylation of aromatic rings by mixed function oxygenases was originally understood in terms of oxo-iron species behaving like 'oxene', giving arene oxides as intermediates on reaction with aromatic compounds.[1-4] The model systems such as the chromyl reagents,[17] CrO_2X_2, and others employing porphyrin - iron oxidants[18] which are likely to contain high valent oxo-iron species, and electrophylic epoxidizing agents such as peroxyacids also exhibit the NIH shift upon reaction with appropriate aromatic compound.[3] On the other hand, oxidations utilizing the Fenton system[6,19] Fe^{2+}/H_2O_2, and other systems containing an iron salt and peroxide or O_2/reductant[20,21] (eg.Udenfriend, Hamilton and Viscontini systems) do not proceed with the NIH shift. The results described here for the single electron transfer oxidation of 1-substituted and 1,4-disubstituted naphthalene derivatives indicate that for obtaining the shift, the crucial intermediate is the hydroxycarbocationic intermediate (Schemes 2 and 4). Although the precursor radical to this intermediate is also formed in the oxidations using the Fenton system through HO. radical addition to the aromatic ring, the shift is not observed unless there is an one electron oxidant capable of oxidizing this radical to the cationic species.[9,19]

The 1,2- shifts observed in the oxidation of the 1- and 1,4- disubstituted naphthalenes with the single electron transfer oxidants illustrate that such 1,2-shifts are not diagnostic of the involvement of arene oxide intermediates in the oxidation of aromatic rings. However, there is a possibility that the arene oxides could result from the intermediates similar to the hydroxy carbocationic intermediate (Scheme 2 and 4), formed through single electron transfer mechanism. There are several recent reports describing the involvement of carbocationic intermediates in the epoxidation of olefins by certain monooxygenases[22] and also by some model systems.[23-25] Needless to say, in view of the carcinogenicity of several aromatic hydrocarbons, it is worthwhile to probe the nature of the precursors to the arene oxides in biological oxidations.

Table 2. Manganese(III) oxidation of 1- and 1,4- disubstituted naphthalenes

S.No	Substrates	Reaction conditions[a] Temp(°C)	Time(h)	Product(s)[b] Yield [%][c]
1.		25	10	
2.		50	3	
3.		50	3	
4.		50	3	

a) Oxidations were carried out in CH_3CN/6M H_2SO_4 mixture using 1 mmol of organic substrate and 6 mmol of Mn(III). Manganese(III) sulphate(~6 mmol) in 6M H_2SO_4 solution(50 ml) was prepared using $KMnO_4$(200 mg) and $MnSO_4$(2g) at 0°C. b) Products were identified by comparison of the samples and data with those obtained in the oxidation(Table 2). c) Yields are of products isolated by preparative TLC.

Experimental Section

General: Melting points reported are uncorrected. Thin layer chromatographic tests and separations were carried out on glass plates(20cm x 5cm and 20cm x 20cm) coated with silica gel(ca. 0.2mm) obtained from NCL, Pune, India; activated at 100°C for 3-4h prior to use. Spots and bands of colourless compounds were rendered visible by short exposure to iodine vapor. Ceric ammonium sulphate $2(NH_4)_2SO_4.Ce(SO_4)_2.2H_2O$, used was of reagent grade. Acetonitrile was kept over anhydrous Na_2SO_4 and then distilled over P_2O_5. Organic substrates were obtained from commercial sources or prepared following cited procedures. The oxidation products were characterized by spectral(i.r. and ^1H-NMR) data and comparison of the physical constant data with the data reported in the literature. The unknown compounds were fully characterized by spectral data and elemental analyses (C +0.3%, H +0.3%).

Oxidation Procedures. Typical procedures followed for the oxidations are given below.

CAS oxidation of 1,4-diphenylnaphthalene: Ceric ammonium sulphate (3.8g, 6mmol) dissolved in 0.5M sulfuric acid (90ml) was added to 1,4-diphenyl- naphthalene (0.28g,1mmol) suspended in acetonitrile (100ml) and 0.5M sulfuric acid (10ml) and the contents were stirred for 3h at 50^{0}C. The mixture was brought to room temperature and extracted with ether (3x50ml). The organic extract was dried over anhydrous Na_2SO_4 and the solvent was evaporated. Chromatographic separation of the residue(TLC benzene/ chloroform, 5:1), gave 5,8-diphenyl-1,4-naphthoquinone (0.06g, 20%), mp.141^{0}C, Lit.[26] mp. 140-142^{0}C, i.r. (nujol) ν^- 1600 cm^{-1}, ^1H-NMR (60MHz,$CDCl_3$) 7.2-7.7δ (12H, m) and 6.7δ (2H, s); and 4-hydroxy-2,4-diphenyl-1(4H)-naphthalenone (0.16g, 52%), mp.152-152^{0}C, i.r.(nujol) ν^- 3350, 1670 and 1605cm^{-1}, ^1H-NMR (270MHz, DMSO-d_6) 8.05-8.09δ (1H, m), 7.2-7.7δ (13H, m), 7.0δ (1H, s) and 6.8δ [1H(OH), s]; Mass(m/e): 312(M^+,80%), 295(60%) and 284 (100%); Analysis: C 84.89% and H 5.50%, $C_{12}H_{16}O_2$ requires C 84.59% and H 5.16%.

When the above experiment was carried out using 6M H_2SO_4 in the place of 0.5M H_2SO_4, 2,3-diphenyl-1,4-naphthoquinone was isolated in 68% yield, mp.140-141^{0}C, Lit[27] mp.138-140^{0}C, i.r.(nujol) ν^- 1650 cm^{-1}, ^1H-NMR(60MHz, $CDCl_3$) 8.0-8.4δ(2H, m), 7.5-7.9δ(2H, m) and 6.8-7.4δ(10H, m).

Mn^{3+} Oxidation of 1,4-diphenylnaphthalene. To a solution of 1,4-diphenyl-naphthalene (0.14g, 0.5mmol) in acetonitrile (30ml), manganese(III) sulphate (3mmol), prepared using $KMnO_4$ (0.1g) and $MnSO_4$ (1g) in 6M sulphuric acid at 0^{0}C, was added and the contents were stirred for 3h at 50^{0}C. After work-up, 2,3-diphenyl-1,4-naphthoquinone (80mg,52%) was isolated. The product was found to be identical to that obtained in the CAS oxidation.

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