# Photochemical Oxygenation of Phenols by Pyrimido[5,4-g]pteridine N-Oxide. Comparative Studies with Pyridazine and Isoalloxazine N-Oxides

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1,3,7,9-Tetrabutylpyrimido[5,4-g]pteridine-2,4,6,8(1H,3H,7H,9H)-tetraone 5-oxide **1** transfers its N-oxide oxygen to phenols, i.e., phenol **5**, p-cresol **6**, L-tyrosine methyl ester **7**, and p-hydroxyacetanilide (acetaminophen) **8**, under photochemical conditions to give the corresponding dihydric phenols as major products without any accompanying photochemical intramolecular rearrangements of the N-oxide group taking place. This oxygenation is reasonably explained in terms of a photo-induced single-electron transfer (SET) followed by oxygen-atom transfer (the SET mechanism) which occurs via the initial formation of a charge-transfer complex between compound **1** and the phenols employed. Comparative experiments with 3,10-dibutylisoalloxazine 5-oxide **3** and 3-methylpyridazine 2-oxide **4** well demonstrate the simplicity and the mechanistic characteristics of the photochemistry of compound **1**.

Previous articles[1] from our laboratory have reported that 1,3,7,9-tetrabutylpyrimido[5,4-g]pteridine-2,4,6,8(1H,3H,-7H,9H)-tetraone 5-oxide **1**[2] functions as an agent for oxygenation or dehydrogenation depending upon the nature of the co-substrate under photochemical conditions, without any accompanying appreciable intramolecular rearrangement of its N-oxide group taking place. For example, benzene, toluene and anisole efficiently undergo photochemical oxygenation by compound **1** to give the corresponding phenols.[3] Chemical and physicochemical results are in accord with the theory that the oxygen-atom transfer occurs via a single-electron transfer (SET) from the benzenes to a singlet-excited oxidant **1**;[3] this is an alternative to the oxene mechanism generally accepted for photo-oxygenation by heterocyclic N-oxides.[4,5] It has also been observed that although the conversion yields of the phenols are high in the initial period of the photoreaction, prolongation of the irradiation time results in a decrease in their yield, indicating the occurrence of further photoreactions between the N-oxide **1** and the produced phenols.

1 *n* = 1
2 *n* = 0
3
4
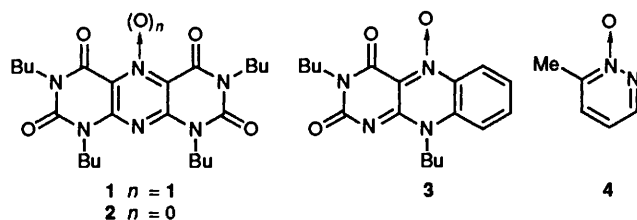
To our best knowledge, the photo-oxygenation of phenols by heterocyclic N-oxides has never been studied in detail, except for the use of flavin 5-oxide.[6]

The above background prompted us to investigate the photoreaction of compound **1** with phenols, i.e., phenol **5**, p-cresol **6**, L-tyrosine methyl ester **7** and p-hydroxyacetanilide (acetaminophen) **8**. The present results demonstrated that N-oxide **1** oxygenates the phenols **5–8** via photo-induced SET in an initially formed charge-transfer (CT) complex to give the corresponding dihydric phenols as major products.

Comparative experiments using 3,10-dibutylisoalloxazine 5-oxide **3**[1b] and 3-methylpyridazine 2-oxide **4**[7] showed the mechanistic characteristics of N-oxide **1** and the different reaction modes among compounds **1**, **3** and **4** for the photochemical oxygenation of the phenols.

Results

(a) *Photo-oxygenation of Phenol* **5** *by the Heterocyclic N-Oxides* **1**, **3** *and* **4**.—A mixture of phenol **5** (2.0 mol dm⁻³) and N-oxide **1** [λ_{max} 370 (ϵ 2.2 × 10⁴) nm] (5.0 mmol dm⁻³) in dry acetonitrile was irradiated with a 400 W high-pressure mercury arc lamp through a BiCl₃ solution filter (>355 nm) at ambient temperature under argon for 1 h. During this period, compound **1** was completely consumed and converted into 1,3,7,9-tetra-butylpyrimido[5,4-g]pteridine-2,4,6,8(1H,3H,7H,9H)-tetraone **2** almost quantitatively. After trimethylsilylation of the reaction mixture with 1,1,1,3,3,3-hexamethyldisilazane (HMDS), the formation of catechol **9** and p-hydroquinone **10** in 43% total yield (based on N-oxide **1** employed; product ratio 9:10 55:45) was confirmed by GC and GC-mass analyses. Appreciable o- and p-benzoquinones which can be formed by dehydrogenation of the diols **9** and **10**, however, were not detected in the reaction mixture.†

The oxygen atom inserted into the products **9** and **10** might originate from a small amount of water or molecular oxygen contained in the medium. In order to rule out this possibility, ¹⁸O-labelled N-oxide **1** was prepared and its photoreaction with phenol **5** was examined.

When a mixture of phenol **5** and the ¹⁸O-labelled N-oxide **1** in dry acetonitrile was irradiated under the conditions similar to the foregoing case, quantitative ¹⁸O-incorporation into the photoproducts **9** and **10** was confirmed by GC-mass analysis of the reaction mixture after trimethylsilylation. This fact clearly indicates that the inserted oxygen atoms of the products **9** and **10** originate from the N-oxide oxygen of compound **1**.

Rastetter et al.[6] have reported that 2,3,5,6-tetramethylphenol is photochemically oxygenated in pyridine by flavin 5-oxide to give the corresponding p-hydroquinone which is further oxidised to a p-benzoquinone derivative under the conditions employed. In the present study, the photoreaction of phenol **5** with the 3,10-dibutylisoalloxazine 5-oxide **3** [λ_{max} 430 (sh, ϵ 5.0 × 10³), 451 (6.0 × 10³) and 475 (sh, 5.0 × 10³) nm], a

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† Independent experiments showed that the photochemical dehydrogenation of compounds **9** and **10** to the corresponding quinones by N-oxide **1** occurs only in the presence of a base such as pyridine.

flavin 5-oxide analogue, was investigated in order to obtain a companion with the case of compound 1.

When a mixture of compounds 3 and 5 was irradiated in dry acetonitrile under the analogous conditions described above, a significant amount of N-oxide 3 (ca. 35%) was recovered even after six hours and the oxygenated products 9 and 10 (9:10 58:42; by GC) were obtained in very poor yield (ca. 5%). In this case, the coupling product of phenol 5, 2,2'-dihydroxybiphenyl, was detected. Analogous oxidative coupling of the phenols has been observed in a previous study of the photoreaction with the flavin 5-oxide in chloroform.[6] The formation of some products originating from compound 3 in addition to the deoxygenated isoalloxazine was indicated by TLC analysis of the reaction mixture.*
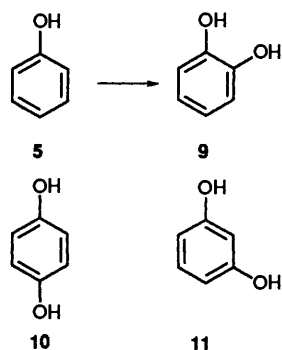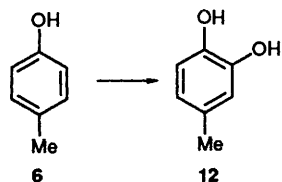

Scheme 1

The 3-methylpyridazine 2-oxide 4 [λ_{max} 323 (ε 1.4 × 10⁴) nm] appears to be an efficient agent for photo-oxygenation among the heterocyclic N-oxides so far investigated.[7]

When a mixture of compounds 4 and 5 in dry acetonitrile was irradiated for 20 min through a Pyrex filter (>280 nm), complete consumption of compound 4 was observed, and compounds 9, 10 and a new oxygenated product, resorcinol 11, were obtained in 37% total yield in the proportions 9:10:11 45:48:7 (by GC). The deoxygenated pyridazine was formed in only 45% yield and some products derived from the N-oxide 4 were also detected as reported previously.[7]

(b) *Photo-oxygenation of* p-*Cresol* 6, L-*Tyrosine Methyl Ester* 7, *and* p-*Hydroxyacetanilide* (*Acetaminophen*) 8 *by the* N-*Oxide* 1.—A mixture of p-cresol 6 (2.0 mol dm⁻³) and N-oxide 1 (5.0 mmol dm⁻³) in dry acetonitrile was irradiated for 40 min under the conditions analogous to the foregoing cases. 4-Methyl-catechol 12 was obtained in 37% yield as a major product. The

Scheme 2

formation of a small amount of isomeric 6-methylresorcinol was shown by GC and GC-mass analyses of the reaction mixture

after trimethylsilylation. p-Hydroxybenzyl alcohol, p-hydroxy-benzaldehyde and Pummerer's ketone,[8] which are possible products, were not detected in the reaction mixture.

The biotransformation of L-tyrosine to dopa is catalysed by tyrosine hydroxylase (tyrosine 3-monooxygenase) which contains tetrahydrobiopterin as a cofactor.[9]

When a mixture of L-tyrosine methyl ester 7 (500 mmol dm⁻³) and N-oxide 1 (5.0 mmol dm⁻³) in 5% aq. acetonitrile was irradiated for 40 min, dopa methyl ester 13 was obtained in 25% yield as the only determined product. The structure of compound 13 was confirmed by spectral comparison with an authentic sample prepared by esterification of dopa.[10]

The metabolism of acetaminophen 8, a widely used analgesic and antipyretic drug, has been extensively studied in view of the toxicity (hepatic necrosis and renal damage) observed in both humans and laboratory animals when high doses are ingested or administered.[11] The biological oxidation of acetaminophen 8 catalysed by cytochrom P-450 or horseradish peroxidase has been known to involve the formation of the acetaminophen phenoxy free-radical *via* an SET process and to produce 3-hydroxyacetaminophen 14 in addition to polymerisation products of acetaminophen 8 and N-acetyl-p-benzoquinone imine intermediate which reacts with reduced glutathione and cysteine residues in cellular macromolecules.
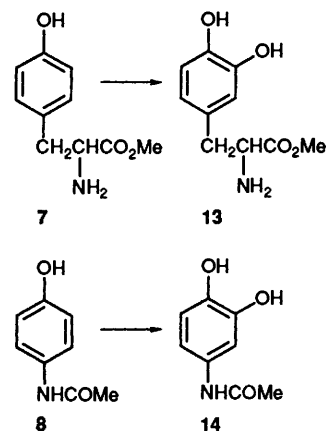
Scheme 3

For comparison with biological oxidation, the photoreaction of compound 8 with N-oxide 1 was investigated. A mixture of acetaminophen 8 (100 mmol dm⁻³) and N-oxide (5.0 mmol dm⁻³) in dry acetonitrile was irradiated for 20 min under conditions analogous to those described above. Isolated oxidation products were compound 14 (6%) and trace amounts of two dimeric products.† The structure of compound 14 was confirmed by comparison with the spectral data reported previously.[12]

Discussion

The efficiency of the N-oxides employed as an oxidant for the photo-oxygenation of phenol 5 was in the order 1 > 4 ≫ 3 with respect to the total yield of dihydric phenols 9 and 10. In the cases of 1 and 4, however, a somewhat different regioselectivity was observed: the resorcinol 11 was obtained only in the case when oxide 4 was the oxidant. The simplicity of the photo-oxygenation by N-oxide 1 is greater than that of other N-oxides 3 and 4 because the latter cases are accompanied by other photochemical reactions of the N-oxides, such as intramolecular rearrangements. Fig. 1 shows the relation between concentration of phenol 5 and consumption of the N-oxides 1, 3 and 4, during the irradiation time-course.

As shown in Fig. 1(c), the N-oxide 4 was rapidly consumed

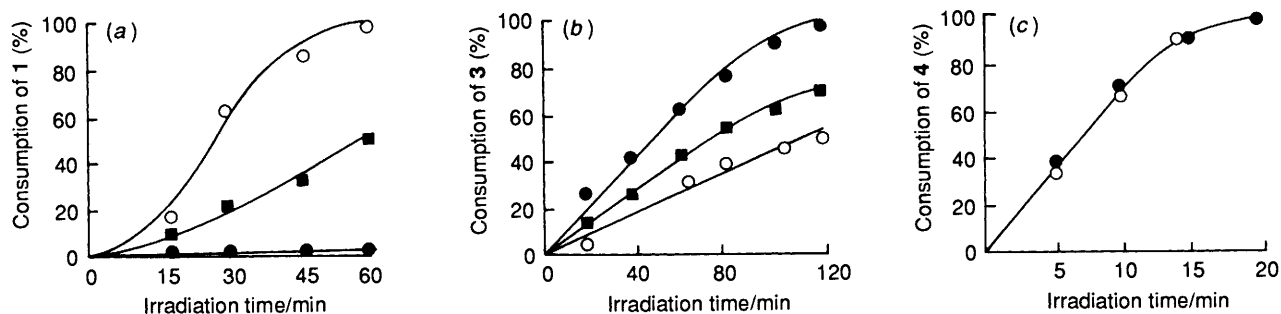* Studies on the structures of the photo-products originating from N-oxide 3 are underway.

† The structures of the dimers were proposed to be 4,4'-dihydroxy-3,3'-biacetaminophen and 4,4'-dihydroxy-N,3'-biacetanilide on the basis of spectral comparison with the products isolated in the enzymatic oxidation of compound 8 (cf. ref. 11a). TLC analysis of the reaction mixture showed the formation of trace amounts of other products.

Fig. 1 Consumption of the N-oxides, 1, 3 and 4, under the photochemical conditions in the absence or presence of phenol 5 as a function of irradiation time; ●: without 5, ■: with 100 equiv. of 5, ○: with 400 equiv. of 5
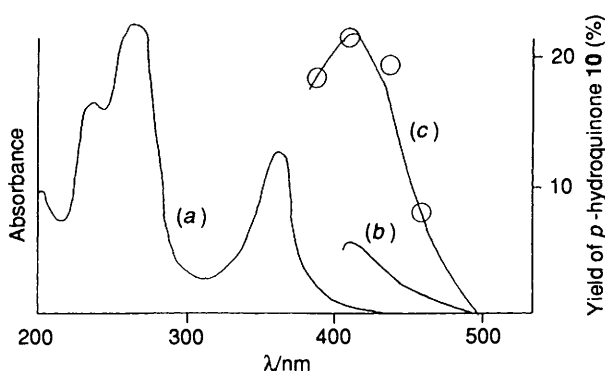
Fig. 2 Wavelength dependence for the formation of p-hydroquinone 10 in the photo-oxygenation of phenol 5 by pyrimido[5,4-g]pteridine N-oxide 1. (a) UV-visible absorption of 1 (0.05 mmol dm^{-3}); (b) difference spectrum of the mixture of 1 (5.0 mmol dm^{-3}) and 5 (2.0 mol dm^{-3}) vs. 1 (5.0 mmol dm^{-3}) in dry acetonitrile; (c) yield of 10. *Reaction conditions:* a mixture of 1 (5.0 mmol dm^{-3}) and 5 (2.0 mol dm^{-3}) in dry acetonitrile (5 cm^3) was irradiated with JASCO CRM-FA spectroirradiator (2 KW Xe lamp and a 4 nm band width) under argon at ambient temperature for 30 min

Table 1 Effects of tetracyanoethylene (TCNE) on the consumption of the N-oxide 1 and the formation of dihydric phenols 9 and 10

TCNE (equivs.)[a]	Consumed 1 (%)	Dihydric phenols (%)[b]
0	91	41
0.1	77	35
1.0	37	24

[a] Molar ratio of TCNE to the N-oxide 1 employed. [b] Total yields of catechol 9 and p-hydroquinone 10. *Reaction conditions:* To a solution of phenol 5 (2.0 mol dm^{-3} and 1 (5.0 mmol dm^{-3}) in dry acetonitrile (5 cm^3), tetracyanoethylene (0.5 or 5.0 mmol dm^{-3}) was added and the mixture was irradiated for 40 min.

regardless of the presence of phenol 5, indicating the uni-molecular nature of the photoreaction which involves liberation of atomic oxygen from its excited state (the oxene mechanism).[4,5,7,13] Contrary to the case of compound 4, N-oxide 1 was very stable under irradiation in the absence of phenol 5, and consumption of compound 1 showed a strong concentration-dependence with respect to the substrate 5 [see Fig. 1(a)]. This fact supports the idea to that an intermolecular collision between reactants 1 and 5 is requisite for the photo-oxygenation of phenol 5.

The N-oxide 3 was fairly unstable under irradiation and consumption of compound 3 was retarded by the addition of phenol 5 with a concentration-dependence as shown in Fig. 1(b),

suggesting that the photochemical behaviour of compound 3 is different from both cases of compounds 1 and 4 (*vide intra*).

Thus, the comparative experiments indicate that compound 1 causes the cleanest photo-oxygenation of phenol 5 in a characteristic manner among the N-oxides employed.

The CT absorption band between substrates 1 and 5 (λ_{max} 278 nm) in the ground state was observed at 408 nm as evidenced in the UV-visible absorption spectra, and excitation at the CT-band resulted in the maximum yield of the product 10 in the photo-oxygenation of phenol 5 by N-oxide 1 as shown in Fig. 2.

No CT-band was observed in the UV-visible spectrum of a mixture of compounds 4 and 5 and the photo-oxygenation of phenol 5 by oxide 4 proceeded most efficiently by excitation at *ca.* 323 nm which is the longest UV absorption band of compound 4. The CT-complex formation between substrates 3 and 5 was demonstrated by the observation of the CT-band (515 nm) in the visible spectrum. The wavelength-dependence experiment, however, showed an obscure result, *i.e.*, excitation at 515 nm is not always most efficient for the oxygenation of phenol 5, which may reflect the complexity of the reaction mechanism.

The photo-oxygenation of phenol 5 by N-oxide 1 was suppressed in a concentration-dependent manner by the addition of tetracyanoethylene, a strong electron acceptor, to the reaction medium (see Table 1). Quenching experiments employing an electron acceptor as an additive are frequently used to attain further evidence for the involvement of the SET process.[14]

Taking into consideration the above facts and previous demonstrations of the SET mechanism for photo-oxygenation by N-oxide 1,[3] we outline a reaction sequence for the photo-oxygenation of phenol 5 by oxide 1 as shown in Scheme 3.

The photoreaction can be initiated by SET from phenol 5 to oxide 1 in an excited CT-complex, followed by proton transfer between resulting radical ions, **A** and **B**, to generate phenoxyl radical **C** and nitroxyl radical **D**. Coupling of radicals **C** and **D**, produces a transient intermediate **E**, which collapses to give products 9 and 10, accompanied by elimination of species 2. Contrary to the case of oxide 4, the oxene mechanism does not operate for oxidation with 1.

Rastetter *et al.*[6] have demonstrated the generation of phenoxyl radicals (such as **C**) in the photo-oxygenation of phenols by flavin 5-oxide in pyridine by ESR spectrometry and proposed that a biradical species generated by its excitation (probably in a triplet state) is responsible for hydrogen abstraction from the phenols. At present, the reaction mode for the photo-oxygenation of phenol 5 by compound 3 under the present conditions, however, is not obvious because of its complexity and inefficiency.

Conclusions.—The present results showed that the photo-oxygenation of phenol 5 by the heterocyclic N-oxides 1, 3 and
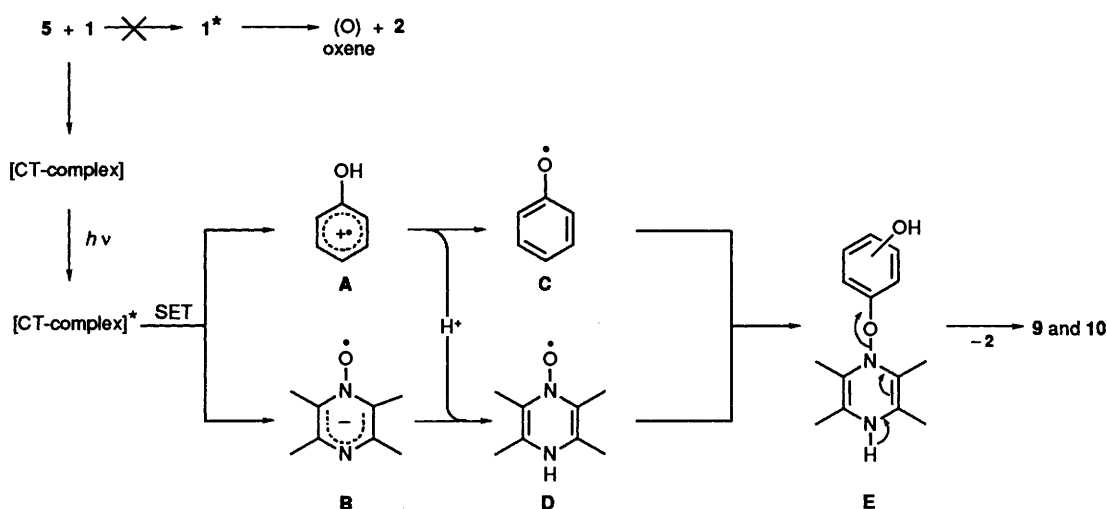
Scheme 4.

4 are different in their reaction modes. The *N*-oxide **1** oxidised phenol **5** in a simple manner without other accompanying photoreactions and in a characteristic manner which involves photo-induced SET *via* CT-complex formation.

The oxygenation of the phenols is of interest in view of the metabolism of phenolic compounds. The photo-oxygenation of species **7** and **8** by *N*-oxide **1** mimics well their biological oxygenations.[9,11]

Experimental

Irradiations were carried out at ambient temperature under argon with a 400 W high-pressure mercury arc lamp (Riko Kagaku Sangyo) through a $BiCl_3$ solution filter (>355 nm) for oxides **1** and **3** or a Pyrex filter for compound **4**. A grating mono-chromater (JASCO CRM-FA spectroirradiator) with 2 kW Xe lamp and a 4 nm bandwidth was used for the wavelength-dependence experiments. The spectroscopic measurements were performed with the following instruments: UV absorption spectra with a Shimadzu-260 spectrophotometer; ^{1}H NMR spectra with a JEOL JNX-270 (270 MHz) spectrometer with tetramethylsilane as internal standard; mass spectra with a JEOL JMS D-300 machine operating at 70 eV. Gas chromatographic (GC) analyses were performed with a Shimadzu GC-8APF instrument with 1.2 m column (PEG 5% on Uniport HP). TLC analyses for the assay of substrates **1, 2** and **3** were performed on silica gel plates (Merck, art 5715) with benzene–ethyl acetate (5:2 for the assay of **1** and **2** or 1:1 for the assay of **3**) as developer and TLC-scanning was carried out with a Shimadzu CS-9000 dual-wavelength flying-spot scanner (detection 370 nm for the assay of **1** and **2**; 450 nm for **3**). Column chromatographic separation was accomplished on silica gel (Wakogel C-300).

Photochemical Oxidation of Phenol **5** *by* 1,3,7,9-*Tetrabutyl-pyrimido*[5,4-g]*pteridine*-2,4,6,8(1H,3H,7H,9H)-*tetraone* **5**-*Oxide* **1**, 3,10-*Dibutylisoalloxazine* **5**-*Oxide* **3**, *or* 3-*Methyl-pyridazine* 2-*Oxide* **4**.—(a) *Photoreaction of phenol* **5** *with oxide* **1**. A solution of phenol **5** (941 mg, 1.0 × 10^{-2} mol) and oxide **1** (12.2 mg, 2.5 × 10^{-5} mol) in dry acetonitrile (5.0 cm³) was irradiated externally through a $BiCl_3$ solution filter. The reaction mixture was sampled every 15 min for one hour. TLC analyses of the mixtures showed the smooth consumption of compound **1** (by TLC densitometry, R_f 0.27) and almost quantitative conversion of this oxide into 1,3,7,9-tetrabutyl-pyrimido[5,4-g]pteridine-2,4,6,8(1H,3H,7H,9H)-tetraone **2** (R_f

0.35). GC analyses of the sampled mixtures were carried out after treatment with excess of HMDS in pyridine at 80 °C overnight, and showed the formation of catechol **9** and *p*-hydroquinone **10** (product ratio **9**:**10** 55:45) in this photo-reaction. No detectable amounts of other products originating from phenol **5** was observed by GC-analysis of the reaction mixture. The structures of products **9** and **10** were assigned by comparison of their GC retention times and GC-mass spectra with those of respective authentic samples after trimethylsilyla-tion. The yields of compounds **9** and **10** during the irradiation were as follows. Total yields of products **9** and **10** based on the employed oxide **1**: 9% (15 min), 21% (30 min), 36% (45 min) and 43% (60 min).

(b) *Photoreaction of phenol* **5** *with oxide* **3**. A solution of phenol **5** (941 mg, 1.0 × 10^{-2} mol) and oxide **3** (8.6 mg, 2.5 × 10^{-5} mol) in dry acetonitrile (5.0 cm³) was irradiated externally through a $BiCl_3$ solution filter. The reaction proceeded very slowly compared with that of oxide **1**. TLC analysis of the mixture after irradiation for 6 h showed *ca.* 35% recovery of starting oxide **3** (R_f 0.31) and the formation of some products originating from this oxide, together with the deoxygenated isoalloxazine (R_f 0.38; 40% yield based on the employed oxide **3**. After trimethylsilylation of the resulting reaction mixture, the formation of products **9** and **10** in *ca.* 5% total yield (**9**:**10** 58:42) and 2,2′-dihydroxybiphenyl (2% yield) was confirmed by GC and GC-mass analyses. The structural assignment of the bisphenol followed from GC co-injection and comparison of GC-mass spectral fragmentation patterns to those of an authentic sample prepared by the oxidation of phenol **5** with di-t-butyl peroxide.[15] The isomeric biphenol, 4,4′-dihydroxybiphenyl, was not detected in the reaction mixture.

(c) *Photoreaction of phenol* **5** *with oxide* **4**. A solution of phenol **5** (941 mg, 1.0 × 10^{-2} mol) and oxide **4** (2.7 mg, 2.5 × 10^{-5} mol) in dry acetonitrile (5.0 cm³) was irradiated externally through a Pyrex filter for 20 min under argon. GC analysis of the reaction mixture showed complete consumption of oxide **4** and the formation of the deoxygenated pyridazine in 45% yield and some products derived from oxide **4**. GC and GC-mass analyses of the reaction mixture obtained after trimethylsilylation showed the formation of products **9, 10** and resorcinol **11** in 45% total yield (**9**:**10**:**11** 45:48:7) based on the employed oxide **4**.

Photochemical Oxidation of p-*Cresol* **6**, L-*Tyrosine Methyl Ester* **7**, *and* p-*Hydroxyacetanilide* (*Acetaminophen*) **8** *by* N-

Oxide **1**.—(a) *Photoreaction of compound* **6** *with oxide* **1**. A solution of *p*-cresol **6** (1.08 g, 1.0 × 10⁻² mol) and oxide **1** (12.2 mg, 2.5 × 10⁻⁵ mol) in dry acetonitrile (5.0 cm³) was irradiated externally for 40 min under conditions analogous to those of the foregoing case. Assay of the reaction mixture by TLC densitometry showed complete consumption of *N*-oxide **1** and its almost quantitative conversion into compound **2**. After trimethylsilylation of the reaction mixture, the formation of 4-methylcatechol **12** in 37% yield and 6-methylresorcinol in 6% yield were confirmed by GC and GC-mass analyses. No formation of detectable amounts of *p*-hydroxybenzyl alcohol, *p*-hydroxybenzaldehyde and Pummerer's ketone[8] in this reaction was found by GC or TLC analysis.

(b) *Photoreaction of ester* **7** *with oxide* **1**. A solution of compound **7** (18.25 g, 1.0 × 10⁻¹ mol) and oxide **1** (488 mg, 1.0 × 10⁻³ mol) in 5% aq. acetonitrile (200 cm³) was irradiated externally for 40 min under conditions analogous to those of the foregoing case. Assay of the reaction mixture by TLC densitometry showed complete consumption of *N*-oxide **1** and the formation of the expected dopa methyl ester **13** as a major product together with species **2** and trace amounts of undetermined minor products. After removal of the solvent, the residue was subjected to column chromatography [eluant chloroform–methanol (10:1)] to isolate compound **13** (62 mg, 25% yield based on the employed oxide **1**). The structure of the product **13** was confirmed by comparison of its ¹H NMR and mass spectra with those of an authentic sample prepared from dopa.[10] *p*-Hydroxybenzyl alcohol and *p*-hydroxybenzaldehyde, which are formed as a result of the oxidation of the side-chain in compound **7**, were not detected in this photoreaction mixture.

(c) *Photoreaction of acetaminophen* **8** *with oxide* **1**. A solution of acetaminophen **8** (3.023 g, 2.0 × 10⁻² mol) and oxide **1** (488 mg, 1.0 × 10⁻³ mol) in dry acetonitrile (200 cm³) was irradiated externally for 20 min under conditions analogous to those of the foregoing case. Assay of the reaction mixture by TLC densitometry showed complete consumption of oxide **1** and its almost quantitative conversion into compound **2**. After removal of the solvent, the residue was subjected to column chromatography [eluant benzene–ethyl acetate (1:1)] to isolate 3-hydroxyacetaminophen **14** (10 mg, 6%) together with 3,3′-acetamido-4,4′-dihydroxybiphenyl (6 mg, 4%) and 4,4′-dihydroxy-*N*,3′-biacetanilide (1.5 mg, 1%). The structures of the products, **14** and the dimers, were assigned by comparison of spectral data with those reported previously.[11,12]

Synthesis of ¹⁸O-*Labelled* N-*Oxide* **1**.—To a solution of 6-amino-1,3-dibutylpyrimidine-2,4(1*H*,3*H*)-dione (239 mg, 1.0 × 10⁻³ mol) in acetonitrile (7.0 cm³) containing H₂¹⁸O (25 mm³; ¹⁸O-content 97%) was added dropwise at 0 °C a solution of nitrosonium tetrafluoroborate[16] (140 mg, 1.2 × 10⁻³ mol) in acetonitrile (7.0 cm³) and the mixture was stirred for 0.5 h, then briefly heated at 50 °C after gas evolution had subsided. After removal of the solvent under reduced pressure, the resulting residue was poured into water and the solution was extracted with chloroform. The extract was washed with saturated aq. NaCl, dried over anhydrous MgSO₄ and evaporated to dryness to isolate almost pure 6-amino-1,3-dibutyl-5-nitrosopyrimidine-2,4(1*H*,3*H*)-dione (267 mg, 99% yield; ¹⁸O-content 29%, by mass spectrometry).

Oxidation of the N¹⁸O-labelled 6-amino-5-nitrosopyrimidinedione (122 mg, 4.5 × 10⁻⁴ mol) with lead tetraacetate (90% purity; 246 mg, 5.0 × 10⁻⁴ mol) gave the ¹⁸O-labelled *N*-oxide **1** (93 mg, 84% yield; ¹⁸O-content 27%, by mass spectrometry).

Photoreaction of Phenol **5** *with* ¹⁸O-*Labelled Oxide* **1**.—A solution of phenol **5** (941 mg, 1.0 × 10⁻² mol) and ¹⁸O-labelled

oxide **1** (12.2 mg, 2.5 × 10⁻⁵ mol) in dry acetonitrile (5.0 cm³) was irradiated externally for one hour under the conditions similar to the foregoing case. After trimethylsilylation of the reaction mixture, ¹⁸O-content values of the oxidation products **9** and **10** were determined by GC-mass spectrometer (¹⁸O-content 27% for both products **9** and **10**).

Concentration-dependence Experiment for the Photo-oxygenation of Phenol **5** *by the* N-*Oxide* **1**, **3** *or* **4**.—A solution of an oxide **1**, **3** or **4** (2.5 × 10⁻⁵ mol) in dry acetonitrile (5.0 cm³) was irradiated in the absence or presence of phenol **5** (2.5 × 10⁻³ or 1.0 × 10⁻² mol) through a BiCl₃ solution filter for oxides **1** and **3** or a Pyrex filter for oxide **4**. The consumption yields of these *N*-oxides **1**, **3** and **4** were determined by TLC densitometry (for **1** and **3**) or GC analysis (for **4**) and plotted as a function of irradiation time in Fig. 1 (see Fig. 1a, 1b and 1c).

Charge-transfer Interaction between Phenol **5** *and the* N-*Oxide* **1**, **3** *or* **4**.—The CT complex formation between phenol **5** and the *N*-oxide **1** or **3** was evidenced in the difference UV–visible absorption spectra of a mixture of oxide **1** or **3** (5.0 × 10⁻³ mol dm⁻³) and phenol **5** (2.0 mol dm⁻³) vs. **1** or **3** (5.0 × 10⁻³ mol dm⁻³) in dry acetonitrile. The observed CT-bands were 408 (ε 149 dm³ mol⁻¹ cm⁻¹) nm for **1** and 515 (ε 111 dm³ mol⁻¹ cm⁻¹) nm for **3**. No formation of CT-complex between substrates **5** and **4** was observed in the UV–visible absorption spectrum of a mixture of phenol **5** (5.0 × 10⁻³ mol dm⁻³) and oxide **4** (2.0 mol dm⁻³).

Wavelength-dependence Experiments for the Photochemical Oxygenation of Phenol **5** *by the* N-*Oxides* **1**, **3** *and* **4**.—A solution of phenol **5** (1.0 × 10⁻² mol) and the *N*-oxide **1**, **3** or **4** (2.5 × 10⁻⁵ mol) in dry acetonitrile (5.0 cm³) was degassed carefully and irradiated with light of various wavelengths (301–540 nm, *ca.* 54 J cm⁻²). The yields of product **10** were determined by GC analysis after trimethylsilylation. The results were as follows. Yields of **10** (wavelength nm): 10% (354), 18% (381), 20% (407), 18% (433), 7% (460) and 0% (486) for *N*-oxide **1** after 30 min; 1.7% (407), 2.1% (433), 1.7% (460), 1.5% (486), 2.2% (513) and 0% (540) for *N*-oxide **3** after one hour; 6.4% (301), 8.2% (328) and 1.2% (356) for *N*-oxide **4** after 10 min.

Inhibitory Effect of Electron-transfer Quencher on the Photo-oxygenation of Phenol **5** *by* N-*Oxide* **1**.—To a solution of phenol **5** (1.0 × 10⁻² mol) and *N*-oxide **1** (2.5 × 10⁻⁵ mol) in dry acetonitrile (5 cm³) was added tetracyanoethylene (2.5 × 10⁻⁶ or 2.5 × 10⁻⁵ mol) and the mixtures were irradiated for 40 min. The consumption yields of *N*-oxide **1** in this reaction were determined by TLC densitometry and the total yields of products **9** and **10** were determined by GC analysis of the irradiation mixtures after trimethylsilylation. The results are shown in Table 1.

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