# The Release of Singlet Oxygen in the Reaction of Dioxiranes with Amine *N*-Oxides

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The reactivity of dimethyldioxirane and methyl(trifluoromethyl)dioxirane towards the amine *N*-oxides **1a–13a** and ammonium derivatives **13b–d** has been investigated. In the dioxirane oxidation of the tertiary amines and nitrogen heteroarenes, the expected *N*-oxides are not always formed. Instead, the in situ generated *N*-oxides are deoxygenated by the dioxirane with the release of singlet oxygen ($^1O_2$) at comparable or even higher rates than the amine oxidation. The amount of $^1O_2$ has been quantified by IR chemiluminescence and by chemical trapping with 9,10-dimethylanthracene. The nucleophilicity of the *N*-oxide determines the efficacy of the $^1O_2$ release in the deoxygenation. Thus, for the less nucleophilic heteroaromatic *N*-oxides, the deoxygenation of the amine oxide competes ineffectively with the oxidation of the amine. The ammonium derivatives **13b–d** do not promote the decomposition of the dioxiranes; as expected, they are epoxidized.

## Introduction

The reaction of heteroarenes and tertiary amines with dioxiranes to give the corresponding *N*-oxides has been of interest in recent years.[1] In early work, the oxidation of pyridine to its *N*-oxide was reported, by using the dioxirane derived from cyclohexanone, which was generated in situ.[2] Murray pointed out the critical reaction conditions required for obtaining good yields of the amine *N*-oxides with the isolated dimethyldioxirane (DMD). It was suggested that in the presence of an excess of DMD, certain *N*-oxides form a labile intermediate which decomposes to regenerate the starting amine with the concomitant release of molecular oxygen; however, the structure of this intermediate and the electronic nature of the evolved dioxygen were not elucidated.[1c] Recently, we detected the release of singlet oxygen in the DMD oxidation of 4-(dimethylamino)pyridine[3] and postulated an $S_N2$ mechanism for the reaction of dioxiranes with heteroarenes.[4]

During the use of DMD and (trifluoromethyl)methyldioxirane (TFD) for the preparation of amine *N*-oxides,[5][6] we encountered some unusual facts that called our attention. As observed with 4-(dimethylamino)pyridine,[3] in some instances it was not possible to achieve complete conversion of the amine to the *N*-oxide in spite of the large excess of consumed dioxirane. In addition, several *N*-oxides of olefinic amines did not undergo epoxidation upon treatment even with an excess of DMD.

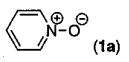
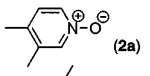
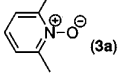
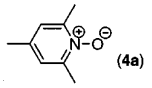
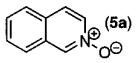
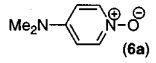
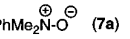
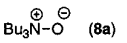
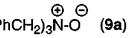
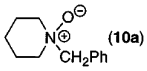
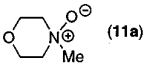
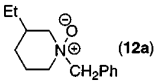
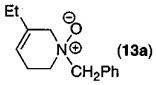
The present contribution reports our results on the reactivity of DMD and TFD towards the amine *N*-oxides **1a−13a** (Table 1) and the ammonium derivatives **13b−d** (Scheme 1). We have found that the dioxiranes are decomposed only by certain amine *N*-oxides and that the previously proposed mechanism, which involves the nucleophilic attack of the amine *N*-oxide functionality on the peroxide bond, operates with final release of singlet oxygen.[3][4] On the basis of quantitative measurements of the evolved singlet oxygen, performed by physical and chemical means, the nucleophilicity of the amine *N*-oxides is considered responsible for their efficiency in deoxygenating the dioxiranes.

## Results and Discussion

The *N*-oxide **13a** (Table 1) could be readily obtained by treatment of the corresponding amine **13** with DMD, but all attempts to oxidize the *N*-oxide **13a** with DMD to its epoxide **14a** resulted only in the consumption of the dioxirane.[5] These facts led us to explore whether the DMD decomposition was caused by the related ammonium derivatives **13b−d** under our anhydrous reaction conditions. In all cases the epoxidation took place quantitatively and the epoxides **14b−d** were obtained in good yields when TFD was used as oxidant. These results demonstrate unequivocally that the dioxirane decomposition is due to the negatively charged *N*-oxy functionality of the *N*-oxides and not the positively charged quaternary nitrogen atom (Scheme 1).

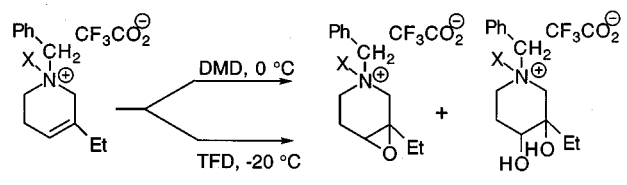
  1434−193X/98/1111−2527 $ 17.50+.50/0 

Table 1. Persistence of the dioxiranes DMD and TFD towards the *N*-amine oxides **1a−13a** and detection of the singlet oxygen by IR chemiluminescence

| entry | *N*-oxide | DMD persistence[a] | DMD $^1O_2$ (%)[b] | TFMD persistence[a] | TFMD $^1O_2$ (%)[b] |
|---|---|---|---|---|---|
| 1 |  (1a) | stable [c] | n.a. [d] | labile [e] | 4.8 |
| 2 |  (2a) | stable | n.a. | labile | 0.2 |
| 3 |  (3a) | stable | n.a. | labile | 1.3 |
| 4 |  (4a) | stable | n.a. | labile | 0.6 |
| 5 |  (5a) | stable | n.a. | labile | 0.02 |
| 6 |  (6a) | labile | 30 | labile | ca. 5 [f] |
| 7 |  (7a) | labile | 0.33 | n.a. [d] | not detected |
| 8 |  (8a) | labile | not detected | labile | 0.12-0.88 |
| 9 |  (9a) | labile | 0.65-1.18 | n.a. | n.a. |
| 10 |  (10a) | labile | 0.04-0.09 | n.a. | n.a. |
| 11 |  (11a) | labile | 0.08-0.60 | n.a. | n.a. |
| 12 |  (12a) | labile | not detected | n.a. | not detected |
| 13 |  (13a) | labile | 0.18 | n.a. | n.a. |

[a] The persistence of dioxirane was monitored by means of the peroxide test (KI/HOAc). − [b] A photodiode detector was used to detect the 1268-nm emission; yields were calculated based on mols of dioxirane divided by two (stoichiometric factor). − [c] Decomposition of DMD required 120 h at room temp. (ca. 20°C). − [d] Not assayed. − [e] TFMD decomposed in less than 3 min, whereas DMD required 5−10 min. − [f] Ref.[3].

Scheme 1




Initial studies on the qualitative stability assays were carried out by the addition of an excess of DMD to the solution of the corresponding *N*-oxide. The results (Table 1) show that except for the electron-rich 4-(dimethylamino)-substituted derivative **6a**, only *N*-oxides derived from the pyridine-type heteroarenes **1−5** did not promote the decomposition of DMD. For all the other aliphatic amine *N*-oxides **7a−13a**, the DMD was consumed within ten minutes at 20°C in acetone solution, as well as in acetone-free dichloromethane or carbon tetrachloride.[7] In contrast, for those cases in which DMD persisted, TFD was rapidly decomposed (Table 1). As for the oxidation products, with the exception of **9a**, the crude reaction mixtures contained only the *N*-oxide. For the amine *N*-oxide **9a**, a mixture of tribenzylamine, dibenzyl nitrone and benzaldehyde was obtained.[5]

Since for 4-(dimethylamino)pyridine *N*-oxide (**6a**) we had shown that the DMD decomposition releases singlet oxygen,[3] it was of interest to ascertain whether this deoxygenation of *N*-oxides is a general process. For this purpose, solutions of DMD in deuteriochloroform or of TFD in trifluoroacetone (TFA) were used[8] and the evolution of singlet oxygen was monitored by its characteristic IR chemiluminescence at 1268 nm with a photodiode detector. The thermal decomposition of 1,4-dimethylnaphthalene 1,4-endoperoxide (E-DMN) was employed as calibration standard[9] and the quantitative results are shown in Table 1. As is clearly evident from these results, the decomposition of TFD by the *N*-oxides of the heteroarenes **1a−5a** afforded quite different yields of singlet oxygen. No singlet oxygen was detected for DMD with the *N*-oxides **8a** and **12a**, whereas a positive response was obtained when **8a** was allowed to react with TFD.

The low yields in singlet oxygen in the above experiments (Table 1) and the fact that in several cases no $^1O_2$ could be detected, implied that alternative mechanisms, e.g. radical-type processes[10] may operate in these decompositions. For this purpose, two experiments were carried out to assess the intervention of radicals in the above DMD decomposition. On the one hand, the NMR analysis of the crude reaction mixture obtained after the addition of a large excess of "acetone-free" DMD solutions in either dichloromethane or carbon tetrachloride to a solution of amine *N*-oxide **8a** revealed acetone as only dioxirane product. Moreover, quantification of the amount of acetone by appropriate correction for the residual contents of this ketone present in the "acetone-free" DMD solutions, indicated that the dioxirane had been quantitatively converted into acetone. On the other hand, when these same reactions were performed under either oxygen or nitrogen, no difference was observed in the rates and product composition of the DMD decomposition. In view of our previous findings for the radical-type decomposition of dioxiranes,[10] the present results suggest that non-radical pathways operate in the decomposition of dioxiranes by amine *N*-oxides.

Another reason for the low $^1O_2$ yields (Table 1) may be quenching by the *N*-oxides and the respective amines,[11] the latter generated in situ in the dioxirane decomposition. To test this possibility, the efficiency of the transfer of singlet oxygen, generated in the thermal decomposition of the 1,4-endoperoxide of 1,4-dimethylnaphthalene to 9,10-dimethylanthracene was conducted in the presence of various

amines and their *N*-oxides (Table 2, method A). The aliphatic tertiary amines tributylamine (**8**), tribenzylamine (**9**) and *N*-benzylpiperidine (**10**) and their *N*-oxides **8a−10a**, and aromatic amine 4-(dimethylamino)pyridine (**6**) and its *N*-oxide **6a** were chosen because of their rapid dioxirane decomposition (Table 1). In all cases assayed, the thermolysis of the naphthalene endoperoxide was conducted to completion and the amine or *N*-oxide was quantitatively recovered. The $^1O_2$ trapping efficiencies, measured in terms of the endoperoxide cycloadduct of 9,10-dimethylanthracene, are given in Table 2 (Method A). Compared to the blank, i.e., no additive (footnote b of Table 2), the amines and their *N*-oxides quench singlet oxygen since the trapping efficiency was in all cases lower than that without additive (86 ± 3%). This explains at least in part the low $^1O_2$ yields obtained in the spectral detection of this relatively long half-life $^1O_2$ in deuteriochloroform and its pronounced reactivity (decay and oxidation) towards amines.[11] Tributylamine (**8**) exhibits the most effective quenching (entry 3, ca. 50%) of singlet oxygen, while the aromatic amine **6** (entry 1, ca. 20%) is ineffective.

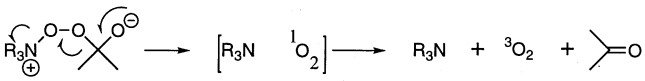
Table 2. Chemical detection of singlet oxygen by [4+2] cycloaddition with 9,10-dimethylanthracene in the thermal decomposition of 1,4-dimethylnaphthalene 1,4-endoperoxide in the presence of various amines and their *N*-oxides (**A**), or in the decomposition of DMD promoted by these amines or *N*-oxides (**B**)[a]

| entry | substrate | method A: $^1O_2$ trapping efficiency (%)[b] | method B: DMD decomposition amine:*N*-oxide [c] | $^1O_2$ (%) [d] |
|---|---|---|---|---|
| 1 | $Me_2N$–  (**6**) | 81 ± 6 | 17 : 83 | 32 |
| 2 | $Me_2N$–  (**6a**) | 98 | 13 : 87 | 30 |
| 3 | $Bu_3N$ (**8**) | 47 | 8 : 92 | 1 |
| 4 | $Bu_3\overset{\oplus}{N}–\overset{\ominus}{O}$ (**8a**) | 77 | 3 : 97 | 3 |
| 5 | $(PhCH_2)_3N$ (**9**) | 79 | [e] | 8 |
| 6 | $(PhCH_2)_3\overset{\oplus}{N}–\overset{\ominus}{O}$ (**9a**) | 83 | [f] | 10 |
| 7 |  (**10**) | 65 | 8 : 92 | 12 |
| 8 |  (**10a**) | 64 | 6 : 94 | 13 |

[a] A fivefold molar excess of dioxirane was used. − [b] Yields (ca. 10% error) were determined by $^1$H-NMR analysis; under the same conditions, 9,10-dimethylanthracene trapped 86% (ca. 3% error) of the singlet oxygen generated from the thermal decomposition of the 1,4-endoperoxide of 1,4-dimethylnaphthalene. − [c] Ratios were determined by $^1$H-NMR analysis (ca. 2% error). − [d] Yields were calculated based on mols of dioxirane divided by two (stoichiometric factor). − [e] A 10:49:41 mixture of amine/nitrone/aldehyde was obtained. − [f] A 23:50:27 mixture of amine/nitrone/aldehyde was obtained.

In the above chemical assay (Table 2, Method A), the singlet oxygen is generated by the thermal decomposition of the 1,4-dimethylnaphthalene 1,4-endoperoxide. In contrast, the source of $^1O_2$ in Table 1 is the reaction of the *N*-oxide with the dioxirane. According to our previous suggestion,[3][4] heterolytic cleavage of the spin-paired, dipolar *N*-oxide-dioxirane adduct must (spin conservation) generate singlet oxygen and that in close proximity of the released amine, as displayed in Scheme 2. Clearly, the amine should act as more efficient singlet-oxygen quencher than in the endoperoxide thermolysis. This fact would account for the lower yields of $^1O_2$ in Table 1.

Scheme 2



To test the cogency of this possibility, the above endoperoxide chemical assay for singlet oxygen was performed in the presence of DMD (Table 2, DMD decomposition, method B). Thus, a five-molar excess of dioxirane was added to a solution of the amine or the *N*-oxide and 9,10-dimethylanthracene in deuterated chloroform and 5 min later, the crude reaction mixture was analyzed by $^1$H-NMR spectroscopy to determine the amount of endoperoxide and also the amine/*N*-oxide ratio. Control experiments confirmed that 9,10-dimethylanthracene had reacted with the dioxirane at slower rates than those observed for the *N*-oxide-promoted decomposition process. In some cases, the amines suffered secondary oxidation reactions to afford unidentified products. The results in Table 2 demonstrate that the amine/*N*-oxide ratios, as well as the $^1O_2$ efficiencies, depend on the *N*-oxide structure. Thus, for the amine with the least quenching of $^1O_2$, namely 4-(dimethylamino)pyridine (**6**), the singlet-oxygen efficiency is highest (entry 1, ca. 32%), while for tri-*n*-butylamine (**8**), the most efficient quencher of $^1O_2$, it is the lowest (entry 3, ca. 1%).

The above results reveal that the reaction of dioxiranes with the *N*-oxides release $^1O_2$ and the corresponding amine, which in turn is in situ reoxidized to the *N*-oxide. Three different pathways may occur: a) The amine oxidation is faster than the deoxygenation of the *N*-oxide and the major reaction product will be the *N*-oxide (e.g. **1a−5a**); b) if these reaction rates are of the same order, mixtures of amines and their corresponding *N*-oxides will be formed in relative ratios that will depend on the respective reaction rates (e.g. **6a**, **8a**, **10a**); c) if the amine oxidation is slower, the major reaction product will be the amine (e.g. **9a**). Furthermore, some by-products may also be formed, particularly for benzyl derivatives due to the oxidation of the sensitive benzylic position by means of the singlet oxygen, either free or directly in the exciplex (Scheme 2).

According to the previously proposed mechanism of singlet-oxygen formation in the *N*-oxide-promoted decomposition of DMD,[3] the amount of $^1O_2$ should be proportional to the quantity of DMD used. When this was tested for the case of tributylamine *N*-oxide (25 μmol) with 9,10-dimethylanthracene (1 equiv.) as singlet-oxygen trap, for 5, 10 and 15 equiv. of DMD, there were obtained 11, 17 and 21% of the endoperoxide of 9,10-dimethylanthracene.

Of the maximally available $^1O_2$ (mol of DMD divided by two), this corresponds to 3 ± 0.5% of trapping by 9,10-dimethylanthracene.

In conclusion, we have shown that the oxidation of tertiary amines and nitrogen heteroarenes by dioxiranes to the expected *N*-oxides is not a general process. Thus, the in situ generated *N*-oxide may react with the dioxirane at comparable or even higher rates than the amine to afford mixtures of both products; the amine/*N*-oxide ratio is dependent on the nucleophilicity of the *N*-oxide. Addition of an excess of dioxirane merely results in the decomposition of the latter to release $^1O_2$. Only for non-nucleophilic heteroaromatic *N*-oxides this competing deoxygenation of the amine oxide is not significant in comparison with the amine oxidation. The more nucleophilic *N*-oxides derived from tertiary aliphatic amines react faster with dioxiranes to promote their deoxygenation and are more prone to release $^1O_2$ than those of heteroaromatic substrates.

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## Experimental Section

The IR spectra were recorded by using a Bomen model MB120 apparatus and the absorptions bands are given in $cm^{-1}$. The NMR spectra ($^1H$ NMR, 300 MHz; $^{13}C$ NMR, 75 MHz) were recorded with a Varian Unity 300 spectrometer in neutralized $CDCl_3$ solutions and the chemical shifts (δ) are given in ppm downfield from tetramethylsilane for $^1H$ and from deuteriochloroform for $^{13}C$ resonances. − DMD solutions in acetone (80 mM) were prepared as described elsewhere.[12] The concentrated, "acetone-free" DMD solutions, were obtained according to the recently reported procedure.[7] Unless stated otherwise, organic extracts obtained in the workup were dried with $MgSO_4$ and the resulting residues were purified after solvent removal as specified for the individual cases.

*Heteroarene and Amine N-Oxides:* These compounds (Table 1) were obtained, with the exception of the *N*-oxide **9a**, by treatment of the corresponding amino derivatives with DMD as described.[5] *N*-Oxide **9a** was prepared by using *m*CPBA as oxidant.

*Preparation and Epoxidation of the Tetrahydropyridinium Salts* **13b−d**

*N-Benzyl-3-ethyl-1,2,5,6-tetrahydropyridinium Trifluoroacetate* (**13b**): Trifluoroacetic acid (0.18 ml, 2.4 mmol) was added dropwise to a solution of *N*-benzyl-3-ethyl-1,2,5,6-tetrahydropyridine (0.400 g, 2.00 mmol) in anhydrous diethyl ether (10 ml) and the mixture was stirred under reflux until the reaction was complete (30 min, TLC monitoring). Removal of the solvent (25°C, 20 Torr) afforded the pure ammonium salt **13b** in quantitative yield. − IR (film): $\tilde{\nu}$ = 3459, 2971, 2606, 1777, 1739, 1671, 1457, 1201, 1143 $cm^{-1}$. − $^1H$ NMR: δ = 10.90 (br., 1 H, NH), 7.39−7.37 (5 H, ArH), 5.55 (br., 1 H, 4-H), 4.25 (br., 2 H, $CH_2$), 3.63 (d, $J$ = 16 Hz, 1 H, 2-$H_a$), 3.46 (m, 1 H, 6-$H_a$), 3.34 (d, $J$ = 16 Hz, 1 H, 2-$H_b$), 2.97 (m, 1 H, 6-$H_b$), 2.48 (br. d, $J$ = 18 Hz, 1 H, 5-$H_a$), 2.25 (br. d, $J$ = 18 Hz, 1 H, 5-$H_b$), 1.90 (q, $J$ = 7.5 Hz, 2 H, $CH_2$), 0.94 (t, $J$ = 7.5 Hz, 3 H, $CH_3$). − $^{13}C$ NMR: δ = 161.0 (q, $J_{C\text{-}F}$ = 37.5 Hz, CO), 132.0 (C-3), 130.7 ($CH_{Ar}$, C-2, C-6), 130.0 ($CH_{Ar}$, C-4), 129.2 ($CH_{Ar}$, C-3, C-5), 128.2 ($CH_{Ar}$, C-1), 117.3 (C-4), 115.8 (q, $J_{C\text{-}F}$ = 288 Hz, $CF_3$), 58.9 (benzyl $CH_2$), 51.6 (C-2), 47.8 (C-6), 26.8 (C-5), 21.3 ($CH_2$), 11.1 ($CH_3$). − HRMS for $C_{14}H_{20}N$: calcd. 202.1596, found 202.1608.

*N-Benzyl-3-ethyl-N-methyl-1,2,5,6-tetrahydropyridinium Trifluoromethanesulfonate* (**13c**): Methyl trifluoromethanesulfonate (0.22 ml, 1.90 mmol) was added dropwise at 0°C to a solution of *N*-benzyl-3-ethyl-1,2,5,6-tetrahydropyridine (0.350 g, 1.7 mmol) in anhydrous dichloromethane (10 ml) and the mixture was stirred at 25°C until the reaction was complete (30 min, TLC monitoring). Removal of the solvent (25°C, 20 Torr) afforded pure ammonium salt **13c** in quantitative yield. − IR (film): $\tilde{\nu}$ = 3546, 2969, 1459, 1258, 1224, 1156, 1029 $cm^{-1}$. − $^1H$ NMR: δ = 7.51−7.36 (5 H, ArH), 5.56 (br., 1 H, H-4), 4.60 (br., 2 H, $CH_2$), 3.90 (d, $J$ = 16.5 Hz, 1 H, 2-$H_a$), 3.59 (d, $J$ = 16.5 Hz, 1 H, 2-$H_b$), 3.51−3.38 (2 H, 6-H), 2.96 (s, 3 H, $NCH_3$), 2.40 (br., 2 H, 5-H), 1.93 (q, $J$ = 7.5 Hz, 2 H, $CH_2$), 0.95 (t, $J$ = 7.5 Hz, 3 H, $CH_3$). − $^{13}C$ NMR: δ = 133.0 ($CH_{Ar}$, C-2, C-6), 132.0 (C-3), 130.6 $CH_{Ar}$, C-4), 129.0 ($CH_{Ar}$, C-3, C-5), 126.4 ($CH_{Ar}$, C-1), 116.2 (C-4), 67.5 (benzyl $CH_2$), 58.9 (C-2), 55.8 (C-6), 46.0 ($CH_3N$), 26.8 (C-5), 20.8 ($CH_2$), 11.1 ($CH_3$). − HRMS for $C_{15}H_{22}N$: calcd. 216.1752, found 216.1770.

*N-Benzyl-3-ethyl-N-methoxy-1,2,5,6-tetrahydropyridinium Trifluoromethanesulfonate* (**13d**): Methyl trifluoromethanesulfonate (0.12 ml, 1.10 mmol) was added dropwise at 0°C to a solution of *N*-oxide **13a** (0.220 g, 1.00 mmol) in anhydrous dichloromethane (15 ml) and the mixture was stirred at 25°C until the reaction was complete (3 h, TLC monitoring). Removal of the solvent (25°C, 20 Torr) afforded pure ammonium salt **13d** in quantitative yield as a 4:1 mixture of conformers ($^1H$ NMR). − IR (film): $\tilde{\nu}$ = 3492, 2971, 1457, 1276, 1257, 1162, 1029 $cm^{-1}$. − $^1H$ NMR: δ = 7.69−7.30 (5 H, ArH), 5.58 (br., 1 H, H-4), 4.99 (d, $J$ = 14 Hz, 1 H, $H_a$, $CH_2$), 4.93 (d, $J$ = 14 Hz, 1 H, $H_b$, $CH_2$), 4.76 (d, $J$ = 14 Hz, 1 H, $H_a$, $CH_2$), 4.68 (d, $J$ = 14 Hz, 1 H, $H_b$, $CH_2$), 4.34 (d, $J$ = 17 Hz, 1 H, 2-$H_a$), 4.12−3.56 (3 H, 2-$H_b$, 6-$H_2$), 3.97 (s, 3 H, $OCH_3$), 2.60−2.22 (2 H, 5-H), 1.95 (2 H, $CH_2$), 0.97 (t, $J$ = 7.5 Hz, 3 H, $CH_3$, conformer a), 0.76 (t, $J$ = 7.5 Hz, 3 H, $CH_3$, conformer b). − $^{13}C$ NMR: δ = 132.9 ($CH_{Ar}$, C-2, C-6, conformer b), 132.6 ($CH_{Ar}$, C-2, C-6, conformer a), 131.2 ($CH_{Ar}$, C-3,conformer b), 130.7 ($CH_{Ar}$, C-4, conformer a), 130.5 ($CH_{Ar}$, C-4, conformer a), 130.1 ($CH_{Ar}$, C-3, conformer a), 129.1 ($CH_{Ar}$, C-3, C-5, conformer a), 128.8 ($CH_{Ar}$, C-3, C-5, conformer b), 126.9 ($CH_{Ar}$, C-1, conformer b), 126.0 ($CH_{Ar}$, C-1, conformer a), 120.6 (q, $J_{C\text{-}F}$ = 255 Hz, $CF_3$), 117.2 (C-4, conformer a), 116.5 (C-4, conformer b), 70.8 (benzyl $CH_2$, conformer b), 64.8 (benzyl $CH_2$, conformer a), 63.6 (C-2, conformer b), 59.3 (C-2, conformer a), 56.1 (C-6), 56.1 ($CH_3O$), 26.5 (C-5), 21.5 ($CH_2$), 11.2 ($CH_3$). − HRMS for $C_{15}H_{22}NO$: calcd. 232.1686, found 232.1701.

*Epoxidation of the Ammonium Salts* **13b−d**. − *General Procedure:* The DMD reactions were carried out by dropwise addition of the oxidant to the substrate in $CH_2Cl_2$ solution of the substrate at 0°C and this temperature was maintained until all the DMD was consumed. In the case of TFD, the oxidant was added to the substrate in $CH_2Cl_2$ at −78°C and the mixture was stirred at −20°C until all the TFD had been consumed. The solvent was evaporated (30°C, 20 Torr) and yields were determined by $^1H$-NMR analysis.

*Epoxides* **14b−d** *and Diol* **15b**: According to the General Procedure, a solution of the ammonium salt **13b** (0.100 g, 0.320 mmol)

in $CH_2Cl_2$ (1 ml) was treated with 1.2 equiv. of DMD (4 h). The $^1$H-NMR analysis of the residue showed 30% conversion and the presence of a mixture of the expected epoxide **14b** and the diol **15b**. Due to the complexity of the product spectra (severe overlap of peaks), the relative composition of the products **14b** and **15b** could not be determined. When the oxidation was performed with TFD, only 30 min were required for completion and the $^1$H-NMR analysis of the residue revealed the same products. Once again, due to severe peaks overlap it was not possible to estimate the relative composition of this mixture.

A portion of the above crude reaction mixture was poured onto a 1:1 mixture of 0.1 M aqueous $KHCO_3$ and *tert*-butyl methyl ether, and the organic phase was separated and dried. The residue obtained after evaporation of the solvent under vacuum was purified by preparative TLC (elution with a 1:1 mixture of hexane and ethyl acetate) to afford pure epoxide **14b**[5] and diol **15b** in a ca. 1:1 ratio. *N*-Benzyl-3-ethyl-3,4-dihydroxypiperidine (**15b**): IR (film): $\tilde{\nu}$ = 3415, 2934, 2803, 1453, 1062 cm$^{-1}$. − $^1$H NMR: δ = 7.40−7.18 (5 H, ArH), 3.67 (t, *J* = 4 Hz, 1 H, 4-H), 3.57 (d, *J* = 13 Hz, 1 H), 3.49 (d, 1 H, *J* = 13 Hz), 2.60−2.30 (3 H, 2-H, 6-$H_a$), 2.06 (m, 1 H, 6-$H_b$), 1.57 (4 H, 5-H, C$H_2$CH$_3$), 0.90 (t, *J* = 7.5 Hz, 3 H, $CH_3$). − $^{13}$C NMR: δ = 138.2 ($C_{Ar}$, C-1), 128.9 ($CH_{Ar}$, C-3, C-5), 128.3 ($CH_{Ar}$, C-2, C-6), 127.1 ($CH_{Ar}$, C-4), 71.7 (C-3), 70.1 (C-4), 62.5 ($CH_2$, benzylic), 58.2 (C-2), 48.3 (C-6), 29.8 (C-5), 26.7 ($CH_2$), 6.4 ($CH_3$). − MS (70 eV); *m/z* (%): 235 [M$^+$], 188, 150, 146, 140 (100).

*Epoxide* **14c**: Treatment of the ammonium salt **13c** with 1.1 equiv. of DMD for 30 h according to the General Procedure led to a 80:20 diastereomeric mixture of the epoxide **14c** (NMR monitoring). When TFD was used, only 30 min were required for completion to afford the same mixture of epoxide **14c**. − IR (film): $\tilde{\nu}$ = 3448, 2967, 1457, 1274, 1258, 1224, 1162 cm$^{-1}$. − $^1$H NMR: δ = 7.55−7.37 (5 H, $H_{Ar}$), 4.77 (d, *J* = 13 Hz, 1 H, benzylic $H_a$, diast. a), 4.62 (br., 2 H, $CH_2$, diast. b), 4.59 (d, *J* = 13 Hz, 1 H, benzylic $H_b$, diast. a), 3.98 (d, *J* = 14.5 Hz, 1 H, 2-$H_a$, diast. b), 3.79 (d, *J* = 14.5 Hz, 1 H, 2-$H_a$, diast. a), 3.53 (d, *J* = 14.5 Hz, 1 H, 2-$H_b$, diast. a), 3.74−3.36 (6-$H_a$, diast. a + b, 2-$H_b$,diast. b), 3.26 (s, 3 H, $NCH_3$, diast. b), 3.13 (s, 3 H, $NCH_3$, diast. b), 3.12−3.03 (6-$H_b$, diast. a + b), 3.03 (s, 1 H, 4-H, diast. a), 3.00 (s, 1 H, 4-H, diast. b), 2.48−2.21 (2 H, 5-H, diast. a + b), 1.64 (q, *J* = 7.5 Hz, 2 H, C$H_2$CH$_3$), 0.92 (t, *J* = 7.5 Hz, 3 H, CH$_2$C$H_3$). − $^{13}$C NMR: δ = 133.3 ($CH_{Ar}$, C-2, C-6, diast. a), 133.2 ($CH_{Ar}$, C-2, C-6, diast. b), 130.9 ($CH_{Ar}$, C-4), 129.3 ($CH_{Ar}$, C-3, C-5), 126.3 ($C_{Ar}$, C-1), 120.5 (q, $J_{C\text{-}F}$ = 324 Hz, $CF_3$), 69.1 (benzylic C, diast. a), 68.0 (benzylic C, diast. b), 60.0 (C-2, diast. b), 59.8 (C-2, diast. a), 58.2 (C-3, diast. b), 57.2 (C-3, diast. a), 54.3 (C-6, diast. b), 53.5 (C-3, diast. a), 53.3 (C-3, diast. b), 52.1 (C-6, diast. a), 48.5 ($CH_3$, $NCH_3$, diast. b), 47.3 ($NCH_3$, diast. a), 28.0 (C-5, diast. b), 26.8 (C-5, diast. a), 20.5 (*C*H$_2$CH$_3$, diast. b), 20.4 (*C*H$_2$CH$_3$, diast. a), 7.8 (CH$_2$*C*H$_3$, diast. a), 7.4 (CH$_2$*C*H$_3$, diast. b).

*Epoxide* **14d**: Treatment of the ammonium salt **13d** with 1.2 equiv. of DMD for 30 h according to the General Procedure led to a 82:18 diastereomeric mixture of epoxide **14d** (NMR monitoring). When TFD was used, only 30 min were required for completion of the reaction to afford the same mixture in a 67:33 diastereomeric ratio. − IR (film): $\tilde{\nu}$ = 3459, 2967, 1731, 1457, 1276, 1257, 1224 cm$^{-1}$. − $^1$H NMR: δ = 7.54−7.38 (5 H, $H_{Ar}$), 4.97 (br., 2 H, $CH_2$ benzylic diast. a), 4.88 (br., 2 H, $CH_2$ benzylic diast. b), 4.07 (s, 3 H, $OCH_3$ diast. a), 4.10−3.94 (3 H, 2-H, 6-$H_a$), 3.83 (s, 3 H, $OCH_3$, diast. b), 3.42 (m, 1 H, 6-$H_b$), 3.26 (br., 1 H, 4-H), 2.40−2.18 (2 H, 5-H), 1.63 (q, *J* = 7.5 Hz, 2 H, C$H_2$CH$_3$, diast. b), 1.62 (q, *J* = 7.5 Hz, 2 H, C$H_2$CH$_3$, diast. a), 0.88 (t, *J* = 7.5 Hz, 3 H, CH$_2$C$H_3$, diast. b), 0.86 (t, *J* = 7.5 Hz, 3 H, CH$_2$C$H_3$, diast. a). − $^{13}$C NMR: δ = 133.0 ($CH_{Ar}$, C-2, C-6, diast. b), 132.7 ($CH_{Ar}$, C-2, C-6, diast. b), 131.1 ($CH_{Ar}$, C-4), 129.5 ($CH_{Ar}$, C-3, C-5, diast. a), 129.3 ($CH_{Ar}$, C-3, C-5, diast. b), 125.9 ($C_{Ar}$, C-1, diast. b), 125.5 ($C_{Ar}$, C-1, diast. b), 120.4 (q, $J_{C\text{-}F}$ = 318 Hz, $CF_3$), 72.9 ($CH_2$, benzylic C, diast. b), 65.8 ($CH_2$, benzylic C, diast. a), 63.7 (C-2, diast. b), 61.5 ($CH_2$, C-2, diast. a), 56.9 (C, C-3, diast. b), 56.7 (C, C-3, diast. b), 56.5 ($CH_3$, $OCH_3$), 55.2 ($CH_2$, C-6, diast. b), 54.1 (CH, C-4, diast. b), 53.8 (C-4, diast. a), 51.4 (C-6, diast. a), 28.0 (C-5, diast. b), 27.9 (C-5, diast. b), 20.6 (*C*H$_2$CH$_3$, diast. a), 20.4 (*C*H$_2$CH$_3$, diast. b), 7.6 (CH$_2$*C*H$_3$).

*Persistence Assays of Dioxiranes Towards the Amine N-Oxides:* To an approx. 0.5 mM solution of the *N*-oxide in acetone, $CH_2Cl_2$ or $CCl_4$ was added a solution of DMD (3 equiv.) in the same solvent[7] and the mixture was stirred at 20°C. When TFD was used as oxidant, a threfold molar excess of the TFD solution in trifluoroacetone was employed. The consumption of the dioxirane was monitored by the peroxide test (KI/HOAc) and the results are shown in Table 1.

The 1,4-endoperoxide of 1,4-dimethylnaphthalene was synthesized according to Turro et al.[9]. IR chemiluminiscence experiments were conducted by using an indium-doped gallium arsenide photodiode detector which was cooled with liquid nitrogen. The spectral window used was 1270 ± 10 nm ($^1O_2$ exhibits a characteristic chemiluminiscent band at 1268 nm). In these experiments TFD was used in trifluoroacetone (TFA) solution, whereas DMD was employed as $CDCl_3$ solution. The assays were conducted in the detector cuvette by addition of five molar equivalents of TFD or DMD to the corresponding *N*-oxide. Quantification of the $^1O_2$ produced was carried out by calibration with that generated by the thermal decomposition of the naphthalene endoperoxide. For this purpose, a solution of the naphthalene endoperoxide in $CDCl_3$ was heated up to 50°C in the detector cuvette and the IR emission at 1268 nm was measured. The yield of singlet oxygen (76%) was previously established by Turro et al.[9] and was employed as reference. The ratio of the areas under the IR emission curves was determined for the decomposition of the naphthalene endoperoxide in the presence of the various *N*-oxides and their absence. From these ratios and the calibration factor for the naphthalene endoperoxide (76% yield of $^1O_2$[9]), the singlet-oxygen yields in the *N*-oxide-promoted decomposition of the dioxiranes were calculated with respect to the amount of dioxirane used. For this purpose it was assumed that total $^1O_2$ was: (mols dioxirane + mols *N*-oxide)/2. The results are summarized in Table 2.

*Chemical Trapping of Singlet Oxygen by 9,10-Dimethylanthracene in the Presence and Absence of the Amines and Their N-Oxides:* A mixture of the 1,4-endoperoxide of 1,4-dimethylnaphthalene (5.0 mg, 0.031 mmol) and 9,10-dimethylanthracene (7.0 mg, 0.034 mmol) in $CDCl_3$ (0.8 ml) was heated for 12 h at 40°C. The $^1$H-NMR analysis of the crude reaction mixture revealed the presence of 9,10-dimethylanthracene 9,10-endoperoxide[9] in yields within 82−91%. The same assay, but with 1.7 equiv. of the particular amine or amine *N*-oxide, was used to determine the ability of these compounds to quench singlet oxygen and the results are shown in Table 2.

*Determination of the Singlet Oxygen Yield Generated in the Decomposition of DMD by the Amines and their N-Oxides:* A solution of DMD (5 equiv.) in $CDCl_3$ was added to a mixture of the amine and of the *N*-oxide (5 mg, ca. 0.03 mmol) and 9,10-dimethylanthracene (1 equiv.) in $CDCl_3$ (0.2 ml) at 20°C, and the reaction was maintained until all DMD had been consumed (monitored by the peroxide test: KI/HOAc). The amount of anthracene endoperoxide

was determined by $^1$H-NMR analysis and results are shown in Table 2.

[1] For reviews on dioxiranes see: [1a] W. Adam., A. K. Smerz, *Bull. Soc. Chim. Belg.* **1996**, *105*, 581−599. – [1b] R. Curci, A. Dinoi, M. F. Rubino, *Pure Appl. Chem*. **1995**, *67*, 811−822. – [1c] R. W. Murray, *Chem. Rev.* **1989**, *89*, 1187−1201. – [1d] W. Adam, R. Curci, J. O. Edwards, *Acc. Chem. Res.* **1989**, *22*, 205−211.
[2] A. Gallopo, J. Edwards, *J. Org. Chem*. **1981**, *46*, 1684−1688.
[3] W. Adam, K. Briviba, F. Duschek, D. Golsch, W. Kiefer, H. Sies, *J. Chem. Soc., Chem. Commun.* **1995**, 1831−1832.
[4] W. Adam, D. Golsch, *Angew. Chem. Int. Ed. Eng*. **1993**, *105*, 771−773.
[5] M. Ferrer, F. Sanchez-Baeza, A. Messeguer, *Tetrahedron* **1997**, *53*, 15877−15888.
[6] M. Ferrer, F. Sánchez-Baeza, A. Messeguer, A. Diez, M. Rubiralta, *J. Chem. Soc., Chem. Commun.* **1995**, 293−294.
[7] M. Gibert, M. Ferrer, F. Sánchez-Baeza, A. Messeguer, *Tetrahedron* **1997**, *53*, 8643−8650.
[8] The halflife of singlet oxygen is ca. tenfold longer in deuterated solvents: P. B. Merkel, D. R. Kearns, *J. Am. Chem. Soc.* **1972**, *94*, 1029.
[9] N. J. Turro, M. Chow, J. Rigaudy, *J. Am. Chem. Soc.* **1981**, *103*, 7218−7224.
[10] W. Adam, R. Curci, M. E. González-Núñez, R. Mello, *J. Am. Chem. Soc.* **1991**, *113*, 7654−7658.
[11] F. Wilkinson, W. P. Helman, A. B. Ross, *J. Phys. Chem. Ref. Data* **1995**, *24*, 663−1021.
[12] W. Adam, J. Bialas, L. Hadjiarapoglou, *Chem. Ber.* **1991**, *124*, 2377.

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