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THE FLUORIDE ION EFFECT IN THE REACTIONS OF SINGLET OXYGEN WITH ENOLS

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Abstract—The fluoride ion effect in the reactions of enolic systems with singlet oxygen has been investigated. β-Dicarbonyl compounds yielded 1,2,3-tricarbonyl derivatives, some of which underwent further hydration, whereas α-diketones suffered oxidative decarboxylation to give open-chain aldehydo-acids or keto-acids.

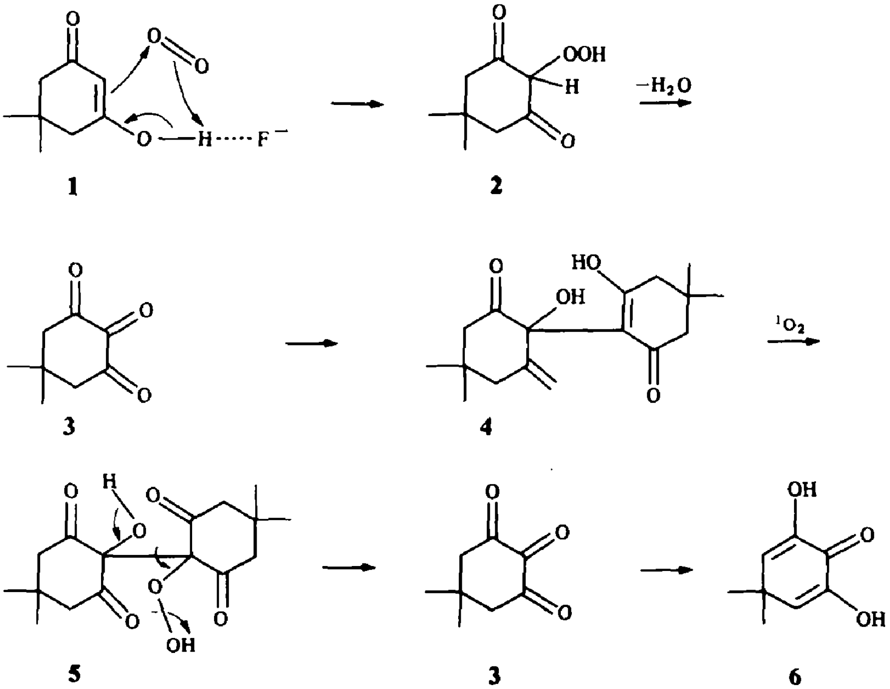
The reactions of singlet oxygen with electron-rich systems, such as enamines and enol ethers, have received considerable attention both in mechanistic studies and in applications to synthetic methodology.[1,2] By contrast, there have been few reports on enol–$^1O_2$ reactions beyond investigations by Matsuura and co-workers on 3-hydroxyflavones,[3,4] by Padwa *et al.* on 3-phenylisocoumaranone[5] and by Young and Hart on enolate anions of β-diketones.[6] In general, it has been found that enols of β-diketones react very sluggishly or not at all with $^1O_2$, presumably because of the conjugation of the double bond with the electron-withdrawing CO group.

Recent findings by Clarke and Miller[7] have shown that fluoride ion may serve to enhance the nucleophilicity of enolic systems by a process involving transfer or electron density to the donor site. This effect has played a significant role in the fluoride-promoted mono-C-alkylation of β-dicarbonyl compounds, in the self-condensation of enols,[8] and in other nucleophilic reactions of phenols, acids and nitro compounds.[9] In all of these cases, evidence has been adduced to show the existence of a H-bond between the acidic substrate and the fluoride ion. We have now found that the fluoride ion effect may be extended to the reactions of enolic systems with $^1O_2$.[10]

Table 1 summarizes the compounds which exhibited an increase in reactivity with $^1O_2$ in the presence of fluoride to give identifiable products. In general, β-dicarbonyl compounds yielded 1,2,3-tricarbonyl derivatives, some of which underwent further hydration, while α-diketones suffered oxidative decarboxylation to give open-chain aldehydo-acids or keto-acids. In all cases listed in Table 1, there was a marked increase in reactivity toward $^1O_2$ upon addition of fluoride. In fact, many of these compounds were totally unreactive in the absence of fluoride. The results of the fluoride-promoted photo-oxidation of selected β-diketonic systems are discussed below.

5,5-*Dimethylcyclohexane*-1,3-*dione* (*dimedone*)

Dimedone (1) reacted very slowly with $^1O_2$ in the absence of fluoride ion, consuming only 0.8 equivalent of O_2 after 16 hr of irradiation in the presence of Rose



Scheme 1.

Table 1.

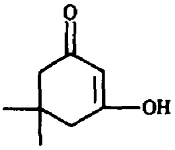
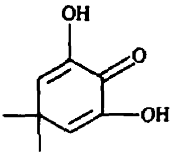
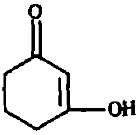
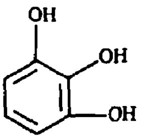
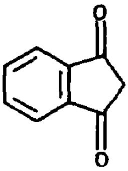
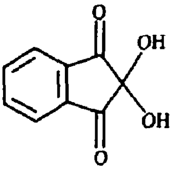
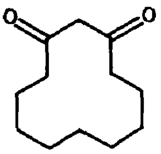
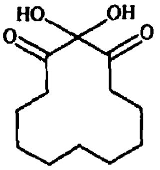
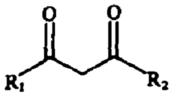
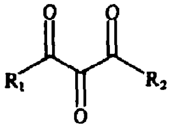
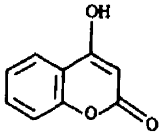
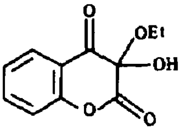
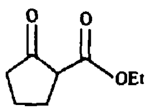
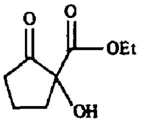
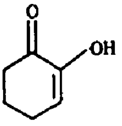
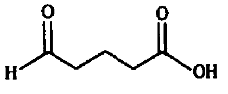
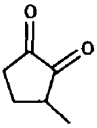
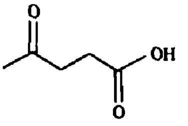
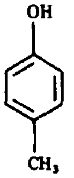
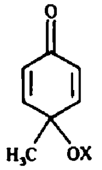
Dicarbonyl substrate	Product[a]	Yield with F^-	Results, absence of F^-
 **1**	 **6**	72%, 1½ hr	[b]
 **8**	 **9**	70%, 2 hr	[b]
 **10**	 **11**	75%, 3 hr	[c]
 **12**	 **13**	60%, 1 hr	[c]
 **15**	 **16**		
$R_1 = Ph, R_2 = Ph$	$R_1 = Ph, R_2 = Ph$	97%, 2 hr	[c]
$R_1 = Ph, R_2 = CH_3$	$R_1 = Ph, R_2 = CH_3$[d]	72%, 3 hr	[c]
$R_1 = CH_3, R_2 = CH_3$	$R_1 = CH_3, R_2 = CH_3$[d]	66%, 2.5 hr	[c]
 **17**	 **18**	70%, 0.5 hr	[c]
 **19**	 **20**	49%, 2 hr (2 equivalents F^-)	[c]

Table 1.—*continued*

 **21**	 + CO **22**	65%, 3 hr	e
 **23**	 **24**	72%, 5 hr	e
 **25**	 X=H,OH **26**	87%, 3 hr	b

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[a] Satisfactory NMR, IR and elemental analyses were obtained for all new compounds.

[b] The reaction was very slow and yielded an intractable mixture of products.

[c] There was no detectable O_2 uptake or change in TLC behaviour after several hours of irradiation.

[d] Isolated as the addition product with *o*-phenylenediamine.

[e] A very slow reaction, accompanied by severe dye bleaching.

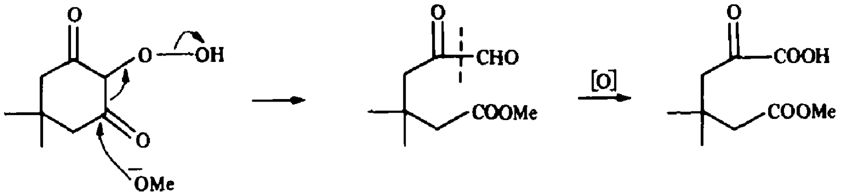
Bengal, to give a mixture of products including the condensation product (**4**). In the presence of 1 equivalent of tetrabutylammonium fluoride in chloroform the photo-oxidation was complete in 90 min to give the vicinal tricarbonyl (**3**) isolated as the dienol (**6**) (72%).[11]

TLC showed that all of the starting material had been consumed after 0.5 equivalent of O_2 had been taken up. If the reaction was stopped at that point, the condensation product **4** could be isolated. Addition of dimedone to pure **6** in the presence of fluoride also gave **4**. Scheme 1 is proposed as a rationale for the reaction. In this process, dimedone (**1**) as a fluoride complex reacts with $^1O_2$ to give hydroperoxide (**2**). Compound **2** then undergoes β-elimination of water to form the trione **3** (or **6**). Unreacted dimedone may then take part in a condensation reaction with **3** to give **4**, which is further oxidized to **5**. Intermediate **5** would be expected to undergo fragmentation with C–C bond cleavage to give two molecules of trione **3** (or the dienol **6**).

The photo-oxidation of dimedone also occurred rapidly in basic media but did not proceed as cleanly. Photo-oxidation in methanol–methoxide previously had been reported to give 3,3-dimethylglutaric acid monomethyl ester (**7**)[6] (Scheme 2). No 3,3-dimethylglutaric acid was found in the fluoride-promoted photo-oxidation. Photo-oxidation of dimedone in the presence of tetrabutylammonium hydroxide gave a complex mixture of products, but no signals in the NMR corresponding to dienol **6** or condensation product **4** were visible. The rate of O_2 uptake was comparable to the fluoride runs.

Cyclohexane-1,3-*dione* (**8**)

Cyclohexane-1,3-dione (**8**) reacted with $^1O_2$ in the presence of fluoride to give pyrogallol (**9**) in 2 hr (70%). In the absence of fluoride, an unidentified mixture of products was formed after 12 hr. No evidence of a condensation product analogous to **4** was obtained, presumably because the initially formed triketone



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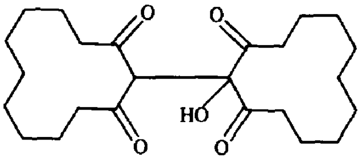
Scheme 2.

underwent rapid aromatization to the final product before condensation with the dione could occur.

Cyclododecane-1,3-*dione* (12)

Cyclododecane-1,3-dione (12) was photo-oxidized in chloroform in the presence of fluoride ion, but less than 1 equivalent of O_2 was consumed even after long irradiation and the addition of excess fluoride. Two products were isolated on work-up: the hydrate of cyclododecane-1,2,3-trione (13; 60%) and the condensation product 14 in 21% yield. Unlike 4, condensation product 14 did not appear to undergo further photo-oxidation.



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Other β-diketones

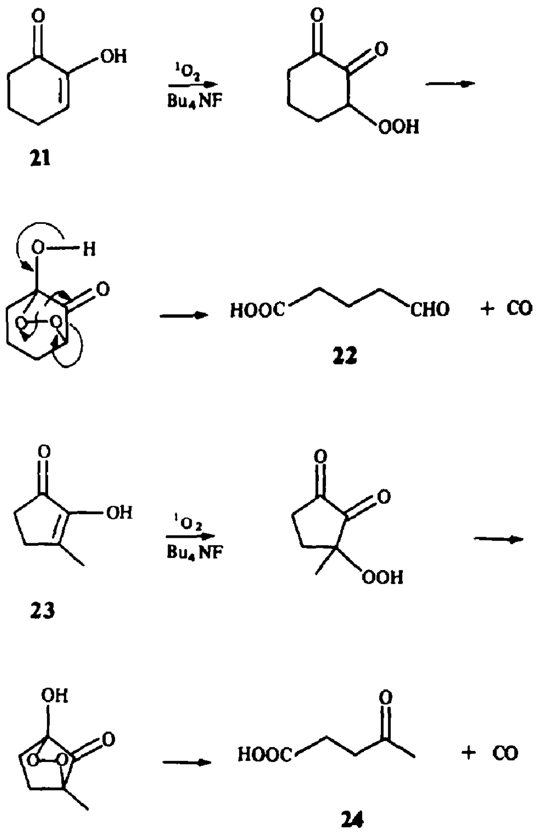
Dibenzoylmethane, 15 ($R_1 = R_2 =$ Ph) reacted with $^1O_2$ in the presence of fluoride to give diphenylpropanetrione, 16 ($R_1 = R_2 =$ Ph) (97%). This appears to be a very convenient synthesis of this vicinal triketone. There was no reaction without fluoride. Likewise, benzoylacetone, 15 ($R_1 =$ Ph; $R_2 = CH_3$) and acetylacetone, 1 ($R_1 = R_2 = CH_3$) gave the corresponding triones upon photo-oxidation in the presence of fluoride. These products, however, were too polar to permit convenient separation from the Bu_4NF and they were, therefore, isolated as their quinoxalines by the addition of *o*-phenylenediamine to the reaction mixtures.

4-*Hydroxycoumarin* (17)

4-Hydroxycoumarin (17), a fully enolic compound, was totally inert toward $^1O_2$ in the absence of fluoride. In the presence of 1 equivalent of fluoride (chloroform soln), however, photo-oxidation was complete within 30 min to give the ethanol adduct of 2,3-benzopyran-4,5,6-trione (18). The ethanol most probably was present as a stabilizer in commercial chloroform.

α-Diketones

Cyclohexane-1,2-dione (21) was very difficult to photo-oxidize in the absence of fluoride due to severe dye bleaching. In the presence of fluoride, the dye was much more stable and all of the starting material was consumed after 3 hr of irradiation. Upon work-up, glutaraldehydic acid (22) was isolated (65%), characterized as its 2,4-dinitrophenylhydrazone. Tests for carbon monoxide in the effluent gas were positive. This type of oxidative degradation of α-dicarbonyl compounds (summarized in Scheme 3) has precedent in the lit.[4,12] (Very recently, Utaka *et al.*[13] have reported new results on the temperature dependency of 1,2-cyclohexanedione photo-oxygenation.) In like manner, 3-methylcyclopentane-1,2-dione (23) was photo-oxidized in the presence of fluoride to yield carbon monoxide and levulinic acid (24), isolated as the ethyl ester (72%).



Scheme 3.

Phenols

Dye-sensitized photo-oxidations of phenols have been extensively studied by Matsuura[3,4] and, in a variety of cases, the intermediacy of $^1O_2$ has been shown by competitive inhibitors, quenching techniques and solvent isotope effects. In our initial studies on the fluoride ion effect in $^1O_2$–phenol reactions, we used *p*-cresol and a number of phenols bearing electron-withdrawing substituents. *p*-Cresol (25) underwent photo-oxidation very slowly without fluoride but, in the presence of 1 equivalent of Bu_4NF, it was photo-oxidized within 3 hr to give a hydroperoxide, 26 (X = OH; 84%) which underwent reduction with triphenylphosphine to the alcohol 26 (X = H). Photo-oxidation of *p*-cresol in the presence of Bu_4NOH did not take place cleanly, yielding a mixture of products. Attempts to extend this procedure to phenols bearing electron-withdrawing groups in the 4-position, such as ethyl *p*-hydroxybenzoate were unsuccessful.

Uptake of $^1O_2$ by *p*-cresol did not occur when methylene blue (triplet energy, 34 kcal/mol) was used as the sensitizer instead of polymer-bound Rose Bengal (40 kcal/mol). These results suggest that the oxidation may not be occurring via a $^1O_2$ mechanism but, rather, by electron transfer with the dye.

Sources of fluoride

Tetrabutylammonium fluoride was found to be a satisfactory source of fluoride for the oxidations with $^1O_2$. It is readily soluble in water, chloroform, methylene chloride, tetrahydrofuran and alcohols, but is not soluble in ether. Reaction mixtures can be partitioned between water and ether or ethyl acetate with the fluoride going cleanly into the water layer. A convenient preparation of the fluoride follows the procedure of Pless,[14] starting with tetrabutylammonium bromide and exchanging the bromide for fluoride on an ion exchange column. For reasons which are not clear, we found that the fluoride salt prepared by neutralization of tetrabutylammonium hydroxide with HF was not effective in promoting these photo-oxidations.

Other counterions for the fluoride were tried. Benzyltrimethylammonium fluoride, prepared by neutralizing Triton B with HF, promoted the photo-oxidation of dimedone, but not as effectively as Bu_4NF. Potassium fluoride in the presence of 18-crown-6 favoured the photo-oxidation of dimedone and *p*-cresol if a full equivalent of the crown ether was used. Reactions with catalytic quantities of the crown ether were very sluggish and, in all cases, a full equivalent of fluoride ion was found necessary. Use of less than 1 equivalent resulted in less than complete reaction.

The nature of the fluoride effect

There is disagreement in the literature over the role of fluoride ion in increasing the nucleophilicity of enols. Clark and co-workers[7–9] have proposed that fluoride ion forms H-bonds with the OH group, thereby increasing the electron density on the oxygen. Mingin and Huisgen, on the other hand, have advanced the hypothesis that the fluoride acts as a base, and that increased reactivity in the presence of fluoride is due to anion formation.[16]

We found that fluoride was the only halide effective in enhancing the photo-oxidation reactions. Tetra-alkylammonium chlorides, bromides and iodides did not increase the rate of dimedone photo-oxidation significantly. The nature of the solvent was important as well. Although very small amounts of ethanol in chloroform, methylene chloride, or dichloroethane did not seem to inhibit the reaction, the rate of photo-oxidation of dimedone in ethanol was nearly the same with or without fluoride (*ca* 12 hr). This finding is consistent with the H-bond theory. Ethanol would be expected to take part in H-bonding with the fluoride ion, thereby reducing the effect of the fluoride on the enol. We are giving further study to the role of fluoride ion in promoting the photo-oxidations of all types of enolic systems.

EXPERIMENTAL

Tetrabutylammonium fluoride. The procedure of Pless[14] was followed. Amberlite IRA 410 CP ion exchange resin (1000 ml) was converted to a slurry with water and packed into a large chromatography column. The following were then passed through the column: 5% NaOH until the effluent was basic, water until neutral, 5% HF until acidic and water until neutral (*ca* 12 l). Then 50 g of Bu_4NBr in 500 ml of water was passed through the column very slowly, followed by the slow addition of water until a qualitative test for fluoride was negative. For this test, a reagent was prepared by dissolving 10 g of $Pb(OAc)_2$ in 100 ml of water and 1 ml of HOAc. One drop of 2 N HCl was added to 1 ml of this reagent and the test tube was shaken until the cloudiness disappeared. Then a few drops of the column effluent was added. A white ppt (PbClF) is a positive test.

The fluoride-containing fractions were evaporated *in vacuo*. EtOH was added and evaporated three times. Finally, enough absolute EtOH was added to make 155 ml of a 1 M soln. The fluoride may be rendered nearly anhydrous by repeatedly adding and evaporating $CHCl_3$ and then keeping the resulting oil overnight *in vacuo* at 60°. The column may be regenerated and re-used.

Photo-oxidation of dimedone (**1**) *in the presence of fluoride. Formation of* 4,4-*Dimethyl* - 2,6 - *dihydroxy* - 2,5 - *cyclohexadieneone* (**6**). Dimedone (1.40 g, 10 mmol) was dissolved in 50 ml of $CHCl_3$, 10.5 ml of a 1 M soln of Bu_4NF in EtOH was added and the solvent was evaporated to a yellow oil. The oil was taken up in 100 ml of $CHCl_3$ and injected into a dried, O_2-purged, ice-cooled oxygenation well. Sensitox[†][15] (*ca* 10 mg) was added and the soln irradiated with visible light from a Pyrex-filtered 650 W tungsten–halogen lamp while O_2 was circulated. O_2 uptake was monitored using a gas buret. After 90 min, 250 ml of O_2 (10 mmol) had been consumed, and the mixture was worked-up by filtering the Sensitox, evaporating the $CHCl_3$, and partitioning the residue between ether and water. The aq layer was extracted with three 50 ml portions of ether. The ether portions were combined, washed with brine, dried with Na_2SO_4 and evaporated to dryness to yield **6** as a sweet-smelling oil that crystallized to an oily solid upon standing: 1.25 g, 72%; IR $\nu_{max}^{CHCl_3}$ 3478, 1632, 1453, 1400, 1375, 1309, 1281, 1196 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.30 (6H, s), 6.21 (2H, s), 6.25 (2H, br s).

The bisphenylhydrazone was prepared in aq H_2SO_4–HOAc and twice recrystallized from MeOH: m.p. 177–178° (lit.[11] 175°). The authentic bisphenylhydrazone had m.p. 177–179°; mixed m.p. with above product was 178°. The IR spectra of the products were superimposable.

Photo-oxidation of dimedone (**1**) *in the presence of fluoride. Isolation of the primary product* (**4**). Dimedone (1.40 g, 10 mmol) was dissolved in 85 ml of $CHCl_3$ in the well of the oxygenation apparatus. Tetrabutylammonium fluoride (16 ml of a 0.63 M soln in $CHCl_3$, 10 mmol) and methylene blue (*ca* 5 mg in $CHCl_3$) were added. The apparatus was purged with O_2, cooled in an ice bath and irradiated with visible light (650 W tungsten–halogen lamp, Pyrex-filtered). After 70 min, O_2 uptake as measured by a gas buret was 140 ml (5.6 mmol), and TLC (silica gel–EtOAc) showed that all of the starting material had been consumed. The soln was then diluted with 70 ml of ether and extracted with 50 ml of water and two 25 ml portions of brine. The combined aq portions were extracted with one 50 ml portion of ether. The combined organic portions were dried with Na_2SO_4 and evaporated to give an oily solid, **4**, which crystallized upon trituration with benzene: 0.46 g, 38%; m.p. 133–134°; IR $\nu_{max}^{CHCl_3}$ 3442, 2957, 1721, 1656, 1615, 1423, 1399, 1264 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 0.85 (3H, s), 1.10 (9H, s), 2.29 (8H, br s), 5.0 (2H, br s). (Found: C, 65.22; H, 7.55%. Calc for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53%.) Addition of dimedone (**1**) to the dienol, **6**, gave a product with chromatographic and spectroscopic properties identical to **4**.

Photo-oxidation of dimedone (**1**) (*absence of fluoride*). Dimedone (1.40 g, 10 mmol) was dissolved in 100 ml of THF and subjected to Rose Bengal-sensitized photo-oxidation at 0°. The dye bleached rapidly and more was added as needed. After 16 hr 195 ml (8 mmol) of O_2 had been consumed. A starch–iodide test for peroxides was negative. The soln was evaporated to give an oily solid which was taken up in ether and washed with 5% Na_2CO_3 and brine, dried with Na_2SO_4 and the solvent removed. Trituration of the product with ether gave 100 mg of a solid, m.p. 130–132°, with a NMR spectrum identical to **4**.

Photo-oxidation of dimedone (**1**) *in* MeOH–*methoxide*. Na metal (0.375 g, 16.2 mmol) was dissolved in 100 ml of MeOH. Dimedone (2.10 g, 15 mmol) was added and the soln subjected to Rose Bengal-sensitized photo-oxidation, O_2 uptake (15.5 mmol) was complete within 1 hr. The mixture was evaporated and partitioned between ether and water. The aq layer was

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[†] Polymer-bound Rose Bengal, available commercially as Sensitox from Hydron Laboratories, New Brunswick, U.S.A.

brought to pH 4 with dil HCl and extracted three times with a total of 150 ml of ether. The combined ether portions were washed once with brine, dried with Na_2SO_4 and evaporated to yield a yellow oil. The NMR spectrum showed a mixture of products including signals consistent with **6**. This oil was taken up in ether and an ethereal soln of CH_2N_2 was added. After addition of formic acid the soln was washed with sat. $NaHCO_3$ aq and brine, dried with Na_2SO_4 and evaporated to give an oil. The oil was distilled to give a fraction, b.p. 86–89° (3–4 Torr), with spectroscopic characteristics identical to those of authentic dimethyl-3,3-dimethylglutarate. IR ν_{max}^{neat} 1735, 1440, 1220 cm^{-1}; NMR ($CDCl_3$, 60 MHz) δ 1.10 (6H, s), 2.39 (4H, s), 3.64 (6H, s). Other unidentified fractions also were obtained.

Photo-oxidation of dimedone (**1**) *in the presence of* Bu_4NOH. Dimedone (1.40 g, 10 mmol) and 6.4 g of 40% aq Bu_4NOH (10 mmol) were dissolved in EtOH and the solvent was evaporated. The residue (repeatedly) was taken-up in EtOH, $CHCl_3$ was added, and the soln evaporated until the solvent was fully exchanged with $CHCl_3$. The $CHCl_3$ soln (100 ml) was then subjected to Sensitox-sensitized photo-oxidation under standard conditions. O_2 uptake (250 ml, 10 mmol) was complete in 90 min. The mixture was filtered, evaporated, acidified and partitioned between ether and water. The ether layer was washed with water and brine, dried with Na_2SO_4 and evaporated to give a yellow oil: 1.20 g, 77% mass recovery. The NMR spectrum showed a complex mixture of products but no signals in the range of δ 6–6.5, indicating that no **6** had been found. There was no signal at δ 0.8 indicating that none of the primary product (**4**) was present.

Photo-oxidation of dimedone (**1**) *in the presence of fluoride in ethanol solution.* Dimedone (0.70 g, 5 mmol), Bu_4NF (5 mmol in EtOH solution) and 5 mg of methylene blue were dissolved in 80 ml of absolute EtOH and subjected to photo-oxidation. O_2 uptake (10 mmol) was complete after 11 hr of irradiation. The EtOH was then evaporated to give an oil and worked-up as described before to yield an oily solid: 0.73 g; 87%. IR, NMR and chromatographic characteristics were identical with those of **6**.

Photo-oxidation of 1,3-*cyclohexanedione* (**8**) *in the presence of fluoride.* 1,3-Cyclohexanedione (1.12 g, 10 mmol) was photo-oxidized in the presence of 10 mmol of Bu_4NF under standard conditions in $CHCl_3$ using Sensitox as the sensitizer. O_2 uptake was complete in 2 hr. The mixture was filtered and evaporated. The resulting residue was taken-up in water and subjected to ether extraction for 48 hr. The ether portion was evaporated to give 0.80 g (70%) of crude **9**. After sublimation of this material, a pure sample was obtained: m.p. 129–131° (authentic sample, 132–133°); IR and NMR spectra were identical with the spectra of authentic pyrogallol. A photo-oxidation run in the absence of fluoride gave a complex mixture of products after 12 hr.

Photo-oxidation of 1,3-*indanedione* (**10**) *in the presence of fluoride.* Indane-1,3-dione (0.292 g, 2 mmol) was photo-oxidized in 150 ml of $CHCl_3$ in the presence of 2 mmol of Bu_4NF and Sensitox under standard conditions. The soln became red upon addition of the fluoride. The oxidation was complete within 3 hr to produce a single product on TLC. The mixture was filtered, evaporated and partitioned between ether and water. The ether layer was dried with Na_2SO_4 and evaporated to yield **11**, 0.265 g (75%), identical in chromatographic and spectroscopic properties to authentic material. Attempted photo-oxidation in the absence of fluoride gave no reaction after 3 hr.

Photo-oxidation of 4-*hydroxycoumarin* (**17**) *in the presence of fluoride.* 4-Hydroxycoumarin (1.62 g, 10 mmol) was photo-oxidized in $CHCl_3$ in the presence of 5 mmol of Bu_4NF and Sensitox. Although 4-hydroxycoumarin itself is only slightly soluble in $CHCl_3$, the complex with fluoride dissolved readily. The oxidation was complete in 30 min to yield a single product (TLC). The mixture was filtered and evaporated, and the resulting residue eluted with $CHCl_3$ through a short silica gel column to yield the EtOH adduct of **18**, 1.55 g (70%), m.p. 86–89°; IR $\nu_{max}^{CHCl_3}$ 3493, 3072, 1752, 1739, 1614, 1479, 1464, 1179 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.23 (3H, t), 4.28 (2H, q), 7.13 (2H, m), 7.65 (2H, m), 4.80 (1H, v br). (Found: C, 59.37; H, 4.58%. Calc for $C_{11}H_{10}O_5$: C, 59.46; H, 4.54%.) Attempted photo-oxidation of **17** in $CHCl_3$ or MeOH–$CHCl_3$ in the absence of fluoride resulted in no reaction after 7 hr.

Photo-oxidation of dibenzoylmethane, **15** ($R_1 = R_2 = Ph$) *in the presence of fluoride.* Dibenzoylmethane (2.24 g, 10 mmol) was photo-oxidized in $CHCl_3$ in the presence of 10 mmol of tetrabutylammonium fluoride and Sensitox under the standard conditions. Oxidation was complete after 2 hr to give a single product on TLC. After the usual ether extraction work-up, **16** ($R_1 = R_2 = Ph$) was obtained, 2.31 g (97%), m.p. 68–70° (lit.[17] 69–70°); IR $\nu_{max}^{CHCl_3}$ 1720 (w), 1683, 1600, 1450, 1330, 1120 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 7.55 (6H, m), 8.15 (4H, dd); MS m/z 238 $[M]^+$, 105. There was no reaction in the absence of fluoride.

Photo-oxidation of benzoylacetone, **15** ($R_1 = Ph$; $R_2 = CH_3$) *in the presence of fluoride.* Benzoylacetone (1.62 g, 10 mmol) was photo-oxidized in $CHCl_3$ in the presence of 10 mmol of tetrabutylammonium fluoride and Sensitox under standard conditions. Oxidation was complete in 3 hr. The product was inseparable from the fluoride by extraction or chromatography and was, therefore, converted to the quinoxaline derivative by adding 1.1 g (10 mmol) of *o*-phenylenediamine to the mixture and refluxing for 1 hr in $CHCl_3$. Removal of the solvent followed by partition between ether and water gave the product as a 1:1 mixture of quinoxalines: 1.78 g, 72%; NMR ($CDCl_3$, 90 MHz) δ 2.70 (s), 2.78 (s), 7.3–8.2 (m). Separation of the isomers by chromatography on silica gel ($CHCl_3$) gave pure samples of 2-methyl-3-benzoylquinoxaline: m.p. 110–111° (lit.[80] 110°). 2-Phenyl-3-acetylquinoxaline: m.p. 88–90° (lit.[18] 88–89°).

Photo-oxidation of acetylacetone, **15** ($R_1 = R_2 = CH_3$) *in the presence of fluoride.* Acetylacetone (1.00 g, 10 mmol) was photo-oxidized in $CHCl_3$ in the presence of 10 mmol of tetrabutylammonium fluoride under the usual conditions. Reaction was complete with 2.5 hr. The mixture was filtered, *o*-phenylenediamine (1.1 g, 10 mmol), was added and the soln was refluxed for 1 hr. Evaporation of the solvent followed by partition between ether and water gave 2-methyl-3-acetylquinoxaline: 1.03 g (66%); m.p. 85.5–86.5° (lit.[19] 85–86°); IR $\nu_{max}^{CHCl_3}$ 3019, 1699, 1564, 1552, 1482, 1425, 1363, 1194, 1126, 1059 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.82 (3H, s), 2.96 (3H, s), 7.7–8.2 (4H, m). There was no reaction in the absence of fluoride.

Photo-oxidation of 1,3-*cyclododecanedione* (**12**) *in the presence of fluoride.* Cyclododecane-1,3-dione (0.392 g, 2 mmol) was photo-oxidized in $CHCl_3$ in the presence of 2 mmol of tetrabutylammonium fluoride and Sensitox. Within 1 hr, 35 ml (1.45 mmol, 72%) of O_2 had been consumed. Further irradiation resulted in no further reaction. Two products were visible by TLC. After the usual extraction work-up, a solid was obtained: 0.39 g. Chromatography on silica gel ($CHCl_3$) yielded **13**: 0.143 g (60%); m.p. 116–120° (d); IR $\nu_{max}^{CHCl_3}$ 3446, 2942, 2872, 1718, 1468, 1402, 1248, 1151, 1101 cm^{-1}; NMR ($CDCl_3$, 270 MHz) δ 5.36 (2H, s), 2.60 (4H, dd), 1.68 (4H, m), 1.34–1.08 (10H, m). (Found: C, 62.95; H, 8.69%. Calc for $C_{12}H_{20}O_4$: C, 63.14; H, 8.83%.) Along with **13**, a second product, **14**, was obtained in the chromatography: 0.085 g, 21%, m.p. 154–155°; IR $\nu_{max}^{CHCl_3}$ 3407, 2956, 1700 (br), 1477, 1444, 1423, 1401, 1361, 1286, 1248 cm^{-1}; NMR ($CDCl_3$, 270 MHz) δ 5.21 (1H, s), 4.76 (1H, s), 2.84 (2H, dd), 2.77 (2H, dd), 2.56 (4H, m), 1.53 (8H, m), 1.2–0.96 (20H, m); m/z 406 $[M]^+$. (Found: C, 70.94; H, 9.31%. Calc for $C_{24}H_{38}O_5$: C, 70.90; H, 9.40%.)

Photo-oxidation of 2-*carboethoxycyclopentanone* (**19**) *in the presence of fluoride* (1-*equivalent*). 2-Carboethoxycyclopentanone (0.78 g, 5 mmol) was photo-oxidized in $CHCl_3$ in the presence of 5 mmol of tetrabutylammonium fluoride and methylene blue under standard conditions. After a total irradiation time of 4 hr, only 65 ml (2.7 mmol) of O_2 had been consumed. After an additional 1.5 hr, no further reaction occurred. TLC showed that much starting material remained. The solvent was then removed by evaporation and the residue eluted through a short silica gel column with $CHCl_3$. The products were separated by preparative gas chromatography

(SE-30 column) into two major components: one was identified as unreacted starting material by IR; the other was shown to be the mono ester of α-ketoadipic acid, IR $\nu_{max}^{CHCl_3}$ 1713 (sh), 1728, 1749, 1250 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.34 (3H, t), 1.95 (2H, quintet), 2.43 (2H, t), 2.92 (2H, t), 4.43 (2H, q). Warming this compound in acidic EtOH overnight produced diethyl α-ketoadipate identical to authentic material in chromatographic, NMR and GC/MS properties: NMR ($CDCl_3$, 90 MHz), δ 1.24 (3H, t), 1.35 (3H, t), 1.94 (2H, quintet), 2.35 (2H, t), 2.92 (2H, t), 4.12 (2H, q), 4.30 (2H, q); MS *m/z* 171 [−OEt] (11.3), 143 [$-CO_2Et$] (100), no $[M]^+$ observed.

Attempted photo-oxidation in the absence of fluoride gave no reaction after 3.5 hr.

Photo-oxidation of 2-carboethoxycyclopentanone (**19**) *in the presence of fluoride* (2 *equivalents*). 2-Carboethoxycyclopentanone (0.78 g, 5 mmol) was photo-oxidized in $CHCl_3$ in the presence of 10 mmol of tetrabutylammonium fluoride and methylene blue under standard conditions. O_2 uptake (120 ml, 5 mmol) was complete after 2 hr and TLC showed that all of the starting material was consumed. After evaporation of the solvent and elution of the residue through a short silica gel column with $CHCl_3$, **20** was isolated as a yellow oil: 0.42 g, 49%; IR $\nu_{max}^{CHCl_3}$ 3530, 2950, 1755, 1729, 1251, 1178 cm^{-1}; NMR ($CDCl_3$, 270 MHz) δ 1.32 (3H, t), 2.13 (3H, m), 2.49 (3H, m), 3.81 (1H, s), 4.30 (2H, q); decoupling the multiplet at 2.49 reduced the signal at 2.13 to a broad singlet and irradiation at 2.13 reduced the signal at 2.49 to two singlets with ratio 1:2. MS *m/z* 172 $[M]^+$. (Found: C, 55.51; H, 7.07%. Calc for $C_8H_{12}O_4$: C, 55.81; H, 7.02%.)

Photo-oxidation of 1,2-*cyclohexanedione* (**21**) *in the presence of fluoride*. Cyclohexane-1,2-dione (0.56 g, 5 mmol) was photo-oxidized in CH_2Cl_2 in the presence of 6 mmol of tetrabutylammonium fluoride and tetraphenylporphine sensitizer under standard conditions. Gas uptake stopped after 1 hr (1 mmol) although TLC showed the reaction to be complete after 3 hr. The gas in the system was then passed through a $Ba(OH)_2$ soln which gave a small ppt (indicating that some CO_2 had formed), and a Tollens soln which gave a heavy ppt indicating that considerable CO had been produced.

The solvent was evaporated and the residue was chromatographed on silica gel (ether–2% HOAc) to yield the product, **24**, 0.368 g, 64%; NMR ($CDCl_3$, 90 MHz) δ 1.94 (2H, quintet), 2.42 (2H, t), 2.57 (2H, t), 9.72 (1H, s), 10.10 (1H, br s); IR ν_{max}^{neat} 3100 (br), 2950, 2720, 1710 (br), 1410, 1250, 1165 cm^{-1}; 2,4-dinitrophenylhydrazone: m.p. 137–139° (lit.[20] 139–140°).

Photo-oxidation in the absence of fluoride resulted in severe dye bleaching and incomplete reaction after 6 hr to yield several unidentified products.

Photo-oxidation of 3-*methyl*-1,2-*cyclopentanedione* (**23**) *in the presence of fluoride*. 3-Methyl-1,2-cyclopentanedione (1.13 g, 10 mmol) was photo-oxidized in $CHCl_3$ in the presence of 10 mmol of tetrabutylammonium fluoride and methylene blue sensitizer under standard conditions. A Tollens soln bubbler placed in line gave a positive CO test. TLC showed that the starting material was totally consumed after 5 hr. The mixture then was evaporated and chromatographed on a short silica gel column with $CHCl_3$ and the product was esterified by refluxing in absolute EtOH overnight with *p*-toluenesulphonic acid catalyst. The EtOH was evaporated and the residue was partitioned between ether and water. The water layer was extracted five times with ether and the ether portions were combined, dried with Na_2SO_4 and evaporated to yield the ethyl ester of **24** (R = Et), 0.815 g, (72%) identical in all respects with authentic material. IR $\nu_{max}^{CHCl_3}$ 2990, 1722, 1420, 1375, 1220, 1165 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.25 (3H, t), 2.19 (3H, s), 2.65 (4H, dt), 4.13 (2H, q).

Photo-oxidation in the absence of fluoride was impossible because of very severe dye bleaching.

Photo-oxidation of p-*cresol* (**25**) *in the presence of fluoride*. *p*-Cresol (1.08 g, 10 mmol) was photo-oxidized to completion (3 hr) in $CHCl_3$ in the presence of 10 mmol of tetrabutylammonium fluoride and Sensitox under standard conditions. The solvent was evaporated and the residue chromatographed on a short silica gel column ($CHCl_3$) to yield **26** (X = OH), 1.22 g, 87%; IR $\nu_{max}^{CHCl_3}$ 3293, 3019, 1675, 1633, 1216, 1068 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.40 (3H, s), 6.22 (2H, d), 6.92 (2H, d), a small singlet at 2.46 was also visible.

Reduction of the peroxide with triphenylphosphine followed by bulb-to-bulb distillation gave the alcohol, **26** (X = H) as an oily solid: IR ν_{max} 3300, 3020, 1667, 1636, 1213, 1045 cm^{-1}; (lit.[21] neat: 3400, 1660, 1630, 1617 cm^{-1}), NMR ($CDCl_3$, 90 MHz) δ 1.46 (3H, s), 4.05 (1H, br s), 6.04 (2H, d, J = 10 Hz), 6.90 (2H, d, J = 10 Hz), [lit.[21] ($CDCl_3$) δ 2.48 (3H, s), 3.07 (1H, br s), 6.13 (2H, d, J = 10 Hz), 6.95 (2H, d, J = 10 Hz)].

Photo-oxidation in the absence of fluoride resulted in only 3% uptake of O_2 after 1 hr.

Photo-oxidation of p-*cresol in the presence of hydroxide*. *p*-Cresol (1.08 g, 10 mmol) was photo-oxidized in dichloroethane in the presence of tetrabutylammonium hydroxide (6.4 g of a 40% aq soln, 10 mmol) and Sensitox under the conditions described for the photo-oxidation of dimedone in the presence of Bu_4NOH. The oxidation was complete in 5.5 hr. After evaporation of the solvent and chromatography on silica gel ($CHCl_3$), the product was isolated: 1.01 g (72%), NMR ($CDCl_3$, 90 MHz) showed the presence of **26**, X = H plus signals corresponding to a new product: δ 2.23 (s), 3.72 (t, J = 6 Hz), 4.15 (t, J = 6 Hz), 6.75 (d, J = 9 Hz), 7.05 (d, J = 9 Hz). This product was not identified.

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