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Charge Transfer Dioxetanes - A Simple Rationalisation

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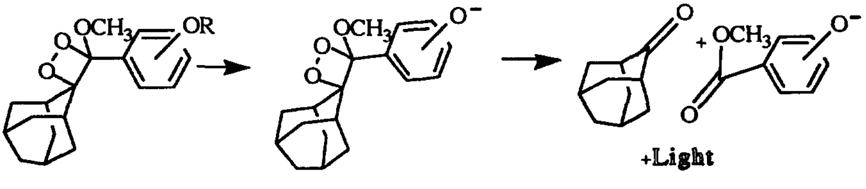
Abstract: A simple explanation for the considerably higher light yield obtained from chemiluminescent dioxetanes with a particular substitution pattern is suggested in the form of an orbital picture which shows how charge transfer enhances excited state formation

Dioxetanes are among the best understood of all chemiluminescent compounds[1,2,] but one of the most intriguing of their properties is the distinction between "simple" dioxetanes and those with electron donating substitution[3,4]

The observation that such dioxetanes will generally show very high yields of singlet excited states on decomposition has been made many times. The mechanism has been characterised as involving charge transfer[3,4]. The consequences of this for visible and easily detected light emission are considerable, particularly in the field of clinical diagnostics,[5,6] The use of chemiluminescence methods in this field has brought a revolution in sensitive, non-isotopic detection of analytes by immunochemical methods[7].

One of the most useful of the new methods is based on the unmasking of the electron donation by the removal of a protecting group so that the dioxetane (hitherto a stable molecule belonging to the class of sterically hindered "simple" dioxetanes) is transformed into a dioxetane decomposing by a charge transfer mechanism[8,9.] In immunoassay, an enzyme, preferably alkaline phosphatase, is attached to the antibody as a label, and its catalytic action on the group R (R = phosphate, Scheme 1)) results in light emission in proportion to the amount of antibody, as the now free oxyanion transfers charge to the dioxetane, causing its decomposition with the emission of light.



Scheme 1

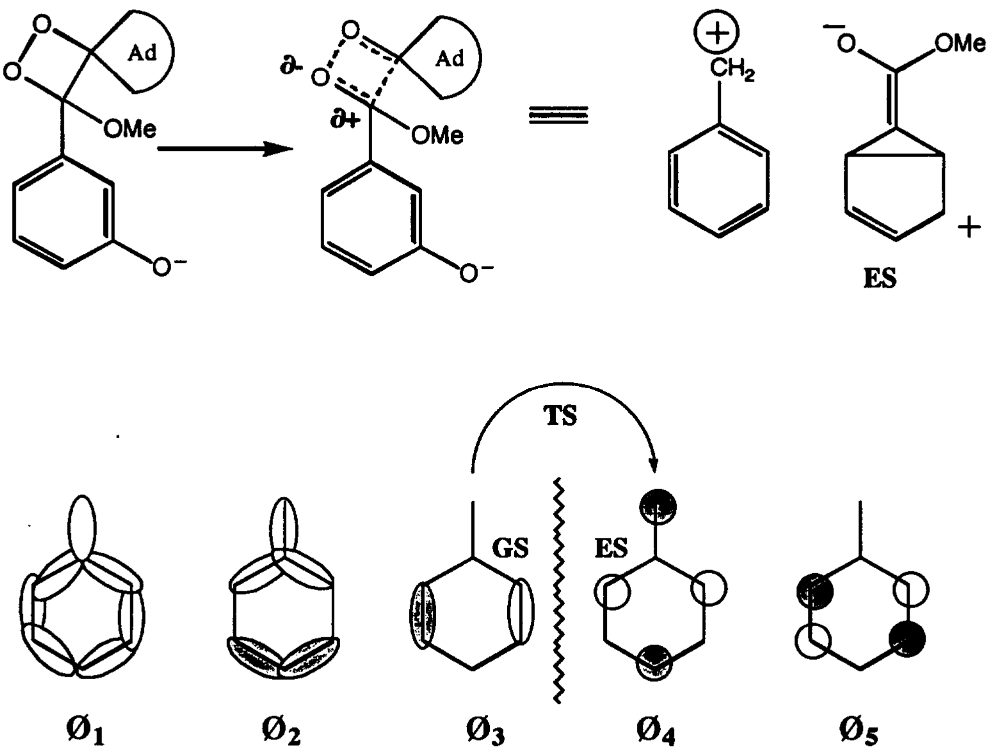
A striking feature of dioxetanes which give the best light yields is that *meta* -substitution leads to a slower rate of reaction and a very much greater light yield. This is true in the phenyl series (the example of Scheme 1) and in the case where the aromatic group is a naphthol. The discoverers of this phenomenon[8,9] have called it "odd" (as opposed to even) substitution. The properties[10] of the three dioxetanes shown in the table demonstrate the effect of releasing charge, and the distinction in rate and efficiency between meta and para substitution.

Molecular orbital calculations provide an explanation[11] but the purpose of this communication is to show that there is an alternative simple, intuitive pictorial description which may serve as a rule of thumb in the design of other chemiluminescent dioxetanes.

Dioxetane	Half-life	Efficiency F_E
RO- (m- or p-)	Years	2×10^{-5}
Para O^-	0.046 sec.	4×10^{-3}
Meta O^-	**180 sec.**	**0.57**

The dioxetane is assumed to decompose in a concerted fashion (a characteristic of the electron rich dioxetanes) forming two new carbonyl groups. As the ester carbonyl develops, the carbon atom becomes electron deficient (note that this is *not* an n,π^* excited state). The simplest analogous system is thus that of the benzyl cation. This is an odd alternant hydrocarbon, and it is proposed that this class of analogue should be sought in the design of future dioxetanes, for high light yields. The reaction scheme and the orbitals concerned are shown below (only five of the seven orbitals are shown).

At the top of the scheme, the transition state (TS) is shown, alongside the valence bond description of an excited state (ES) of the ester product, with a polarised carbonyl group, taken as being equivalent to a benzyl cation. On this representation, the addition of an electron donating group at the *meta* position clearly stabilises this excited state over the ground state. Similarly, in the MO representation, charge is transferred from the meta position to the oxygen atom of the carbonyl, as required in a charge transfer transition. The excited state is thus stabilised by an electron donating group in the meta position as before. The ***ground*** state, by contrast, is stabilised by para substitution. It would be expected that para-substituted dioxetanes would decompose faster than the meta-substituted isomer, with a lower light yield (the barrier to the excited state is likely to be higher, whether stabilised or not). This is exactly what is observed (see table).



Ad = Adamantyl

Scheme 2

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