QUARTERLY REVIEWS

THE CHEMILUMINESCENCE OF ORGANIC COMPOUNDS

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Although the study of luminescence in living systems originated in antiquity,[1] it was not realised until the late nineteenth century that the phenomenon could be associated with a relatively simple organic reaction. Thus Radziszewski,[2] in 1877, demonstrated that lophine (16) reacted with oxygen in alcoholic potassium hydroxide solution, with the emission of light. The same author observed[3] that a large number of materials of biological origin, such as essential oils, glucose, lecithin, etc., gave light on similar treatment. Trautz[4] later added a further very large number of compounds to this list. Indeed, it appears that most organic compounds, or impurities therein, are capable of luminescence under these conditions. The early use of pyrogallol[5] as a photographic developer led to the inclusion of this substance among those organic compounds exhibiting what is now known as chemiluminescence. Chemiluminescence was also observed[6] in the ubiquitous Grignard reagent, thus serving to make the phenomenon well known. The discovery of luminol (1) in 1928,[7] until recently the brightest of all such chemiluminescent materials, gave impetus to work in the field. The dimethylbiacridinium salt, lucigenin (25),[8] was added to this class of compound also about this time. It, too, must be considered particularly effective.

Since the advent of sensitive photomultiplying devices, much work[9,10,11] has been devoted to very weak chemiluminescent reactions, but unless very strict precautions[11] are taken to ensure the greatest purity of substrate, results will be confusing. Reference has already been made to the astonish-

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* Present address: The Chemical Laboratory, University of Sussex, Brighton.

[1] (*a*) E. N. Harvey, "A History of Luminescence", American Philosophical Society, 1957, vol. 44; (*b*) E. N. Harvey, "Bioluminescence", Academic Press, New York, 1952.

[2] B. Radziszewski, *Ber.*, 1877, **10**, 70, 321; K. Hofmann, "Imidazole and Derivatives" The Chemistry of Heterocyclic Compounds, ed. A. Weissberger, Interscience, New York, 1953, p. 11.

[3] B. Radziszewski, *Annalen*, 1880, **203**, 305.

[4] M. Trautz, *Z. phys. Chem.*, 1905, **53**, 1.

[5] P. Lenard and M. Wolf, *Wied. Ann.*, 1888, **34**, 918; J. M. Eder, *Photog. Mitth.*, 1877, **24**, 74.

[6] E. Wedekind, *Z. wiss. Phot.*, 1907, **5**, 29.

[7] H. O. Albrecht, *Z. phys. Chem.*, 1928, **136**, 321.

[8] K. Gleu and P. Petsch, *Angew. Chem.*, 1935, **48**, 57.

[9] T. I. Quickenden, *J. New Zealand Inst. Chem.*, 1964, **28**, 10.

[10] R. Audubert, *Trans. Faraday Soc.*, 1939, **35**, 197; R. Audubert, *Compt. rend.*, 1935, **200**, 918; J. Stauff, *Photochem. and Photobiol*, 1965, **4**, 1199; V. I. Papisova, V. Ya. Shlyapitokh, and R. F. Vassil'ev, *Russ. Chem. Rev.*, 1965, **34**, 599.

[11] E. J. Bowen and R. A. Lloyd, *Proc. Roy. Soc.*, 1963, *A*, **275**, 465.

ingly widespread occurrence of fairly weak chemiluminescence on oxidation of a very wide range of organic compounds.[3,4] It may be assumed that an understanding of the visible examples will lead to a clarification of the mechanism of the weaker reactions. Typically, those in the former category emit one photon for every 10 to 10^5 molecules reacting, while the latter produce one photon for 10^8 to 10^{15} molecules of reactant destroyed.[9,10] The relationship between the threshold of visibility and number of quanta emitted has been derived.[12a]

The earlier work on the brighter compounds has been extensively reviewed,[13,14,15] and some recent reviews are also available.[9,16,17,18] A general symposium on chemiluminescence[19] contains reports showing greatly increased interest in chemiluminescence of organic compounds in solutions.

This Review summarises later developments, and hopes to stimulate further work. Selection is largely restricted to those compounds which provide light easily observable by the human eye. The reactions, with few exceptions, are all of oxidative type, and take place on relatively complex organic molecules in solution.

General Mechanism

There is surprisingly little fundamental work published concerning the physical processes underlying organic chemiluminescent reactions. There is no doubt, however, that the source of the light is a product molecule formed in an electronically excited state, as a result of an exothermic chemical reaction. Emission of the radiation occurs when this molecule, which is not necessarily a direct product of the reaction, forms the ground state. Thus, unless there is evidence to the contrary, it is usually assumed that singlet excited states are involved, and efforts are made to relate the fluorescence of the suspected emitter to the observed chemiluminescence. An early description of the process has been given in terms of thermodynamics.[20]

There is not available an extension of this view which would fit the case of complex organic molecules, and any description of the process is purely illustrative (Figure). It is assumed that relatively unlikely events such as absorption of black body radiation,[20] and higher than average collisional

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[12] (*a*) H. H. Seliger and W. D. McElroy, "Light: Physical and Biological Action", Academic Press, New York, 1965; (*b*) F. Wilkinson, "Electronic Energy Transfer between Organic Molecules in Solution", Advances in Photochemistry, ed. W. A. Noyes, G. S. Hammond, and J. N. Pitts, Interscience, New York, 1964 vol. 3.

[13] A. Bernanose, *Bull. Soc. chim. France*, 1950, 567; 1951, 329; 1952, 39D.

[14] W. Vaughan, *Chem. Rev.*, 1948, **43**, 447.

[15] R. S. Anderson, *Ann. New York Acad. Sci.*, 1948, **49**, 337.

[16] H. Stork, *Chem.-Ztg.*, 1961, **85**, 467.

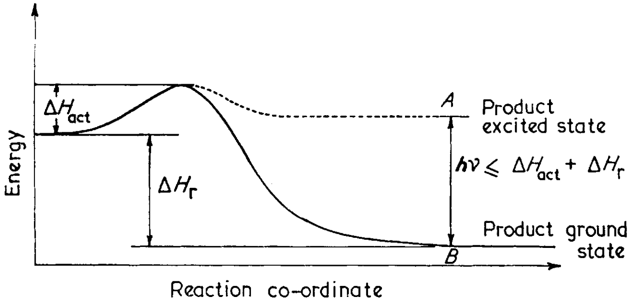
[17] K.-D. Gundermann, *Angew. Chem. Internat. Edn.*, 1965, **4**, 566.

[18] E. N. White, "Light and Life", ed. W. D. McElroy and B. Glass, Johns Hopkins Press, Baltimore, 1961, p. 183.

[19] Symposium on Chemiluminescence, *Photochem. and Photobiol.*, 1965, **4**, 957.

[20] M. G. Evans, H. Eyring, and J. F. Kincaid, *J. Chem. Phys.*, 1938, **6**, 349.

energies, are not involved in the fairly efficient chemiluminescent reactions to be discussed.



In outline, the excited state could be considered as arising from a "cross-over" process (broken line in Figure), perhaps from a high vibrational level of the ground state of the product. Thus the disposition of the reactant in the transision state, particularly if this resembled the geometry of the product in its excited state, could influence the number of molecules taking path *A*. Unknown equilibrium processes between vibrationally excited ground state molecules and the electronically excited state could also affect the efficiency of the luminescent reaction. It is often pointed out[17,18,21] that the energy released in the reaction must at least equal the energy represented by the wavelength of light emitted. For light of wavelength 440 mμ this means that 65 kcal.mole^{-1} must be available (ΔH_r). This is a fairly strict requirement, and the importance of the formation of the products by a concerted mechanism has been emphasised.[22] Exact correspondence between the enthalpy (ΔH_r) of the reaction and the energy of radiation, $\boldsymbol{h\nu}$, however, is not necessary since $\boldsymbol{h\nu}$ includes the activation energy, which is not often known. This enthalpy, ΔH_r, can be calculated from standard bond energies, knowing the nature of the reactant and the product which emits light. Nothing is known about the activation energy, or lack of it, as a barrier to the excited state, and the Figure could be modified accordingly.

Recently[23-26] a type of chemiluminescent reaction has been discovered

[21] H. Eyring, F. H. Johnson, and M. J. Polissar, "The Kinetic Basis of Molecular Biology", John Wiley and Sons, New York, 1954, p. 123.

[22] M. M. Rauhut, D. Sheehan, R. A. Clarke, and A. M. Semsel, ref. 19, p. 1097.

[23] M. M. Rauhut, D. L. Maricle, G. W. Kennedy, and J. P. Mohns, American Cyanamid Company, Chemiluminescent Materials, Technical Report No. 5, 1964.

[24] D. M. Hercules, *Science*, 1964, **145**, 808.

[25] (*a*) E. A. Chandross and F. I. Sonntag, *J. Amer. Chem. Soc.*, 1964, **86**, 3179; (*b*) E. A. Chandross, J. W. Longworth, and R. E. Visco, *J. Amer. Chem. Soc.*, 1965, **87**, 3259; (*c*) E. A. Chandross and F. I. Sonntag, *J. Amer. Chem. Soc.*, 1966, **88**, 1089; (*d*) R. E. Visco and E. A. Chandross, *J. Amer. Chem. Soc.*, 1964, **86**, 5350; (*e*) S. W. Feldberg, *J. Amer. Chem. Soc.*, 1966, **88**, 390; (*f*) R. A. Marcus, *J. Chem. Phys.*, 1965, **43**, 2654.

[26] K. S. V. Santhanam and A. J. Bard, *J. Amer. Chem. Soc.*, 1965, **87**, 139.

which involves no bond alterations, and thus is amenable to a description based on simple molecular orbital theory. Electron transfer from an aromatic hydrocarbon radical anion to an electron acceptor results in the formation of the hydrocarbon in an excited state. It has been suggested[25a] that this process could play a part in the older, more complex chemiluminescent reactions. It is, in fact, surprising that a reaction in solution, involving many nuclei in the transition state, does result in an electronically excited molecule. Since electron transfer is generally faster than a molecular vibration, there is indeed less opportunity for deactivation by vibrational routes in this case. However, it is difficult to reconcile the known facts of many of the reactions discussed with the mechanism of this simpler case.

Another reaction of potential general import has received much attention.[27,28,29] Since many oxidations of organic compounds in solution are chemiluminescent only when oxygen or peroxides are involved,[18] the recent discovery that oxygen itself is often formed in an excited state deserves discussion. Thus Browne and Ogryzlo,[27] following earlier work,[29] have shown that the red (635 mμ) light observed in the reaction between chlorine and hydrogen peroxide in alkaline solution, is due to a complex of two excited ($^1\Delta_g$) oxygen molecules. Other bands, due to vibrationally excited $^1\Delta_g$ molecules, and the $^1\Delta_g \longleftrightarrow {}^3\Sigma_g^-$, $^1\Sigma_g^+ \longleftrightarrow {}^3\Sigma_g^-$ systems generally, are observed. The well known red glow to be seen on oxidation of pyrogallol in the presence of formaldehyde is probably due to a similar excited system.[30]

Peroxides are undoubtedly involved in the majority of organic chemiluminescent reactions[31,32] in solution, and further recent discoveries concerning the alkaline H_2O_2–Cl_2 system have given rise to a general theory of chemiluminescence.[29c] Although the energy available from excited oxygen will not normally exceed 37·8 kcal.mole^{-1}, ($^1\Sigma^+_g$), the dimer ($2\,^1\Delta_g$) previously mentioned does provide more (44·8 kcal.mole^{-1}). If the predominately blue (60-70 kcal.mole^{-1}) emission of the typical organic system is to be explained by energy transfer from excited oxygen, energy greater than this (even including vibrational quanta) must be available. The observation[29c] of a band at 478 mμ in the Cl_2–H_2O system provides 59·8 kcal.mole^{-1}, owing to the combination $^1\Delta_g + {}^1\Sigma_g^+$. With the assumption that the Cl_2 absorption masks the emission from the dimer $2\,^1\Sigma_g$ (75·1 kcal.mole^{-1}), a general role for excited oxygen is obviously possible.

However, several organic chemiluminescent reactions do not show the

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[27] R. J. Browne and E. A. Ogryzlo, *Proc. Chem. Soc.*, 1964, 117.

[28] C. S. Foote and S. Wexler, *J. Amer. Chem. Soc.*, 1964, **86**, 3879.

[29] (*a*) L. Mallet, *Compt. rend.*, 1927, **185**, 352; (*b*) A. U. Khan and M. Kasha, *J. Chem. Phys.*, 1963, **39**, 3105; (*c*) A. U. Khan and M. Kasha, *J. Amer. Chem. Soc.*, 1966, **88**, 1574; (*d*) H. H. Seliger, *ibid.*, 1964, **40**, 3133.

[30] E. J. Bowen and R. A. Lloyd, *Proc. Chem. Soc.*, 1963, 305.

[31] H. Hock, H. Kropf, and F. Ernst, *Angew. Chem.*, 1959, **71**, 541.

[32] See ref. 19, papers concerning chemiluminescence in solution.

required square dependence on peroxide concentration, neither do they form very great amounts of oxygen. The emission spectrum is also often characteristic of a *product* molecule formed by breakage of the O–O peroxide bond, so that the transfer of energy from excited oxygen to this molecule is easily shown to be impossible by the kinetics of the reaction. In spite of the doubtful general application of this type of reaction, it seems to be involved in cases of sensitised luminescence,[29c] and in very weak cases of the phenomenon.[10,11] A more likely mechanism for relatively efficient peroxidic luminescent reactions has been suggested,[22,33,34] comprising the formation of carbonyl compounds in a concerted and exothermic manner. Most of the classical examples of chemiluminescence can be discussed on this basis.

Thus, although complete proof is still lacking, it is possible to include all the known examples of organic chemiluminescence in solution under the three general types; peroxide decompositions, electron-transfer reactions, and formation of excited oxygen.

Before discussing the details of the various reactions, we should mention several relevant experimental problems common to them all. The spectra observed are broad-banded, often with ill-defined maxima, so that apparent congruence of chemiluminescence and fluorescence curves is not necessarily diagnostic of the excited product molecule. Absorption of the emitted light by coloured reaction media can shift the emission maximum, considerably more in the case of the chemiluminescence than for the stronger fluorescence. Transfer of the energy of excitation, by one of several known processes,[12] can result in emission from a fluorescent contaminant molecule. Absorption of the radiation by an impurity, and re-emission, can also superimpose a spurious band on the emission spectrum. For these reasons, even where the products are satisfactorily characterised, doubt in interpretation often remains.

A final general point is also related to the reactions appropriate to excited molecules in solution. The efficiency of chemiluminescent reactions must be the product of two separate efficiencies. That is, the chemical mechanism which leads to the excited molecule is subject to factors which affect the yield of any organic compound. In this context, the excited molecule can be thought of as an alternative product which must be formed in high yield, at the expense of others. Even in those cases[35] where it can be shown that the excited product is formed efficiently, processes such as internal radiationless transitions and external quenching may intervene. The latter factors can be investigated by a consideration of the fluorescence efficiency of the appropriate product molecule when placed in an environment similar to that of the chemiluminescent reaction. This is unfortunately not often

[33] F. McCapra and D. G. Richardson, *Tetrahedron Letters*, 1964, 3167.

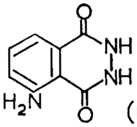
[34] F. McCapra, D. G. Richardson, and Y. C. Chang, ref. 19, p. 1111; F. McCapra and Y. C. Chang, *Chem. Comm.*, 1966, 522.

[35] E. H. White, O. Zafiriou, H. M. Kägi, and J. M. Hill, *J. Amer. Chem. Soc.*, 1964, **86**, 940; E. H. White and M. M. Bursey, *ibid.*, p. 941.

done, so that speculation based on changes in efficiency with, say, substitution could be misleading. The expression "quantum yield" (*Q*) is often applied to chemiluminescent reactions, and refers to the number of photons emitted as a proportion of the reactant molecules destroyed. Problems rather similar to those in the determination of absolute fluorescence efficiencies arise, and a detailed discussion of the techniques available has been published.[36]

Chemiluminescent Organic Compounds

Luminol.—The chemiluminescence of luminol or 5-amino-2,3-dihydro-1,4-phthalazinedione (1) was first reported by Albrecht.[7] In aqueous alkaline solution, hydrogen peroxide and a catalyst such as potassium ferricyanide or hæmin are needed for maximum emission of light.[7,14,18,37] The spectrum consists of a broad band, with λ_{max} 424 mμ. Various demonstrations based on this reaction are well known.[38] Early work, well reviewed,[13,14,18] showed that although the 5-aminophthalazinedione was most efficient, electron-donating substituents generally increased the intensity of emission while electron-withdrawing groups on the benzenoid ring had the opposite effect.[39] It is known[40] that electron-donating substituents enhance autoxidation, but the rates of oxidation of the phthalazinediones are substantially unchanged by substitution,[41] while the brightness increases as mentioned above. The increased intensity is thus perhaps mainly due to the raised quantum yield of fluorescence in the emitting product molecule. Recent work has produced several derivatives, such as (2)[35] and (3)[42] which are more efficient than luminol by about 30% and 300% respectively.



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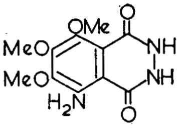

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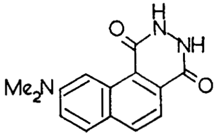

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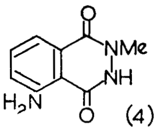

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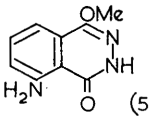

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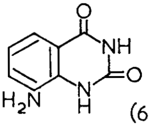

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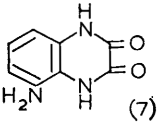

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[36] J. Lee and H. H. Seliger, ref. 19, p. 1015.

[37] A. K. Babko and L. I. Dubovenko, *Z. analyt. Chem.*, 1964, 428.

[38] E. H. Huntress, L. N. Stanley, and A. S. Parker, *J. Chem. Educ.* 1934, **11**, 142; E. H. White, *ibid.*, 1957, **34**, 275.

[39] H. D. K. Drew and F. H. Pearman, *J. Chem. Soc.*, 1937, 586.

[40] C. Walling, "Free Radicals in Solution", John Wiley, New York, 1957.

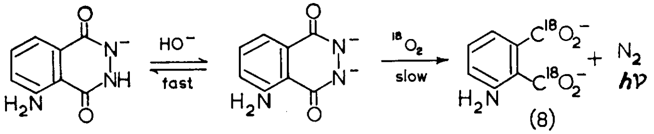
[41] C. N. Zellner and G. Dougherty, *J. Amer. Chem. Soc.*, 1937, **59**, 2580.

[42] K. D. Gundermann, W. Horstmann, and G. Bergmann, *Annalen*, 1965, **684**, 127; K. D. Gundermann and M. Drawert, *Chem. Ber.*, 1962, **95**, 2018.

The importance of avoiding steric inhibition of resonance has been discussed.[42] Any substitution of the heterocyclic ring [*e.g.*, (4), (5)][43] or transposition of the hetero-atoms [as in (6) and (7)][44] prevents chemiluminescence. Since the reaction in aqueous solutions is inhibited[45,46] by quinol, phenols, and cyanide ion, and enhanced by inorganic oxidising agents containing ferric or cupric ions, a radical process is indicated. Organic initiators such as benzoyl peroxide[18] are also effective.

It seems that the recent well supported findings of White and his colleagues[35] must be satisfactorily explained by any suggested mechanism for chemiluminescence of luminol. A significant advance on previous investigations is the use of dimethyl sulphoxide as solvent for the reaction, and, as sole reactants, oxygen and a strong base, such as potassium t-butoxide. By use of 70% aqueous dimethyl sulphoxide and excess of sodium hydroxide, it was possible to isolate nearly quantitatively 3-aminophthalic acid as almost the sole product. When these conditions were employed with oxygen enriched in $^{18}O_2$ it was found that, when exchange reactions were allowed for, quantitative incorporation of oxygen into the aminophthalate ion had occurred. This imposes a rather severe restriction on any possible mechanism. Kinetic studies in this system give the stoicheiometry and relative rates shown in Scheme 1, the reaction being of the first order in base, luminol, and oxygen. Radical chain processes are not involved under these conditions. The very close correspondence of the observed chemiluminescence spectrum and the fluorescence spectrum of the aminophthalate ion leaves little doubt as to the identity of the emitting molecule. The maximum of *both* fluorescence and chemiluminescence in water is at 424 $m\mu$ and in dimethyl sulphoxide at 485 $m\mu$. The chemiluminescence exhibits both peaks in mixtures of these solvents, as does the fluorescence. This identification of the excited product has been supported by other workers.[47] Another very satisfactory feature of this work is the proof that the aminophthalate isolated must indeed be formed as the sole product of the emission step. Thus the chemiluminescence quantum yield in dimethyl sulphoxide is 5 %, and the fluorescence quantum yield for the aminophthalate ion is between 5 and 10% in the same solvent;

SCHEME 1



[43] H. D. K. Drew and R. F. Garwood, *J. Chem. Soc.*, 1937, 1841.

[44] E. H. Huntress and J. V. K. Gladding, *J. Amer. Chem. Soc.*, 1942, **64**, 2644.

[45] A. Spruit van der Burg, *Rec. Trav. chim.*, 1950, **69**, 1536.

[46] F. H. Stross and G. E. K. Branch, *J. Org. Chem.*, 1938, **3**, 385; K. Weber, *Chem. Ber.*, 1942, **75**, 565.

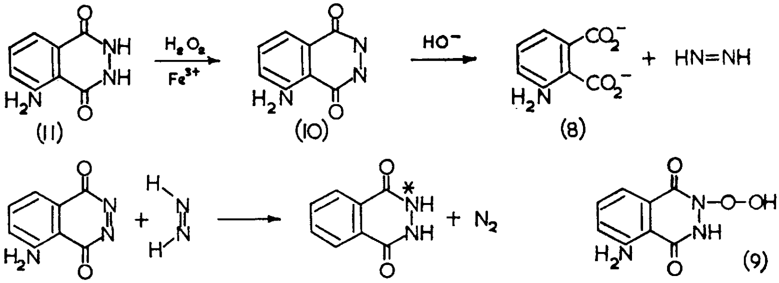
[47] W. A. Armstrong and W. G. Humphreys, *Canad. J. Chem.*, 1965, **43**, 2576.

coupling of this information with a yield of 90% for the ion suggests that the *excited state* of (8) is formed in greater than 50% yield. This finding is of great significance for other very bright systems, since it implies that it is possible to prove that the products isolated by standard organic techniques are formed in the excitation step. It has recently been estimated[48] that even in the gas-phase reaction of SO with O_3, many of the excited SO_2 molecules produced are quenched by collision, giving a relatively low quantum yield, and this may hold for other chemiluminescent reactions.

The mechanism suggested by White tentatively involves the exothermic loss of N_2 from a triplet-state adduct of oxygen and luminol dianion or similar reactant. Intersystem crossing to a singlet state, then radiation from this state, would lead to the observed emission. An earlier mechanism,[18] also outlined by White, implicates a peroxide such as (9), and thus is capable of inclusion in the general class of chemiluminescent decompositions of peroxides. Although these mechanisms are compatible with these recent findings, earlier suggestions are not.

The search for the emitting molecule was hampered in aqueous solution by the vigorous conditions used,[7] thus tending to destroy the products of the reaction leaving only small amounts of unchanged luminol. Hence early suggestions[7,49] were that luminol itself was the emitter, and attempts were made to evolve a mechanism which re-produced luminol during the reaction. Albrecht's original mechanism has been seriously considered by several subsequent workers (Scheme 2).[46,49,50] Oxidation to the diazaquinone (10), with subsequent hydrolysis to produce the di-imide,[51] would lead to a reductive excitation step. There are some objections to this mechanism. Luminol in alkaline solution is not fluorescent,[18] and is definitely not considered the emitter by recent investigators. Secondly, in the absence of evidence to the contrary, it is reasonable to assume that the mechanism in water is closely related to that in highly

SCHEME 2



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[48] C. J. Halstead and B. A. Thrush, *Chem. Comm.*, 1965, 213.

[49] H. Kautsky and K. H. Kaiser, *Z. Naturforsch.*, 1950, **5b**, 353.

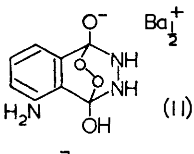
[50] W. S. Metcalf and T. I. Quickenden, *Nature*, 1965, **206**, 506.

[51] E. E. van Tamelen and R. J. Timmons, *J. Amer. Chem. Soc.*, 1962, **84**, 1067, and references cited.

aqueous dimethyl sulphoxide. In the latter conditions, the direct incorporation of an oxygen molecule into the product (8) is intimately involved in the excitation step. An early attempt[49] to isolate the unstable diazaquinone (10), after oxidation of luminol with $Ca(OCl)_2$ at low temperatures, was unsuccessful. Although the crude product did give light on addition of alkali, no information on the relative efficiency of this route is available, and it is possible that unchanged luminol was the source of the light observed. The unsubstituted diazaquinone[52] has been isolated fairly recently, and its chemistry studied. Unfortunately it now appears that the unsubstituted phthalhydrazide is not, in fact, chemiluminescent. This is in accord with the conclusion that, in the luminol reaction, the aminophthalate ion is the emitter, for phthalic acid dianion is not visibly fluorescent. Reports of chemiluminescence from phthalazinedione itself, while correct, must involve a fluorescent contaminant.[53] Very recently, luminescence has been observed from luminol solutions, in the presence of di-imide generated from toluene-*p*-sulphonhydrazide.[50] This apparently is not a particularly efficient process, and it is not clear how the reactants are expected to form an excited state of 3-aminophthalic acid dianion. Thus, if the latter compound is, in fact, the excited product of the reaction, and oxygen is incorporated in association with the excitation step, it must be assumed that the mechanism discussed above does not explain the facts available.

Another suggestion, which has received much attention, was originally made by Drew and Garwood.[54] The basis for this was the isolation of a compound purported to be (11). In spite of recent repetitions of this statement,[9] it is fairly certain[18] that (11) has the constitution of a simple barium salt of luminol solvated by hydrogen peroxide [as (12)].

Nevertheless, addition of hydrogen peroxide to the diazaquinone (10) which could be formed as an unstable intermediate, to give (13),[35,55] is attractive in view of the highly exothermic route to the observed products.



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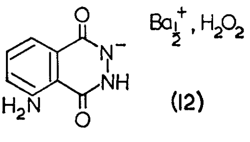

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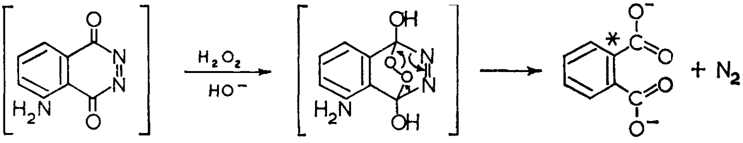

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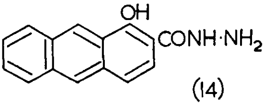
[52] T. J. Kealy, *J. Amer. Chem. Soc.*, 1962, **84**, 966; R. A. Clement, *J. Org. Chem.*, 1960, **25**, 1724.

[53] E. H. White, personal communication.

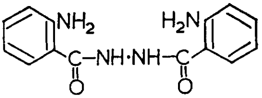
[54] H. D. K. Drew and R. F. Garwood, *J. Chem. Soc.*, 1938, 791.

[55] P. C. Wilhelmsen, R. Lumry, and H. Eyring, "The Luminescence of Biological Systems", ed. F. H. Johnson, Amer. Assoc. Adv. Sci., Washington, 1955, p. 96.

A further advantage of this modification of Drew's hypothesis is the way in which it accounts for the almost quantitative incorporation of $^{18}O_2$ into the isolated methyl phthalate derivative. Since linear hydrazides[49,56] such as (14) and (15) are often brightly chemiluminescent, it seems that a mechanism capable of embracing non-cyclic compounds would be more acceptable. The anthracene derivative[35] (14) is in fact almost as efficient as luminol, such efficiency being rare even in the cyclic phthalhydrazides.



(14)



(15)

Lophine.—Interest in lophine, 2,4,5-triphenylimidazole (16), the first pure organic chemiluminescent compound, has recently been revived. Earlier workers[2,57] oxidised lophine directly, using strong base and oxygen, and noted the influence of catalysts. The spectrum of the resulting yellow glow was roughly recorded.[2] Kautsky and Kaiser[58] found that luminescence was associated with the formation of a purple transient intermediate, presumably a radical. This radical, and its dimer, have now been extensively studied,[59,60] and shown to react with oxygen to form an isolable peroxide (17).[61,62] This peroxide had previously been prepared,[63] although it appears that the *endo*-structure suggested is not actually isolated.

Addition of base, as sole reagent, to the peroxide (17) (Scheme 3) results in the emission of light at 530 mμ much more intense than can be obtained from lophine itself under the usual reaction conditions. These conditions resemble those for luminol, with catalysis by halogens and ferric salts,[2,57] and the necessity for oxygen or hydrogen peroxide. The dihydro-derivative, amarin (18), is also chemiluminescent[64] but is very easily oxidised to lophine,[57] suggesting a common reaction path. Hydrobenzamide (19), although non-cyclic, has a similar structure, formation of a stable radical by abstraction of a hydrogen atom being expected.

The major products from the very mild decomposition of the peroxide (17) are lophine and the dibenzoylbenzamidine (20). It is doubtful if the elimination of oxygen is sufficiently exothermic to account for the light emitted (530 mμ), so that lophine itself is an unlikely choice for the excited

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[56] J. Kroh and J. Luszewski, *Roczniki Chem.*, 1956, **30**, 647; H. Ojima, *Naturwiss.*, 1961, **48**, 600.

[57] K. Hoffmann, "Imidazole and Its Derivatives", The Chemistry of Heterocyclic Compounds, ed. A. Weissberger, Interscience, New York, 1953, p. 11.

[58] H. Kautsky and K. H. Kaiser, *Naturwiss.*, 1943, **31**, 505.

[59] T. Hayashi and K. Maeda, *Bull. Chem. Soc. Japan*, 1962, **35**, 2057; 1960, **33**, 565.

[60] D. M. White and J. Sonnenberg, Abstracts, 144th National Meeting of the Amer. Chem. Soc., April, 1963, p. 55M.

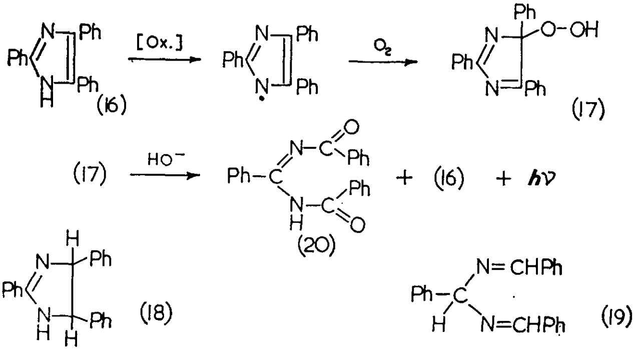
[61] D. M. White and J. Sonnenberg, *J. Amer. Chem. Soc.*, 1964, **86**, 5685.

[62] (*a*) E. H. White and M. J. C. Harding, *J. Amer. Chem. Soc.*, 1964, **86**, 5686; (*b*) E. H. White and M. J. C. Harding, ref. 19, p. 1129.

[63] C. Dufraisse, A. Etienne, and J. Martel, *Compt. rend.*, 1957, 970.

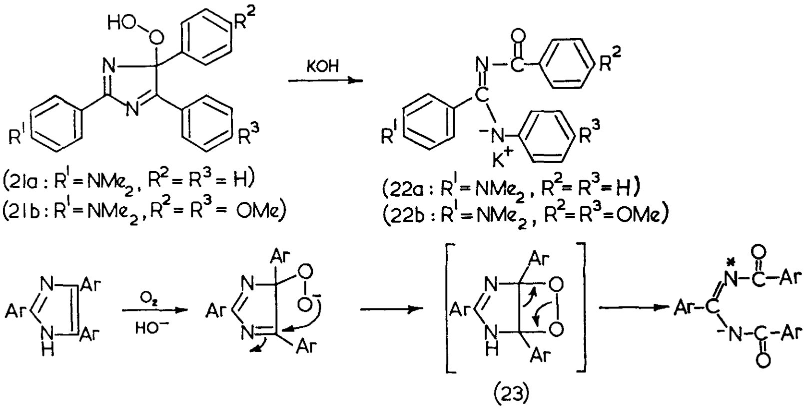
[64] S. S. Bhatnagar and K. G. Mathur, *Z. physikal. Chem.*, 1932, **159**, 454.

SCHEME 3



product. The report[61] that the phosphorescence spectrum of lophine had a maximum at 528 mμ has been challenged,[62b] and a figure of 500 mμ reported. Further, there are objections to invoking radiation from a long-lived triplet state at room temperature in solutions, particularly in the presence of oxygen.[65] On the other hand, the dibenzoylbenzamidine (20) is very weakly fluorescent in basic solution, and appears to fluoresce at wavelengths considerably shorter than 530 mμ. Thus the exact nature of the emitter, and hence the mechanism, is at present unknown. However certain derivatives of lophine[62b] show a satisfactory correspondence in wavelength between the fluorescence of the salt of the dibenzoylbenzamidine formed in the reaction and the chemiluminescence (Scheme 4).

SCHEME 4



The fluorescence of (22a) and chemiluminescence of (21a) had a maximum at 491 mμ (2 × 10^{-3}M) and the respective figure for (22b) and (21b)

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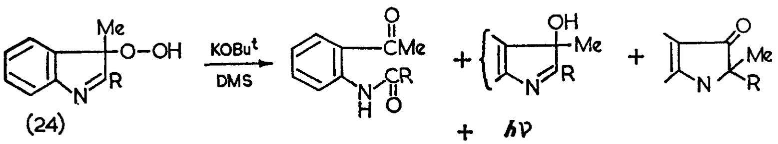
[65] C. A. Parker, "Phosphorescence and Delayed Fluorescence from Solutions" Advances in Photochemistry, John Wiley, New York, 1864, vol. 2, p. 310.

was 485 mμ at the same concentration. As with luminol the intensity of light is directly proportional to the concentration of the substituted lophine, and oxidation (in this case proved to be a peroxidation) is the slow step. The suggested mechanism is shown as occurring *via* the intermediate (23). The relative intensities emitted by a similar series[66] of substituted lophines give a linear plot of log I/I_0 against σ, where I is the intensity observed for the derivative and I_0 is the intensity for lophine oxidation, σ being the Hammett substituent constant.

It is not completely clear whether the relationship is due to rate of oxidation (presumably formation of peroxide) or enhanced fluorescence efficiencies. In fact, a later study[62b] strongly suggests the latter cause. The claim that the maximum (530 mμ) observed for the chemiluminescence of all these derivatives is the same is not substantiated by later work,[62] although it is suggested that the discrepancy between the results of the two investigations is caused by the use of different solvents.[66] Thus the mechanism previously shown explains the facts so far observed, with ethanol as solvent, the four-centred nature of the reaction being supported[62b] by the fact that the chemiluminescence is undiminished in anhydrous dimethyl sulphoxide when dry potassium t-butoxide is used as base. A related study of chlorosubstituted lophines has been made,[67] following earlier work,[68] but no additional mechanistic conclusions can be drawn at present.

A similar series of peroxides,[34] which produce related products, are also chemiluminescent. The indolen-3-yl hydroperoxides (24) have been shown to emit light when heated, or on treatment with potassium t-butoxide in dimethyl sulphoxide. The reaction under the latter conditions gives only those products shown, and the amide anion (formed in very high yield) is the excited product. For example, the chemiluminescence of (24a) and the fluorescence of the corresponding amide anion both have maxima at 518 mμ; (24b) provides light with a maximum at 495 mμ, again identical to the fluorescence of the appropriate amide anion. A four-membered peroxide pathway to the amide has been shown by the use of $^{18}O_2$ in the preparation of the peroxides, and the luminescent reaction is clearly first order with respect to the peroxide concentration.

These peroxides are of significance in that the luciferin isolated from the



(24)

(a) R = Me

(b) R = $C_6H_4 \cdot OMe$

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[66] G. E. Philbrook and M. A. Maxwell, *Tetrahedron Letters*, 1964, 111; G. E. Philbrook, M. A. Maxwell, R. E. Taylor, and J. R. Trotter, ref. 19, p. 1175.

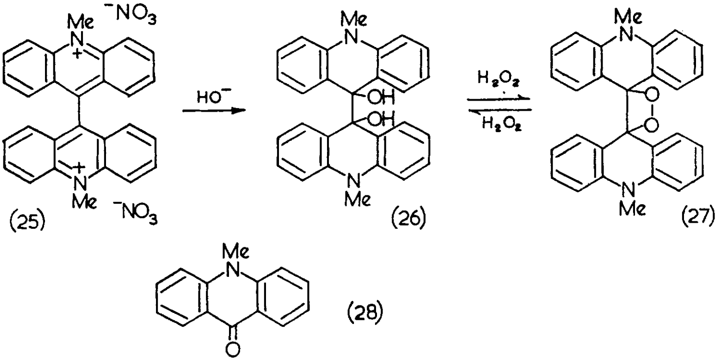
[67] I. Nicholson and R. Poretz, *J. Chem. Soc.*, 1965, 3067.

A. H. Cook and D. G. Jones, *J. Chem. Soc.*, 1941, 278.

bioluminescent sea pansy *Renilla reniformis* has been shown to contain an indolic substituent.[69] Simple indoles are also chemiluminescent[34,69] on oxidation in basic solution, a reaction which most probably involves the indolen-3-yl hydroperoxides.

Lucigenin.—This compound, whose chemiluminescence was first reported in 1935,[2] is of comparable efficiency with luminol and has thus received much attention.[70] Lucigenin, *NN*-dimethyl-9,9′-biacridinium dinitrate (25) emits blue-green light on oxidation with alkaline hydrogen peroxide. The original workers suggested a mechanism based on the oxidation of the carbinol base (26). However, the reaction suggested for the energy-producing step cannot yield the observed energy of excitation. Furthermore, it is doubtful if hydrogen peroxide[71] can function in the way required by the mechanism of Scheme 5.

SCHEME 5



The discoverers of the reaction dismissed *N*-methylacridone (28), which is the major product, as a product of a side reaction, with the step (27)→(26) leading to light emission. However, later workers,[58] using dilute solutions at 40—50°c, observed a blue emission whose spectrum corresponded reasonably well with the fluorescence spectrum of *N*-methylacridone. They also showed that the fluorescence of lucigenin is perhaps the major component of the chemiluminescence at 18° in more concentrated solution. This identification of *N*-methylacridone as the primary emitting molecule has been recently substantiated.[72] It has, however, been pointed out that lucigenin itself, which is green-fluorescent, is not present in great amounts

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[69] M. J. Cormier and C. G. Eckroade, *Biochim. Biophys. Acta*, 1962, **64**, 340; G. E. Philbrook, J. B. Ayers, J. F. Garst, and J. R. Trotter, *Photochem. and Photobiol.*, 1965, **4**, 869.

[70] R. M. Acheson, "Acridines", The Chemistry of Heterocyclic Compounds, ed. A. Weissberger, Interscience, New York, 1956, p. 282.

[71] J. O. Edwards, ed., "Peroxide Reaction Mechanisms", Interscience, New York, 1962; "Organic Peroxides", A. G. Davies, Butterworths, London, 1961.

[72] J. R. Totter, *Photochem. and Photobiol.*, 1964, 3, 231.

in basic solution, formation of the pseudo-base (26) occurring readily.[45] Yet the strongly basic solution is indeed yellow-fluorescent, and the convincing evidence available concerning transfer of energy to, for example, added fluorescein[73,74] supports the interpretation that the blue-fluorescent *N*-methylacridone excites some yellow-fluorescent material in the solution, giving rise to the usual blue-green colour of the chemiluminescence.

The evidence on which a mechanism must be based is as follows. There is a first-order relationship between the initial light intensity and the concentration of hydrogen peroxide, but the kinetic relationship involving base is more complex.[75] A variety of materials, such as glycerol, glycols, urea, ascorbic acid, and aliphatic alcohols enhanced the intensity. It seems that this effect is associated with solvation or hydrogen bonding, and is probably not of major significance. However pyridine,[76,77] piperidine,[76] and ammonia[77] have a more pronounced effect, as does osmium tetroxide. Osmium tetroxide is not effective when ammonium hydroxide is present, and therefore probably has a similar effect on the reaction. There is evidence[76] that the total light emitted is not altered by these additions, so that there is perhaps no change in mechanism, the effect being purely catalytic. As previously indicated, a certain confusion exists about the identity of the emitter. *N*-Methylacridone is not formed quantitatively, and since much of the reaction takes place in presence of lucigenin or its flourescent degradation products, different emission spectra are obtained depending on the conditions. Nevertheless, the fact that the blue emission from *N*-methylacridone is the most energetic observed, strongly suggests that it is the primary excited molecule, and that in certain circumstances, other molecules are induced to emit by a transfer of this energy. A suggestion has been made[78] that a transannular peroxide of unspecified structure decomposes to form a "biradical" which emits the observed light. If *N*-methylacridone is indeed the excited product, then this fact, together with the difficulty of formulating such a structure, seems to lend little support to this view.

Lucigenin in aqueous solution, and in the presence of reducing agents,[8] luminesces in contact with atmospheric oxygen. Since the chemiluminescent reaction is very sensitive to hydrogen peroxide, the presence of traces of this, produced either directly from the appropriate reducing agent or by autoxidation of dihydrolucigenin (*NN*-dimethyl-9,9′-biacridan) seems likely. Various substituted derivatives[70] of lucigenin have been tested for luminescence and most do in fact emit light, with a colour related to the fluorescence of the material used. No change in the mechanism is to be expected.

A series of acridinium salts which are chemiluminescent on the addition

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[73] B. D. Ryzhikov, *Bull. Acad. Sci. U.R.S.S., phys. ser.*, 1956, **20**, 487.

[74] L. Erdey, *Acta. Chim. Acad. Sci. Hung.*, 1953, **3**, 81.

[75] K. Weber and W. Ochsenfeld, *Z. phys. Chem.*, 1942, **51**, 63.

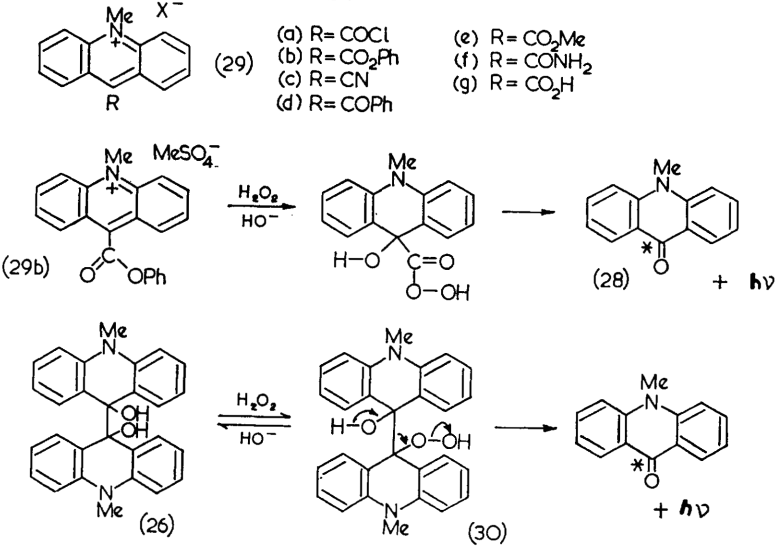
[76] K. Weber, *Z. phys. Chem.*, 1941, **50**, 100.

[77] O. Schales, *Chem. Ber.*, 1939, **72**, 1155.

[78] A. V. Kariakin, *Optics and Spectroscopy*, 1959, **7**, 75.

of alkaline hydrogen peroxide has been described.[34] They give solutions which are free from any colour or fluorescence other than that of *N*-methylacridone. This allows unambiguous identification of *N*-methylacridone as the sole excited product. It seems reasonable that lucigenin and these compounds (29) are related in their chemiluminescent reactions. Thus the probable mechanisms for both lucigenin and compounds of type (31) are shown in Scheme 6. The acid chloride (29a) has been discovered independently,[22,79] and will be discussed later. Compounds (29a) and (29b) are comparable in brightness with lucigenin, and the order of intensity is as given, with (29f) and (29g) not chemiluminescent. Substitution of the phenyl group of (29b) with electron-withdrawing and electron-donating groups gives rate differences confirming that attack of peroxide ion on the carbonyl group is connected with light emission.

SCHEME 6



Kautsky and Kaiser[49] have already suggested oxidation of (26) to (28) as the source of the luminescence, and their suggestion can be accommodated as shown. The intermediates in both classes of acridinium salt could also involve a four-membered peroxide[33] similar to other examples discussed previously.

As adumbrated above, the brightest of the organic chemiluminescent compounds can be considered to react by way of a peroxidic cleavage mechanism. This idea has also been suggested and extensively investigated by another group.[22,79] During an investigation of the recently discovered[80]

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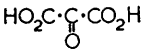
[79] M. M. Rauhut, D. Sheehan, R. A. Clarke, B. G. Roberts, and A. M. Semsel, *J. Org. Chem.*, 1965, **30**, 3587.

[80] E. A. Chandross, *Tetrahedron Letters*, 1963, 761.

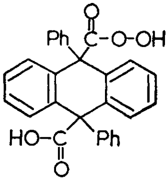
chemiluminescence of oxaloyl chloride and hydrogen peroxide, a large number of acyl peroxides were found to give light on decomposition. The simple aliphatic members of this class of compound do not, of course, yield fluorescent products, and various fluorescent acceptors of the reaction energy are used. With added 9,10-diphenylanthracene, acid chlorides such as (31) in the presence of hydrogen peroxide, and acids (32) and (33) with dicyclohexylcarbodi-imide and hydrogen peroxide, emit light characteristic of the fluorescence of diphenylanthracene.

$Cl{\cdot}CO{\cdot}COCl$ (31)


$HO_2C{\cdot}\underset{\underset{O}{\|}}{C}{\cdot}CO_2H$ (32)

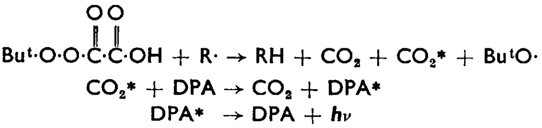
$HO_2C{\cdot}CO_2H$ (33)


$RO{\cdot}\overset{\overset{O}{\|}}{C}{\cdot}\overset{\overset{O}{\|}}{C}{\cdot}O{\cdot}OR'$ (34)


(35)

Use of t-butyl hydroperoxide also gave rise to chemiluminescence. It is assumed that an acyl peroxide such as (34, R = H, R′ = H or t-butyl) is formed *in situ*. No significant luminescence is observed when compounds of the type (34, R = Me, Et, or Bu^t; R′ = H or Bu^t) are used. The authors suggest that the most important requirements for a chemiluminescent decomposition are met by Scheme 7, with emphasis on those reactions which proceed in a fully concerted manner. No distinction can be made between transfer of energy directly from an excited molecule of CO_2 and decomposition of a complex of the acyl peroxide and the acceptor molecule. Evidence for a chemiluminescent emission from excited CO_2 in the gas phase is available.[81] Decomposition of the acyl peroxide (35), prepared from the corresponding anhydride, is also chemiluminescent. A fairly detailed study of the 9-chlorocarbonyl-10-methylacridinium chloride (29a) has also been made by this group, and the quantum yield of the reaction found to be 1·1 %.[79] This is similar to the highest yields found for luminol,[35,36] which is considered to be the brightest, well investigated organic compound. The mechanism suggested is similar to that already shown, presumably related to other acyl peroxide decompositions, since CO_2 would be a product of the reaction. Thus it is not yet clear whether the direct formation of *N*-methylacridone in an excited state is involved, or whether energy is transferred from the CO_2. It is noteworthy that CO_2 is of course a "carbonyl" product, and that its excited state[81] is non-linear. The products from the reactions so far discussed are all obtained from

SCHEME 7



$$Bu^t{\cdot}O{\cdot}O{\cdot}\overset{\overset{O}{\|}}{C}{\cdot}\overset{\overset{O}{\|}}{C}{\cdot}OH + R{\cdot} \rightarrow RH + CO_2 + CO_2{}^* + Bu^tO{\cdot}$$
$$CO_2{}^* + DPA \rightarrow CO_2 + DPA^*$$
$$DPA^* \rightarrow DPA + h\nu$$

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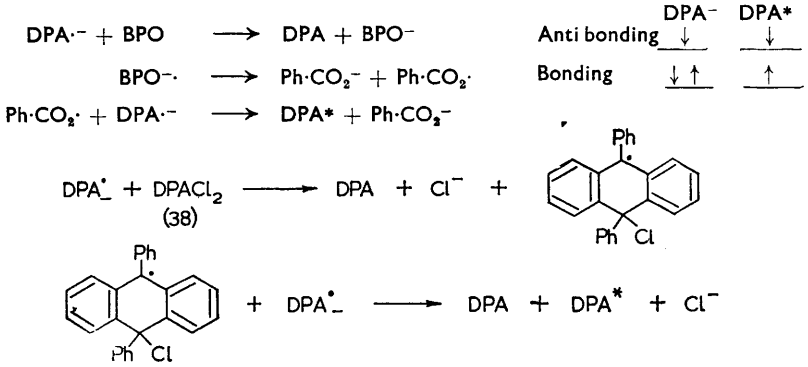
[81] M. A. A. Clyne and B. A. Thrush, *Proc. Roy. Soc.*, 1962, *A*, **269**, 404, and references cited.

peroxide decompositions, and all contain a carbonyl group in at least one product. Many other examples of chemiluminescence are perhaps also of this type, but much further work is required on all of them.

Chemiluminescence of Aromatic Radical Ions.—Recently, a type of chemiluminescence in solution has been discovered independently by several workers.[23–26] It is, perhaps, conceptually the simplest of all, and a brief theoretical discussion has been published.[25f] The reaction involves the removal of an electron from a radical anion, or the addition of an electron to a radical cation, resulting in the direct formation of the excited state of the parent polynuclear hydrocarbon. For example, sodium 9,10-diphenylanthracenide[23,25c] can be oxidised to the anthracene by a variety of electron acceptors. Chlorine and bromine, but not iodine, when added to a solution of the dark-coloured radical anion in tetrahydrofuran give a clear solution of 9,10-diphenylanthracene (DPA) and light corresponding to its fluorescence. Oxaloyl chloride, benzoyl peroxide, nitrogen dioxide, ceric ion, and lead tetra-acetate are also effective, but oxygen is not.[23] It is possible that insufficient energy is released in the oxidations using oxygen and iodine. A large number of polycyclic aromatic hydrocarbons on treatment with sodium naphthalenide give the corresponding radical anion, which luminesces on oxidation. 9,10-Dichloro-9,10-diphenylanthracene (36) can be considered an oxidising agent in this context, and mixing of solutions of it and DPA gives light.[23,25]

The similarity between photo-induced recombination luminescence in the solid state[82] and this type of liquid chemiluminescence has been noted, especially with reference to the reaction of a radical anion with the corresponding radical cation.[25c] In the recombination phenomenon, radiation removes an electron from an organic molecule at low temperatures. The electron returns from a "trap" in the system on warming, with consequent fluorescent emission. Thus transfer of an electron from the highest bonding orbital of the radical anion to an oxidising agent creates a molecule with

SCHEME 8



$$DPA\cdot^- + BPO \longrightarrow DPA + BPO^-$$

$$BPO^-\cdot \longrightarrow Ph\cdot CO_2^- + Ph\cdot CO_2\cdot$$

$$Ph\cdot CO_2\cdot + DPA\cdot^- \longrightarrow DPA^* + Ph\cdot CO_2^-$$

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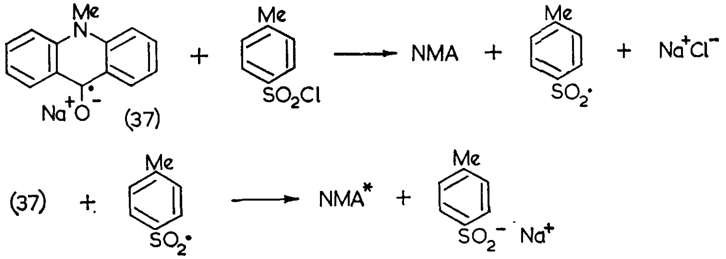
[82] G. N. Lewis and J. Bigeleisen, *J. Amer. Chem. Soc.*, 1943, **65**, 2424; G. N. Lewis and M. Kasha, *ibid.*, 1944, **66**, 2100.

the configuration of its first excited state. The return of the previously added electron (necessarily in an antibonding orbital) to the "vacated" ground state orbital gives rise to the observed chemiluminescence. The mechanism suggested for the case of benzoyl peroxide (BPO) and sodium diphenylanthracenide[25c] is shown in Scheme 8.

The ketyl (37) derived from *N*-methylacridone (NMA) undergoes an analogous reaction with benzoyl peroxide, and a presumably related reaction with toluene-*p*-sulphonyl chloride as electron acceptor, is shown in Scheme 9.

SCHEME 9



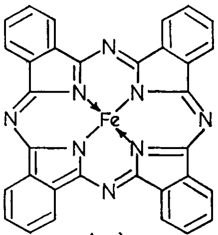
Complete proof of the details suggested in these reactions is not yet available, and the observation of what might be emission from the triplet state of *N*-phenylcarbazole (*i.e.*, a phosphorescence) at room temperature in a similar reaction suggests that further investigation should prove of interest.

The generation of the radical cation $Ar^{\cdot+}$ in the presence of the radical anion $Ar^{\cdot-}$ would be expected to form a product in an excited state, either by removal of an electron from the highest bonding orbital of $Ar^{\cdot-}$ or the addition of an electron to a non-bonding orbital or $Ar^{\cdot+}$. Several independent reports of chemiluminescence in such circumstances have appeared.

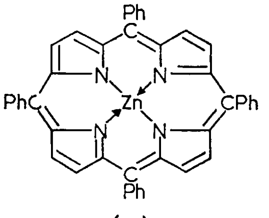
Electrolysis[23–26] of solutions of anthracene, rubrene, perylene, and related polycyclic hydrocarbons in acetonitrile or dimethylformamide, with supporting electrolyte, gives rise to luminescence at the cathode. The colour of the light matches the fluorescence of the hydrocarbon under study. Reaction takes place in the body of the solution, not on the electrode surface, and a variety of effects is obtainable with stirring and with differently shaped electrodes.[24] The reaction appears to be $Ar^{\cdot-} + Ar^{\cdot+} \rightarrow Ar^* + Ar$. A lifetime of up to 10 seconds has been found for the shorter-lived $Ar^{\cdot+}$,[25d] while the anion $Ar^{\cdot-}$ is more stable. The dark colour of the latter, as it is generated, is often observable in room light.[24]

The question arises as to whether the luminescence is a specific result of the $Ar^{\cdot+} + Ar^{\cdot-}$ reaction, or whether independent reduction and oxidation, respectively, is also taking place. Studies[23,25c] with a three-electrode electronic polarograph give cyclic voltammograms, and permit the rapid reversal of electrode polarity. Consequently, the two species involved are generated in the same region of the solution. Further, by use of a square-wave input to generate the radical anion of rubrene ($R\cdot^-$), it is possible to measure the generation potential, and the potential for its oxidation.[23] Thus, measured against the standard saturated aqueous calomel electrode, the potential for the generation of $R\cdot^-$ is $E_{1/2} - 1{\cdot}37$ v, and for $R\cdot^+$ $E_{1/2} + 0{\cdot}91$ v. During the reversal of polarity, the preformed $R\cdot^-$ is oxidised at approximately $+0{\cdot}5$ v, which is below the potential of generation of $R\cdot^+$, demonstrating that the reaction $R\cdot^- - e \rightarrow R^*$ is luminescent. However, it appears that the electron acceptor in this case is not the electrode itself but an electro-generated, fairly long-lived oxidant[25d] perhaps derived from the solvent or supporting electrolyte.[26] Similarly, the electro-reduction of $R\cdot^+$ at $-0{\cdot}9$ v produces light, there being no appreciable concentration of radical anion present. The light observed agrees with the fluorescence spectrum of rubrene, and is thus derived from an excited singlet state. The potentials involved in the similar reaction using 9,10-diphenylanthracene strongly suggest that the threshold of oxidation lies slightly above the spectroscopic singlet energy, and very far above the triplet state energy of this molecule. Emission from excimers (a complex excited state formed from two molecules of hydrocarbon) has been observed for anthracene, dimethylanthracene, phenanthrene, and perylene.[25d] The more hindered rubrene and 9,10-diphenylanthracene show the sharper singlet monomer emission only. Thus the annihilation process $R\cdot^+ + R\cdot^- \rightarrow R^*\text{–}R$ (excimer) can also take place in these solutions. The use of A.C. electrolysis results in a cleaner reaction, as both species are generated in the Nernst diffusion layer surrounding the electrode.[25d] The theory of electrogenerated chemiluminescence has been discussed.[25e]

Porphyrins.—The decomposition of organic peroxides, such as tetralin hydroperoxide, in the presence of metal porphyrins and phthalocyanines results in the emission of light of the same colour as the porphyrin fluorescence.[83,84] Iron phthalocyanine (38) catalyses the exothermic decomposition of tetralin hydroperoxide at room temperature with the emission of light,[83] but generally, higher temperatures, in an inert solvent such as



(38)



(39)

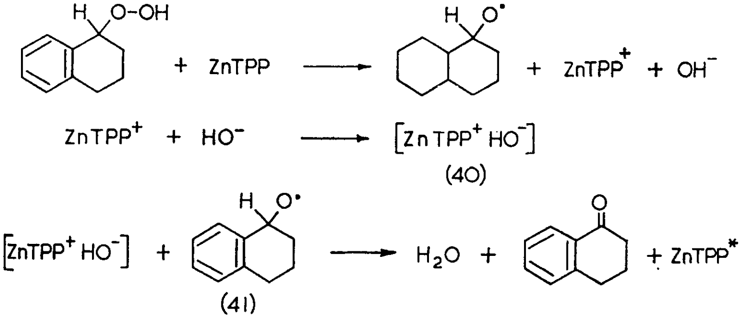
[83] A. H. Cook, *J. Chem. Soc.*, 1938, 1774, 1845.

[84] J. H. Helberger, *Naturwiss.*, 1938, **26**, 316; J. H. Helberger and D. B. Hever, *Chem. Ber.*, 1939, **72**, 11.

[85] H. Linschitz, "Light and Life", Johns Hopkins Press, Baltimore, 1961, p. 173.

boiling toluene, are required. Beryllium phthalocyanine is stated to be the most brilliant. The major products from these reactions are tetralone and phthalimide from the degradation of the phthalocyanine.

A recent investigation[85] of zinc tetraphenylporphine (ZnTPP) (39) established that the light emitted corresponds to the fluorescence of the metalloporphyrin, and confirmed that a metal is a requirement for light emission. The reaction is overall of the second order, first order in both peroxide and porphyrin. The mechanism suggested resembles, in one important aspect, the suggestions for radical-ion luminescence. The charge-transfer product (40) is reduced, either by radical (41) or the peroxide itself, chain processes being considered likely.



The electron abstracted in the last step will enter an excited rather than a ground-state orbital, the result being similar to that discussed for the polynuclear hydrocarbons. As previously mentioned, the possibility exists that most chemiluminescent reactions involve electron-transfer reactions since the conservation of energy combined with the speed of such transfers would be more likely to result in an electronic excited state than a vibrationally excited ground state.[25c] Another suggestion[29c] involving energy transfer from excited oxygen (two $^1\Delta g$ molecules) is not in agreement with the kinetic results indicated above.

Chemiluminescent Grignard Reactions.—The discovery of luminescence during oxidation of the Grignard reagent was made in 1906,[6] but little very recent work has been reported. The brightest emissions are noted when an aromatic Grignard reagent is oxidised by a stream of oxygen.[86] The products of the reaction have not been adequately investigated, although in the case of *p*-bromophenylmagnesium bromide[87] *p*-bromophenol and bromobenzene have been isolated, with insoluble, uncharacterised material. A related luminescent reaction of phenyl-lithium[88] gave biphenyl, *p*-phenylphenol, and phenol as products. There is some disagree-

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[86] R. T. Dufford, S. Calvert, and D. Nightingale, *J. Amer. Chem. Soc.*, 1923, **45**, 2058.

[87] W. V. Evans and R. T. Dufford, *J. Amer. Chem. Soc.*, 1923, **45**, 278.

[88] M. A. Pacevitz and H. Gilman, *J. Amer. Chem. Soc.*, 1939, **61**, 1603.

ment[89,90] as to whether aliphatic magnesium halides give light, since the very faint light observed could be due to impurities. Apparently the reaction between oxygen and *p*-chlorophenylmagnesium bromide is the brightest so far reported, with an emission maximum at 475 mμ as recorded by a photographic method.[86,91] The weaker *p*-bromophenylmagnesium bromide had a similar maximum.[91] The fluorescence spectrum of the mixture of products had many bands, probably owing to the presence of unidentified fluorescent compounds. Extensive lists[86,89] of arylmagnesium halides exhibiting chemiluminescence showed that magnesium bromides are brightest, and that the order of brightness for substituents is chloro$>$bromo$>$iodo, with *para* substitution much more effective than *ortho* or *meta*. Other seemingly effective materials are 2-naphthyl-[86] and 9-phenanthryl-magnesium[92] bromides. From the reported emission maximum and the conditions of the reaction, it is probable that a mechanism involving peroxide decomposition or electron transfer would make a reasonable basis for further investigation. In this connection, it is interesting that two effective electron acceptors, chloropicrin[6] and picryl chloride, gave rise to an emission with the arylmagnesium halides although other potential acceptors such as N_2O, NO, NO_2, and $CH_3{\cdot}COCl$ were without effect.[93] The isolation and investigation of peroxides of the type R–O–OMgX is of interest,[94] and studies[95] of the oxidation products of phenylmagnesium bromide reveal a variety of products which are obviously the result of a radical reaction. The application of a magnetic field to the chemiluminescent solution concentrated the light at the strongest part of the field.[90] Electrolysis of the ethereal solutions also resulted in luminescence, usually at the anode.[90] It is doubtful whether these observations can be related to more modern work on, for example, aromatic radical ions, and re-investigation of the whole phenomenon is obviously desirable.

Pyrogallol.—The oxidation of pyrogallol in alkaline solution, with chemiluminescence, was also noted over sixty years ago[7] but only very recently has there been a convincing suggestion as to the source of the red light observed. Bowen and Lloyd[30] have identified a band at about 630 mμ as part of the excited oxygen system examined in detail by Browne and Ogryzlo.[27] The intensity of the light produced is considerably enhanced in a mixture of pyrogallol, potassium carbonate, and formaldehyde, and is then often called the Trautz–Schorigin[96] reaction. Decomposition of an

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[89] W. V. Evans and E. M. Diepenhorst, *J. Amer. Chem. Soc.*, 1926, **48**, 715.

[90] R. T. Dufford, D. Nightingale, and L. W. Gaddum, *J. Amer. Chem. Soc.*, 1927, **49**, 1858.

[91] R. T. Dufford, D. Nightingale, and S. Calvert, *J. Amer. Chem. Soc.*, 1925, **47**, 95.

[92] W. E. Bachmann, *J. Amer. Chem. Soc.*, 1934, **56**, 1363.

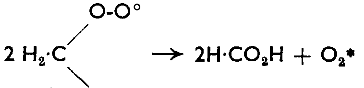
[93] J. Schmidlin, *Ber.*, 1912, **45**, 3172.

[94] C. Walling and S. A. Buckler, *J. Amer. Chem. Soc.*, 1955, **77**, 6032; H. Hock, H. Kropf and F. Ernst, *Angew. Chem.*, 1959, **71**, 541.

[95] H. Wuyts, *Bull. Soc. chim. belges*, 1927, **36**, 222; C. W. Porter and C. Steele, *J. Amer. Chem. Soc.*, 1920, **42**, 2650.

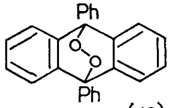
[96] M. Trautz and P. Schorigin, *Z. wiss. Phot.*, 1905, **3**, 121.

intermediate peroxide is suggested,[97] with oxygen formed in an excited state by collision of two radicals (42). The role of pyrogallol is not particularly clear, although it could obviously be involved in the formation of the radical (42). Other polyphenols are also active in a similar reaction, ozone being used as oxidant.[98]

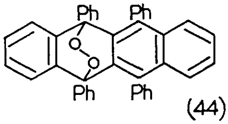

$$2\,H_2C(O{-}O^{\circ})(OH) \rightarrow 2H{\cdot}CO_2H + O_2^{*}$$

(42)

Aromatic Endoperoxides.—Many linear polycyclic aromatic hydrocarbons rapidly oxidise under irradiation to form endoperoxides[99] such as (43). The reaction is usually reversible[100,101] and certain of the peroxides emit light as they evolve oxygen at temperatures ranging from 25° to 200°. Anthracene 9,10-endoperoxide does not produce much oxygen on heating, and anthraquinone is a product. Light intensity is low. In general, peroxides of acenes such as those of rubrene (44) and 1,4-dimethoxy-9,10-diphenylanthracene (45), which release oxygen almost quantitatively, are most efficient in light emission.[100] Thus it seems that the original hydrocarbon is formed in an excited state, and not some product such as anthraquinone. In addition the spectrum of the light observed[100] is usually very similar to that of the fluorescence of the hydrocarbon, although this point probably requires confirmation. It is superficially attractive to invoke the reverse of the formation of the peroxide as a light-producing step, but unfortunately the heat of formation,[102] at least for anthracene peroxide, is much too low to account for the energy of the radiation observed.



(43)



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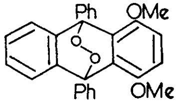

(45)

The activation energy for the decomposition must also be low since, for example, (45) dissociates at 20° releasing 98·5% of its oxygen in 80 hr.[100] Further theoretical and experimental contributions in this area would be helpful.

Tetrakis(dimethylamino)ethylene.—Exposure of tetrakis(dimethylamino)ethylene (46) (TDE)[103] as the neat liquid to air results in a bright

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[97] E. J. Bowen, "Organic Photochemistry", International Symposium, Strasbourg 1964, Butterworths, London, p. 473.

[98] D. S. Bersis, *Z. phys. Chem. (Frankfurt,)* 1960, **26**, 359.

[99] R. M. Hochstrasser and G. B. Porter, *Quart. Rev.*, 1960, **14**, 146, and references cited.

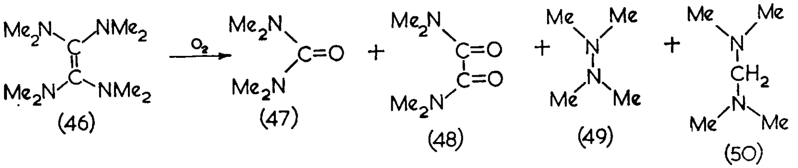
[100] C. Dufraisse and L. Velluz, *Bull. Soc. chim. France*, 1942, **9**, 171.

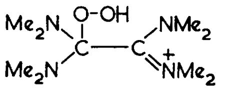
[101] G. M. Badger, "Structures and Reactions of the Aromatic Compounds", Cambridge University Press, 1954, p. 374.

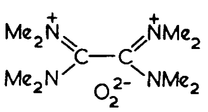
[102] P. Bender and J. Farber, *J. Amer. Chem. Soc.*, 1952, **74**, 1450.

[103] R. L. Pruett, J. T. Barr, K. E. Rapp, C. T. Bahner, J. D. Gibson, and R. H. Lafferty, *J. Amer. Chem. Soc.*, 1950, **72**, 3646.

chemiluminescence which has a spectrum identical to the fluorescence spectrum of TDE (46) itself.[104] Recent intensive effort[104–107] devoted to elucidation of the mechanism of this phenomenon has so far not given a completely convincing result. A very thorough investigation,[106] making full use of nuclear magnetic resonance spectroscopy, revealed several products [(47)—(50)] of the reaction with oxygen under various conditions. These products are explained on the basis of the formation of a peroxide (*e.g.*, 51) and indeed in two-phase systems (52) is isolated in very high yield. Thus the tetramethylurea (47), perhaps formed in an excited state




(51)


(52)

by the exothermic decomposition of (51), could transfer energy to the fluorescent TDE (46). This process may involve a quasi-four-membered peroxide, related to other chemiluminescent autoxidations discussed previously. Two detailed kinetic studies,[105,107] unfortunately not related to such a careful analysis of products, lead to different views of the process. No evidence is yet available to substantiate the implication of a carbene intermediate,[104] and its genesis is not convincingly portrayed.[107] Catalytic solvation by alcohols has been noted, and direct formation of excited TDE by an electron-transfer reduction of the dication such as (52) suggested.[104,105] It is of interest that strong electron spin resonance signals are observed during the oxidation of TDE.[108] The fluorescence quantum yield is low (about 0·05) and the chemiluminescence yield is 3 × 10^{-4}, suggesting that only 1 % of the TDE molecules oxidised result in an excited state of the emitter, TDE itself. Further work on this important chemiluminescence will be awaited with interest.

The only other series of organic compounds spontaneously chemiluminescent in air was described by Delépine[109] in 1910. Thioesters and compounds related to them [(53), (54), and (55)] on vaporisation give a blue light on contact with atmospheric oxygen.

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[104] H. E. Winberg, J. R. Downing, and D. D. Coffman, *J. Amer. Chem. Soc.*, 1965, **87**, 2054; H. E. Winberg, J. E. Carnahan, D. D. Coffman, and M. Brown, *ibid.*, 1965, **87**, 2055, and references cited.

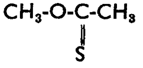
[105] A. N. Fletcher and C. A. Heller, ref. 19, p. 1051.

[106] W. H. Urry and J. Sheeto, ref. 19, p. 1067.

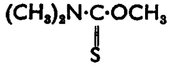
[107] J. P. Paris, ref. 19, p. 1059.

[108] K. Kuwata and D. H. Geske, *J. Amer. Chem. Soc.*, 1964, **86**, 2101.

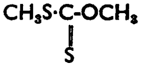
[109] M. Delépine, *Compt. rend.*, 1912, **154**, 1171, and previous references.


$CH_3\text{-}O\text{-}\underset{\underset{S}{\|}}{C}\text{-}CH_3$

(53)


$(CH_3)_2N\cdot\underset{\underset{S}{\|}}{C}\cdot OCH_3$

(54)


$CH_3S\cdot\underset{\underset{S}{\|}}{C}\text{-}OCH_3$

(55)

The brightest of these is (53), apparently owing to its volatility, and consequent high concentration in the vapour phase. Only sulphuric acid has been identified as a product of the reaction. It is perhaps worth suggesting that reports of "Will o' the Wisp" and similar phenomena[1a] associated with decomposing organic matter could be due to related compounds.

Uses of Organic Chemiluminescence

Maximum chemiluminescence in aqueous solutions of luminol is dependent on three factors; hydrogen peroxide concentration, metal catalysis, and pH. Each of these factors can thus be assessed by the use of a sensitive photomultiplier to measure the intensity of light produced. Visual detection is also easily possible.

Flow boundaries can be studied[110] during the mixing of an alkaline hydrogen peroxide solution with a solution containing ferricyanide and luminol. Acid–base titrations[111,112] in opaque or coloured solutions are also feasible, and studies of the accuracy of the method with respect to conventional techniques have been made. A recent modification,[113] with use of added fluorescein to enhance the light observed, has been described. The striking catalysis of luminol chemiluminescence, in aqueous solution, has been used in forensic medicine,[114] where traces of hæm from blood cause a very bright emission of light. Transition metals generally are detectable in concentrations of 10^{-8} to 10^{-9}M.[115] An early use of phthalhydrazides in the detection of hydrogen peroxide[116] has been extended to the quantitative estimation of short-wavelength radiation.[117] A recent improvement of this approach has led to a dosimeter capable of use in the range 30—3,000 rads, using luminol and a commercially available spectrophotofluorometer.[118] Thus, irradiation of water in the presence of the luminol system produces concentrations of hydrogen peroxide of 5×10^{-8} to 10^{-8}M. The intensity of the light detected is a function of the initial radiation intensity. Lucigenin has also been successfully used as an acid–base indicator[119] for coloured solutions. Since the chemiluminescence is

[110] A. S. Friedman, *J. Appl. Phys.*, 1956, **27**, 416.

[111] F. Kenny, *Trans. N. Y. Acad. Sci.*, 1954, **16**, 394.

[112] L. Erdey, *Ind. Chemist*, 1957, **33**, 459, 523, 575.

[113] L. Erdey, W. F. Pickering, and C. L. Wilson, *Talanta*, 1962, **9**, 371.

[114] W. Specht, *Angew. Chem.*, 1937, **50**, 155; A. Steigman, *Chem. and Ind.* 1941, **60**, 889.

[115] A. K. Babko and L. I. Dubovenko, *Z. analyt. Chem.*, 1964, **200**, 488.

[116] W. Langenbeck and U. Ruge, *Ber.* 1937, **70**, 367.

[117] W. V. Mayneord, W. Anderson, H. D. Evans, and D. Rosen, *Radiation Res.*, 1955, **3**, 379.

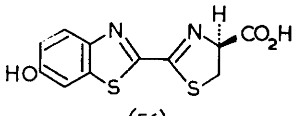
[118] W. A. Armstrong and W. G. Humphreys, *Canad. J. Chem.*, 1965, **43**, 2576.

[119] L. Erdey, J. Takacs, and I. Buzacs, *Acta. Chim. Acad. Sci. Hung.*, 1963, **39**, 295.

affected by the presence of aliphatic alcohols,[76] analysis of the latter has been attempted[120] by the effect of the alcohol on the pH at which luminescence is observed.

Bioluminescence

Several excellent reviews[121] of the subject are available, particularly with respect to the biochemistry which has been most intensively investigated.[122] However, only one system, that of the North American firefly, *Photinus pyralis*, has yet reached the status of a chemiluminescent problem.[123] This organism has yielded the only unambiguous structure for the luminescent organic molecule, generally called a luciferin, presumably present in most bioluminescent organisms. Firefly luciferin (56) has, in addition, been synthesised by two routes.[123,124] The chemiluminescence of (56) has been reported,[125] but no study has been made of the products of the reaction, nor has a satisfactory mechanism been advanced. The products of the bioluminescent reaction are also difficult to identify. Several analogues of (56) have been made,[126] but only (57) and (58) were active in the enzymic reaction, giving red light. The yellow light (562 mμ) normally emitted apparently represents a quantitative conversion of a luciferin molecule into an unknown product, with an emission efficiency of nearly 100%.[127] The chemiluminescence is weaker. It seems that no clear analogy exists between the structure of firefly luciferin and the known cases of efficient chemiluminescence. In view of the requirement for an equivalent of oxygen in the enzymic reaction, a pathway involving a peroxide may be expected.



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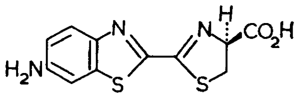

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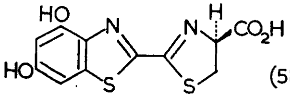

(58)

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[120] E. Michalski and M. Turowska, *Chem. Analit.*, 1960, **5**, 625 (*Chem. Abs.*, 1961, **55**, 4254g).

[121] E. N. Harvey, "Bioluminescence", Academic Press, New York, 1952; P. C. Wilhelmsen, R. Lumry, and H. Eyring, "The Luminescence of Biological Systems", Amer. Assoc. Adv. Sci., Washington, 1955.

[122] M. J. Cormier and J. R. Totter, *Ann. Rev. Biochem.*, 1964, **33**, 431.

[123] E. H. White, F. McCapra, G. F Field, and W. D. McElroy, *J. Amer. Chem. Soc.*, 1961, **83**, 2402; E. H. White, F. McCapra, and G. F. Field, *ibid.*, **85**, 337.

[124] S. Seto, K. Ogura, and Y. Nishiyama, *Bull. Chem. Soc. Japan*. 1963, **36**, 332.

[125] W. D. McElroy and H. H. Seliger, *Fed. Proc.*, 1962, **21**, 1006.

[126] E. H. White, H. Wörther, G. F. Field, and W. D. McElroy, *J. Org. Chem.*, 1965, **30**, 2344.

[127] W. D. McElroy and H. H. Seliger, *Arch. Biochem. Biophys.*, 1960, **88**, 136.

Other bioluminescent organisms[122] are under active investigation in an attempt to define the oxidative reaction responsible for light emission. Two such organisms, *Renilla reniformis*,[69] the luminescent sea pansy, and *Cypridina hilgendorfii*, a luminescent small crustacean, should yield structures for the respective luciferins shortly. The published structure[128] for *Cypridina* luciferin apparently requires modification, and evidence for a more satisfactory structure is to be published.[129]

Conclusions

The number of known chemiluminescent organic compounds is, of course, greater than that noted in this Review. However, in general, insufficient evidence is presented for a proper discussion of them. Even in those cases where a fairly detailed investigation has been made, there is quite certainly no fully satisfactory description of why a particular exothermic reaction should give rise to an electronically excited state of the product. The radical-ion reactions are notable exceptions to this. It is probable that much information on the distribution of energy in reacting molecules would be obtainable from a full investigation of the phenomenon, and it is to be hoped that investigators of various disciplines will be induced to tackle the formidable problems involved.

[128] Y. Hirata, O. Shimomura, and S. Eguchi, *Tetrahedron Letters*, 1959, No. 5, 4.

[129] Personal communication from Dr. T. Goto, Nagoya University, Japan.