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Chemiluminescence in decomposition of bridged 1,2,4,5-tetraoxanes catalyzed by ferrocene

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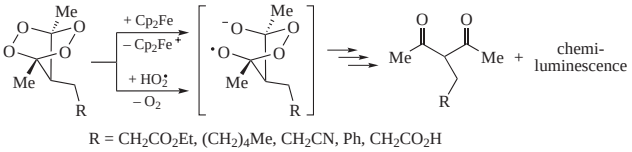
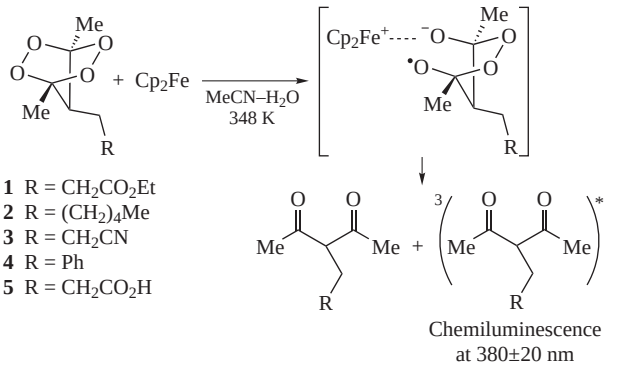
Chemiluminescence was observed in ferrocene-catalyzed decomposition of bridged 1,2,4,5-tetraoxanes, namely, 2,3,5,6-tetraoxabicyclo[2.2.1]heptanes. The chemi- and photoluminescence spectra revealed the main products and luminescence emitters to be β-diketones. The reaction intermediate, the OOH radical, was found to catalyze the decomposition of the 1,2,4,5-tetraoxanes.



The chemiluminescence (CL) method is a highly informative and convenient tool for studying the mechanisms and kinetics of reactions of various peroxides, *viz.*, organic peroxides, including dioxetanes,[1–3] and organometallic peroxides.[4] 1,2,4,5-Tetraoxanes (TOXs) containing two peroxy groups in the six-membered heterocycle possess a broad spectrum of biological activity, including antimalarial and antihelmintic ones,[5] and among peroxides they are most promising for practical purpose. Despite the considerable progress reached in the studies on TOX chemistry, it should be admitted that the mechanism of their therapeutic effect is still a matter of discussion.[5,6] It is believed that the key step of chemical action of TOX involves cleavage of the peroxy bond induced by Fe^{II} ions of human blood heme. In continuation of studies on the regularities of TOX decomposition in reactions with Fe^{II} compounds, this paper reports the first results of studies on the CL emerging in Cp_2Fe-catalyzed TOX decomposition (Cp = C_5H_5). The CL caused by emission of TOX decomposition products was first detected in TOX thermal decomposition,[7] as well as in the reaction of TOX with inorganic Fe^{II} compounds.[8,9] Decomposition of TOX catalyzed by zinc tetraphenylporphyrin was also found to result in CL,[10] where excited zinc(II)–porphyrin moiety served as the emitter.

The standard experimental procedure† is described in detail elsewhere.[14,15] It has been found that, unlike the reactions with inorganic salts of Fe^{II},[8,9] decomposition of all of the TOXs studied in the presence of Cp_2Fe is a catalytic process. In fact, according to iodometric titration data, reactions of TOX (10 mmol dm^{-3}) with even small amounts of ferrocene ($[Cp_2Fe]_0$ = 0.05–1 mmol dm^{-3}) result in nearly complete (⩾ 95%) TOX decomposition in 2 h at 348 K in O_2 atmosphere. The conversion in thermal decomposition of these TOXs under similar conditions does not exceed 8%. Discovery of the catalytic action of Cp_2Fe appears important since catalytic redox reactions involving $Fe^{II/III}$ ions also occur in the living biosystem of the human organism.[5]

Taking into consideration the similar structures and chemical properties of TOX, the regularities of CL and the products of catalytic decomposition of TOX with ferrocene were studied for TOX **1** (Scheme 1), which gives the most intense CL, as an example. It has been found by spectral methods that TOX **1** decomposition affords ethyl 4-acetyl-5-oxohexanoate as the main (~70% according to GC MS) product.‡ Based on the charac-



Scheme 1

† The studied TOXs (99%) were synthesized at N. D. Zelinsky Institute of Organic Chemistry (Moscow) according to published procedure.[11,12] Ferrocene (Aldrich, 98%, 102-54-5), MeCN (Sigma-Aldrich, 99.8%, 75-05-8), Rhodamine 6G (Rd6G, Sigma, 989-38-8), 9,10-dibromoanthracene (DBA) and 9,10-diphenylanthracene (DPA) were of 'chemically pure' grade. Water and gases (Ar, O_2) were purified prior to use.[13]

A solution of TOX in MeCN (40 mmol dm^{-3}, 0.5 ml), a solution of Rd6G in H_2O (4 mmol dm^{-3}, 0.5 ml) or H_2O (0.5 ml) were loaded into a Pyrex reactor (d = 20 mm, V = 10 ml) in an argon or oxygen atmosphere. After that, the volume of the reaction solution was adjusted to 1.8 ml with water (0.5 ml) and MeCN (0.3 ml). Further, a solution of Cp_2Fe in MeCN (10 mmol dm^{-3}, 0.2 ml) was syringed through a penicillin stopper and, CL was recorded.

‡ *Ethyl 4-acetyl-5-oxohexanoate*. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.30 (m, Me), 1.60 (s, 2 Me), 1.95 (d, CH_2), 2.50 (m, CH_2), 2.71 (m, CH), 4.20 (m, CH_2). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 9.81 (s, 2 Me), 14.23 (s, Me), 19.12 (s, CH_2), 31.77 (s, CH_2), 58.20 (s, CH), 60.88 (s, CH_2), 172.37 (s, OCO). MS, m/z (%): 200 (1) $[M]^+$, 158 (15), 113 (37), 84 (23), 71 (15), 55 (15), 43 (100).

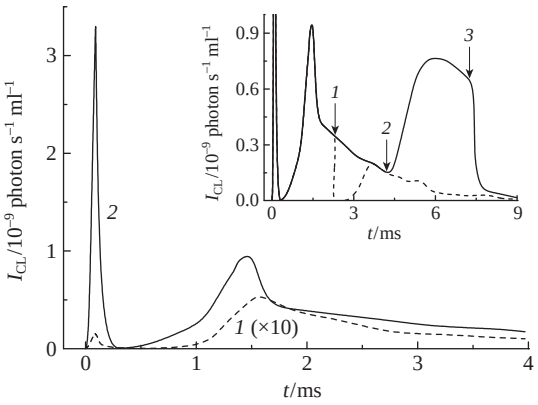


Figure 1 CL kinetic curves of TOX **1** (10 mmol dm^{-3}) with Cp_2Fe (1 mmol dm^{-3}) in aqueous MeCN (2 ml), (*1*) without and (*2*) in the presence of Rd6G (1 mmol dm^{-3}). *T* = 348 K. A chemiluminometer with a FEU-39 photomultiplier. The inset shows the effect of additives on the CL. The arrows point the following moments: ionol addition (*1*, dashed line); start of (*2*) oxygen or (*3*) argon bubbling. $[ionol]_0$ = 1 mmol dm^{-3}.

teristic[16] maximum at 616 nm in the UV absorption spectrum of the reaction solution, we detected an intermediate in ferrocene oxidation, namely, the Cp_2Fe^+ cation. At the same time, analysis of the IR and mass spectra of the products indicates that Cp_2Fe is not consumed during subsequent contact at $[TOX\ \mathbf{1}]_0$ = 10 mmol dm^{-3} and $[Cp_2Fe]_0$ = 1 mmol dm^{-3}. Decomposition of TOX catalyzed by Cp_2Fe gives weak CL (I_{max} = 5.6×10[8] photon s^{-1} ml^{-1} for TOX **1**). The shapes of the CL kinetic curves for all TOXs are similar. Each of them contains a narrow maximum and a broad one that appear at 1–2 and 20–30 min, respectively (Figure 1). Calculations[§] of CL quantum yields (φ_{CL}) have shown the highest value for TOX **1** [φ_{CL} = (3.4±0.2)×10^{-9}]. The φ_{CL} values for the other TOXs are much smaller [(5.2±0.2)×10^{-11}]. The CL spectrum of TOX **1** measured using cut-off-filters contains one diffuse maximum at 380±20 nm (Figure 2, curve *1*). The reaction solution does not display any PL at 298–348 K. However, at 77 K it was found to manifest weak phosphorescence (PS), the PS spectrum containing a broad maximum at 420–450 nm. The lifetime of the PS emitter is 1.8±0.1 ms. Various CL enhancers differently affect the CL of TOX **1**. In fact, addition of DBA (an enhancer of 'triplet' emitters[17]) increases the CL intensity more than twofold. The CL intensity does not change upon addition of DPA (an enhancer of 'singlet' emitters). Thus, based on the proximity of the maxima in the CL and PS spectra, identification of the nature of CL emitters using DBA and DPA, as well as the results of spectral analysis of products from reaction of TOX **1** with Cp_2Fe, one can conclude that it is ethyl 4-acetyl-5-oxohexanoate which is the CL emitter in TOX **1** decomposition. Relatively high yield of this product confirms that CL is truly due to formation of its excited state. Note that singlet oxygen $^1O_2$, which was repeatedly detected previously in other CL systems involving organic peroxides,[18] was not found in the system being studied.

Based on the results obtained, we believe that CL is generated as outlined in Scheme 1. First, electron transfer from Cp_2Fe to TOX occurs to give a ferrocenium cation and a TOX radical anion, which is similar to the first stage of CL-decomposition of peroxides by the known CIEEL mechanism.[19] Clarification of the details of the second stage will be a subject of our future studies.

As it is known,[8] the CL that accompanies TOX decomposition is considerably enhanced by Rd6G dye. In our case, addition of Rd6G also enhances the CL. In fact, the quantum yield of 'indirect' CL of TOX **1** in the presence of Rd6G (φ_{CL} = 1.3×10^{-7}) is 40 times higher than that of 'direct' CL (φ_{CL} = 3.4×10^{-9}) without Rd6G. In this case, the kinetic plots of direct and indirect CL are nearly symbate (see Figure 1). The latter fact indicates that the CL enhancement is of physical nature, *i.e.*, Rd6G is not involved in the chemical processes of TOX catalytic decomposition but only accepts energy from β-diketone. This is also confirmed by the close positions of the maxima in the spectra of enhanced CL (φ_{max} = 595±20 nm, Figure 2, curve *3*) and the PL of the reaction solutions before (λ_{max} = 573±2 nm, Figure 2, curve *4*) and after (λ_{max} = 578±2 nm, Figure 2, curve *5*) TOX **1** decomposition. The close values of the measured lifetimes of excited states of Rd6G in aqueous acetonitrile (8.7 ns) and in the reaction solution (8.1 ns) is an additional argument in favor of the physical nature of the CL enhancement.

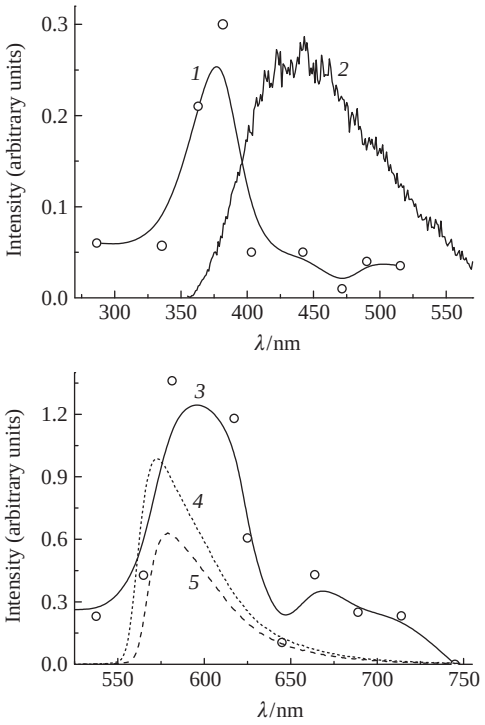
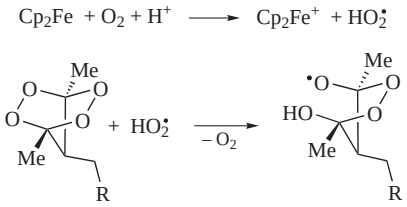


Figure 2 (*1*), (*3*) CL and (*2*), (*4*), (*5*) PL spectra measured upon decomposition of TOX **1** (10 mmol dm^{-3}) catalyzed by Cp_2Fe (1 mmol dm^{-3}) in aqueous MeCN solution (2 ml); (*1*), (*2*) without and (*3*)–(*5*) in the presence of Rd6G (1 mmol dm^{-3}). λ_{exc} is (*2*) 300 and (*4*), (*5*) 425 nm, *T* is (*2*) 77, (*4*), (*5*) 298 and (*1*), (*3*) 348 K.

On addition of ionol, a radical reaction inhibitor, the CL intensity decreases abruptly (down to zero). However, it is restored nearly to the original level after some induction period (see Figure 1). These effects indicate that CL emitters are generated in free radical reaction(s). In contrast, addition of oxygen (bubbling) results in an abrupt CL intensity increase. The promoting effect of O_2 is also clearly demonstrated by CL quenching on changing the atmosphere from O_2 to Ar. It means that oxygen or one of its reactive forms is involved in the processes of TOX decomposition or CL generation. One of these potential reactions is TOX decomposition catalyzed by the $HO_2^{\bullet}$ radical. The formation of $HO_2^{\bullet}$ in the reaction of Cp_2Fe with molecular O_2 in acidic medium was reported previously.[20] As it turned out, the pH value decreases from 3.5 to 3.0 during TOX **1** decomposition but is restored to 3.4 in 1.6 h. Hence, it can be concluded that electron transfer from Cp_2Fe to O_2 in the course of TOX decomposition results in $HO_2^{\bullet}$ radical that can catalyze TOX decomposition (Scheme 2).

In conclusion, the CL intensity and light sum increase proportionally to $[TOX]_0$ in the range studied (10^{-2}–10^{-8} mol dm^{-3}). Using the model TOX **1** as an example, the concentration range of TOX detection using Rd6G-enhanced CL was determined. This CL makes it possible to detect TOX **1** in a very broad concentration range, namely, 10^{-2}–10^{-12} mol dm^{-3}. Thus, owing to the high

[§] $\varphi_{CL} = S_{CL}\times10^3/[TOX]_0$, where φ_{CL} is the CL quantum yield and S_{CL} is the CL light sum (photon ml^{-1}).



Scheme 2

catalytic activity of Cp_2Fe and efficiency of CL enhancement by Rd6G, the CL method allows one to reach picomolar TOX detection limits.

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