Harnessing singlet-oxygen release through endoperoxide-decorated low molecular weight OTHO gelators

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Singlet-oxygen ($^1O_2$) therapy, where this highly reactive oxygen species is used as cytotoxic agent, has recently emerged as an alternative, less damaging treatment for certain types of cancer. In its current form as photodynamic therapy (PDT), it involves the photogeneration of $^1O_2$ in situ from oxygen present at the target region.[1] Its main drawback involves the reliance on the presence of oxygen on the tumor, as hypoxic regions (naturally present or induced by PDT) are immune to the treatment. Endoperoxides (EPOs), consisting in $^1O_2$ reversibly binded to organic moieties such as 9,10-diphenylanthracene (DPA), are an effective solution to hypoxia, although dosage remains a challenge due to difficulties controlling diffusion.[2] In this work, we developed EPO carriers based on supramolecular gels to provide spatiotemporal control over $^1O_2$ release. The oxotriphenylhexanoate (OTHO) gels are prepared through a modular stereoselective multicomponent process (Figure 1),[3] which constitutes a significant advantage over state-of-the-art EPO supports. Thus, we present a series of OTHOs with DPA-based EPOs and their rheological and $^1O_2$ release profile, showcasing the diffusion-limiting effect of the gel matrix.[4]

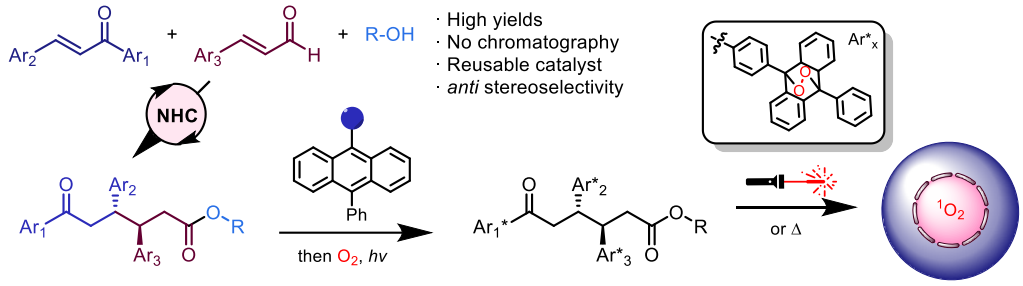

Figure 1. Multicomponent preparation of EPO-OTHOs and release mechanics

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