

Anionically induced decomposition of 2-ethoxycarbonylprop-2-enyl peroxides

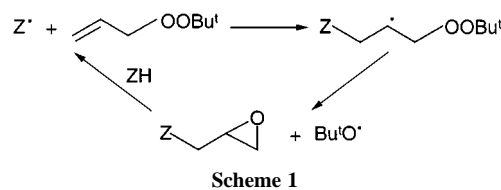
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Treatment of 2-ethoxycarbonylprop-2-enyl peroxides with potassium alkylperoxylate, the sodium enolate of diethyl malonate and a primary or secondary amine yields epoxides *via* a two-step process: (i) addition of the nucleophile to the acrylic unsaturated bond and (ii) intramolecular anionic substitution on the peroxidic bond.

2,3-Epoxy esters are useful synthons, in particular for the production of 2-, 3-, 2,3-di-hydroxy and 3-amino-2-hydroxy esters.¹ The general methods of synthesis are the Darzen's condensation² and the various epoxidations² of 2,3-ethylenic esters. Many years ago the formation of epoxides was identified³ in the homolytically induced decomposition of allyl *tert*-butyl peroxide. Subsequently, the free radical addition of reactive hydrogen donor solvents to allylic peroxides was used to prepare functionalised epoxides^{4,5} (Scheme 1). Such a reaction, applied to acrylic peroxy derivatives, led to the formation of an epoxide with the simultaneous creation of a C–C bond, affording a new method for generation of 2,3-epoxy esters.⁶ However, in some cases, synthetic interest in this reaction was limited by the formation of a mixture of several epoxides in low yields. For example, an attempt to prepare 1-ethoxycarbonyl-1-[2,2-bis(methoxycarbonyl)ethyl]oxirane⁷ by free radical addition of dimethyl malonate to *tert*-butyl 2-ethoxycarbonylprop-2-enyl peroxide **1** failed mainly for two reasons:⁷ (i) both possible radicals were generated from dimethyl malonate by hydrogen abstraction by radicals Bu^o· and Me· and (ii) inefficient addition of the electrophilic radical ·CH(CO₂Me)₂ to the electron-poor double bond of the acrylic peroxide.

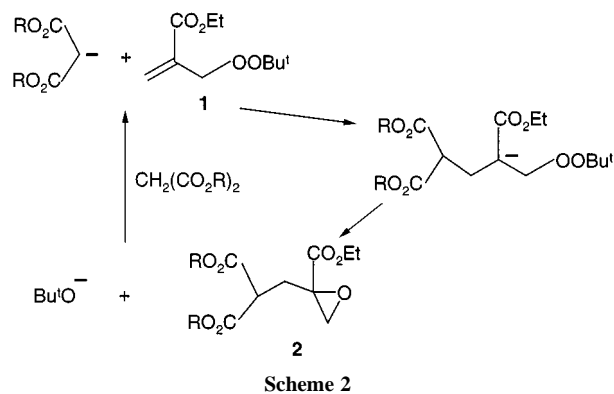
The selective production of the desired radical from dimethyl malonate was brilliantly solved by Roberts *et al.*⁸ by application of reverse polar effects resulting from the addition of an aminoborane to the medium in the induced decomposition of allyl *tert*-butyl peroxide. Following the same approach and considering the existence of an *umpolung* effect on changing from the radical (electrophilic) to the anion (nucleophilic)⁹ we designed an anionic-induced decomposition of **1** to produce epoxides **2** (Scheme 2). Indeed, the Michael addition¹⁰ of [−]CH(CO₂Et)₂ to ethyl acrylate suggested a possible addition of this carbanion to the unsaturation of **1**. The formation of an epoxy peroxide as a by-product in the synthesis of **1**¹¹ has to be considered as a good argument in favor of the feasibility of the intramolecular attack of the O–O bond, even if Yang and Finnegan¹² identified the adduct peroxide in the addition of Bu^oOOH to ethyl acrylate under basic conditions. The capacity of the *tert*-butoxide anion to abstract a proton from malonate would make this anionic-induced decomposition a chain process. The validity of this proposal was verified *via* the

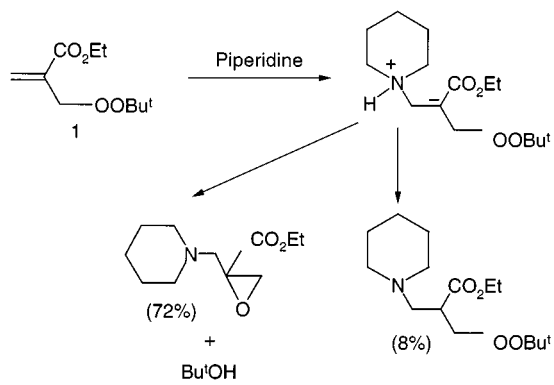
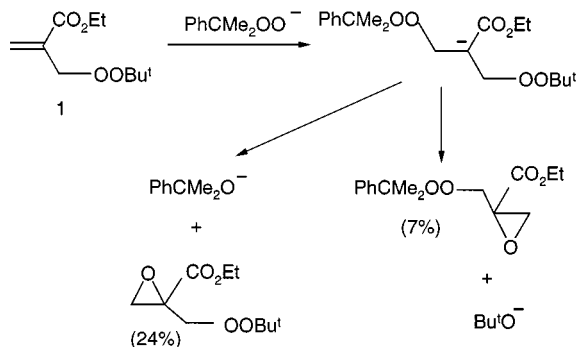


formation of **2** (R = Et, yield 60%) by the addition of 1 equiv. of peroxide **1**, at -10°C , to a THF solution of diethyl malonate, previously treated with 0.1 equiv. of NaOEt.

The success of this reaction, the first synthetic example of an anionic decomposition of an allylic peroxide, prompted us to extend this work to other nucleophiles with the objective of gaining a better knowledge of its mechanism. The possible existence of either a concerted, or a two-step process must be considered. The simple way to prove that the adduct carbanion was a real intermediate was to offer it a chance to take a pathway other than the S_Ni reaction on the *tert*-butylperoxy group. This was arranged in the anionically induced decompositions of peroxide **1** induced by the potassium cumylperoxide anion, with the formation of two different epoxy peroxides, or by piperidine with the simultaneous production of an amino peroxide and an amino epoxide (Scheme 3). In the addition of potassium *tert*-butylperoxide to peroxide **3** the generation of two peroxy epoxides (Scheme 4) confirmed the existence of a general two-step process for the anionic-induced decomposition of unsaturated peroxides.

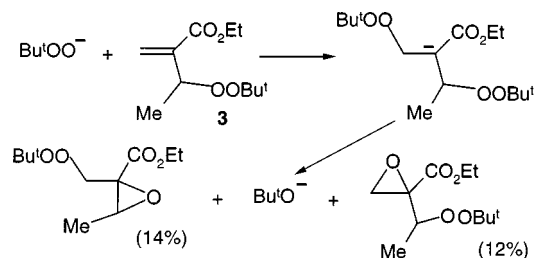
These preliminary results showed that allylic peroxides having an electron-poor double bond can suffer an anionically-induced decomposition consisting of two steps: (i) Michael addition of a nucleophile to the unsaturation and (ii) S_Ni reaction on the peroxidic function. Such steps may be part of a chain mechanism if the eliminated alkoxide is sufficiently basic to regenerate the nucleophile by proton abstraction from NuH, as in the reaction using diethyl malonate or an hydroperoxide; then only catalytic amounts of base are necessary. In the case of amines there is no need for a base because the nucleophile is provided by the lone pair of the nitrogen atom. The third case of interest appears to be when the eliminated alkoxide is not efficient enough to produce the nucleophile: it is then necessary to provide a stoichiometric amount of nucleophile to react with the unsaturated peroxide. This last possible induced decomposition was checked using ethyl 2-methylpropanoate as the precursor of the nucleophile,¹³ the base being LDA. The addition at -78°C of a THF solution of Me₂C–CO₂Et¹³ to peroxide **1** afforded after classical treatment the expected epoxy diester in a yield of 74%.





Scheme 3

In conclusion, anionically-induced decomposition of unsaturated peroxides having electron-poor double bonds by an addition- $\text{S}_{\text{N}}\text{i}$ process was clearly identified for the first time and appears a promising way to obtain oxygenated heterocycles such as epoxides (these reactions are currently under study in our group). This approach complements the homolytically induced decomposition of such unsaturated peroxides according to the *umpolung* effect identified in the replacement of a radical by the corresponding anion.



Scheme 4

Notes and References

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