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Novel Ring Enlargement of Cyclobutane Derivatives by Oxidative Radical Decarboxylation[1]

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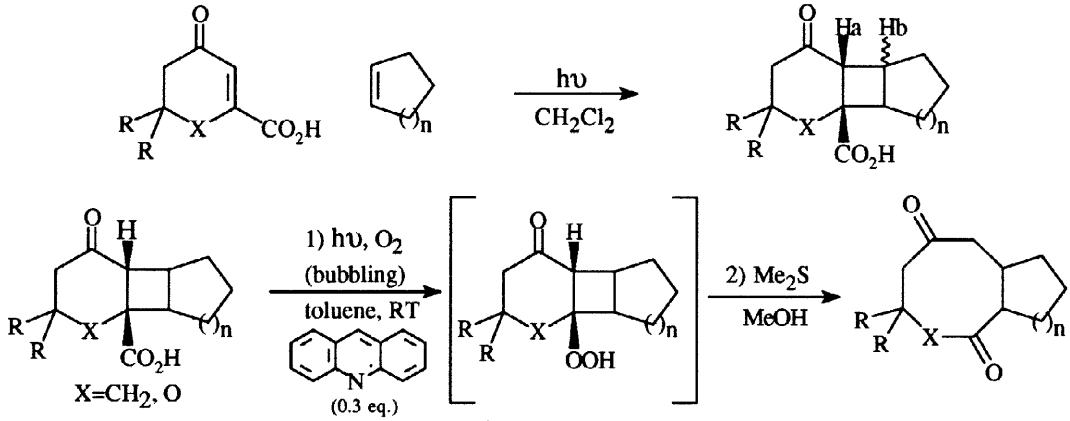
Abstract:

Cycloadducts obtained via [2+2] photocycloaddition between an unsaturated oxoacid and cycloalkene are readily opened by irradiation at 366nm, in the presence of catalytic amounts of acridine in toluene and under an oxygen atmosphere, leading after treatment with dimethylsulfide to the formation of polycyclic diketones or ketolactones.

Keywords: Decarboxylation, ring transformations, cyclobutanes, acridines.

Cyclobutane framework represent important intermediates for the synthesis of natural products.[3] In connection with our work devoted to the photochemistry of unsaturated oxoesters and oxoamides[4,5] we were interested to develop new efficient procedures to realize the ring enlargement of [2+2] cycloadducts. We have previously reported the use of TMS-I to obtain spiranic adducts and also reductive conditions to promote selective C-C bond cleavage[4] and subsequent formation of medium-size rings. In this communication, we report a new two step photochemical process which allows from oxoacids, an easy access to polycyclic compounds (Scheme 1).

Irradiation in methylene chloride of oxoacids and a slight excess of a cycloalkene afforded in few hours and in quantitative yields a *cis-anti-cis* / *cis-syn-cis* mixture (85/15) of the expected [2+2] cycloadducts.[6] After concentration, the cyclobutane carboxylic acids were irradiated in toluene in the presence of small amounts of acridine (0.3 eq) with continuous bubbling of oxygen, according to a decarboxylation procedure already described for linear or aromatic carboxylic acids toward the formation of the corresponding alcohols.[7]



Scheme 1

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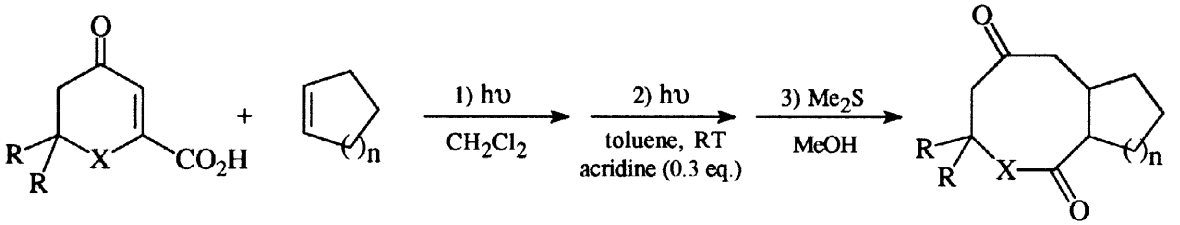
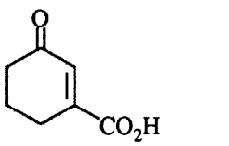
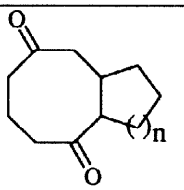
Under these conditions, we were able to obtain bicyclic diones ($X=CH_2$) and ketolactones ($X=O$) *via* the presumably formation of a cyclobutane hydroperoxide intermediate which could be first reduced by action of dimethylsulfide. Therefore the cyclobutanol formed underwent a ring enlargement *via* a retroaldol process. The reaction has been applied to different substrates and the results are summarized in the following table.[8] This reaction corresponds to a formal and well known [2+2] de Mayo's cycloaddition process.[9] However, it is important to note that in our case, a rapid access to bicyclic medium-ring ketolactones is possible from the readily available 4-oxa-oxoacides.

Table: *Ring enlargement of [2+2] cycloadducts by oxidative decarboxylation.*



	n=1		48%
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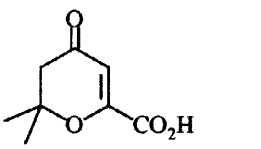
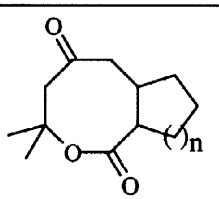
	n=1		48%
	n=2		32%

In conclusion, the radical decarboxylation of adducts derived from the cycloaddition of an unsaturated oxoacid and a cycloalkene can be readily achieved by using acridine as activator. Performed in the presence of oxygen, a new ring-opening procedure takes place *via* a retroaldol process leading to the formation of bicyclic diketones or ketolactones.

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Typical procedure: A solution of the oxoacid (60 mmol) and the cycloalkene (300 mmol) in CH_2Cl_2 (120ml) was irradiated at 366 nm and at RT. After complete disappearence of the starting material (TLC control), the solvent and excess of alkene were removed by concentration giving a mixture of *syn/anti* cycloadducts which was purified by chromatography on silica. The cyclobutane carboxylic acids (10 mmol) were then dissolved in toluene (60 ml) containing acridine (3 mmmol). The resulting solution was bubbled with O_2 and irradiated at 366nm for 12h. Toluene was removed by distillation and the crude mixture was then dissolved in MeOH (10 ml) and stirred overnight with Me_2S (1 ml). After concentration under vacuum, the product was purified by flash-chromatography (AcOEt/hexanes: 20/80).

References and notes:

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