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Photochemical reductive desulfonylation of β-ketosulfones by ascorbic acid

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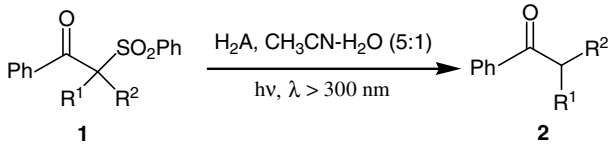
Abstract—Photoinduced electron-transfer reaction between excited β-ketosulfones and ascorbic acid provides an efficient and green approach for the desulfonylation of β-ketosulfones.

β-Ketosulfones are useful intermediates in organic synthesis.[1] The sulfonyl group can stabilize the adjacent carbanions, thus facilitating the carbon–carbon bond formation via alkylation or condensation reaction. However, the usefulness of the sulfonyl group is dependent, in most cases, on the ease of its subsequent removal from the molecule.[2] Several reducing agents, such as Al(Hg),[3] Zn/HOAc,[4] Bu_3SnH,[5] $Na_2S_2O_4$,[6] Mg/MeOH,[7] SmI_2,[8] and $TiCl_4$–Zn,[9] have been used to accomplish this desulfonylation. Desulfonylation of β-ketosulfones could also be realized under photochemical conditions with Hantzsch ester in pyridine in the presence of Ru(II).[10]

Ascorbic acid (vitamin C) is a well-known natural antioxidant, which has been widely used in people's daily life for treatment and prevention of various diseases. The structure of ascorbic acid, which features a 2,3-enediol group on a five-membered lactone ring, renders it an effective electron donor in single electron-transfer reactions. However, only limited reports have appeared in the literature dealing with the application of this compound in organic synthesis.[11,12] Pandey et al.[11] and others[12] have successfully used ascorbic acid as a primary and/or secondary and sacrificial electron donor in synthetically useful photoinduced electron-transfer (PET) reactions. In our ongoing research program on the synthetic potentials of PET reactions,[13] we found that when α-phenylsulfonyl acetophenone derivatives (**1**) were irradiated in the presence of ascorbic acid (H_2A), the reductive desulfonylation could take place effectively (Scheme 1).



1 **2**

Scheme 1.

In a typical procedure, a mixture of α-phenylsulfonyl acetophenone (**1a,** 1 mmol) and H_2A (3 mmol) was irradiated in CH_3CN–H_2O (5:1, 20 mL) with a Pyrex-filtered high-pressure mercury lamp ($\lambda > 300$ nm) under an argon atmosphere at ambient temperature. After completion of the reaction as monitored by TLC, the solvent was removed under reduced pressure and the product **2a** was isolated from the residue by chromatography over silica gel in 88% yield (Table 1, entry 1). No reaction took place in the absence of H_2A under the otherwise same conditions. This method worked well with a variety of α-substituted substrates (**1b**–**g**), and the double bond or triple bond incorporated in the substrates (**1c**–**e**) was left intact under the photoreductive conditions (Table 1, entries 3, 4 and 5). Desulfonylation of α-disubstituted **1g** was also achieved in high yield (entry 7).

It is believed that the reaction proceeded via a photoinduced electron-transfer mechanism as illustrated in Scheme 2. In the scheme the electron transfer from ascorbate to the excited β-ketosulfone (**1**) produces

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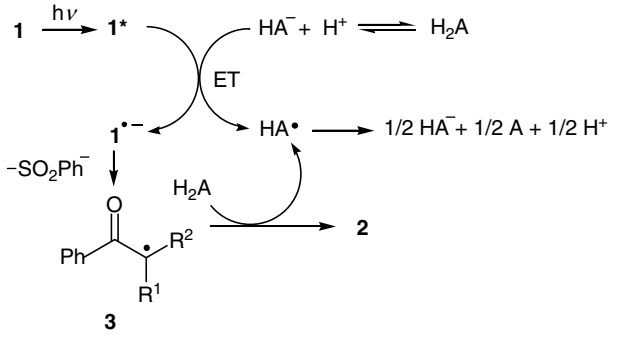
Table 1. Photoinduced desulfonylation of β-ketosulfones **1** by ascorbic acid[a]

Entry	Substrate **1**			Time (h)	Product **2**	Yield (%)[b]
		R^1	R^2			
1	**1a**	H	H	4	**2a**	88
2	**1b**	H	Me	10	**2b**	96
3	**1c**	H	$H_2C{=}CHCH_2$	15	**2c**	94
4	**1d**	H	$HC{\equiv}CCH_2$	15	**2d**	90
5	**1e**	H	$(CH_3)_2C{=}CHCH_2$	24	**2e**	75[c]
6	**1f**	H	$PhCH_2$	15	**2f**	98
7	**1g**	Me	Me	12	**2g**	89

[a] The reaction conditions see text.
[b] Isolated yields. All products are known compounds and were characterized by EI-MS, ^1H and ^{13}C NMR.
[c] 15% **1e** was recovered after irradiation.

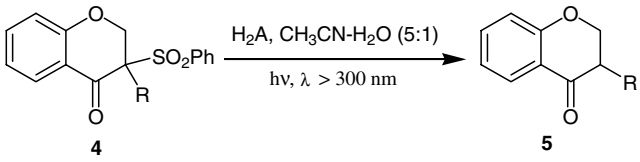


Scheme 2.

ascorbic acid radical HA· and the radical anion of **1**. It is well known that the formation of radical ions would remarkably weaken the chemical bond in the species,[14] hence the mesolystic cleavage[15] of the radical anion of **1** facilitates the desulfonylation. The α-ketone radical (**3**) thus formed abstracts a hydrogen atom from ascorbic acid, producing the corresponding ketone **2**. HA· would disproportionate to dehydroascorbic acid (A) as reported in the literatures.[11a,b,16]

The present desulfonylation method can also be applied for the synthesis of 3-substituted chromanones. It has been reported that the alkylation of 3-phenylsulfonyl-4-chromanone at the 3-position provides a facile approach for the synthesis of 3-substituted chromanones, which constitute an important class of biologically active compounds.[17] The necessity of using 3-phenylsulfonyl substituent to activate the adjacent 3-carbon for alkylation is due to the fact that the direct alkylation of 4-chromanone gave quite unsatisfactory result. For this purpose, several 3-substituted-3-phenylsulfonyl-4-chromanones (**4**) were prepared according to the literature procedure,[17a] then the phenylsulfonyl group was removed using the protocol described above, giving corresponding 3-substituted chromanones (**5**) in high yield (Scheme 3 and Table 2).

In summary, a simple photochemical method employing ascorbic acid as the reducing agent has been developed for the desulfonylation of β-ketosulfones. The reaction



Scheme 3.

Table 2. Photochemical desulfonylation of 3-phenylsulfonyl-4-chromanones **4** by ascorbic acid[a]

Entry	Substrate	R	Time (h)	Product	Yield (%)[b]
1	**4a**	H	6	**5a**	86
2	**4b**	Me	8	**5b**	90
3	**4c**	$H_2C{=}CHCH_2$	10	**5c**	81
4	**4d**	$HC{\equiv}CCH_2$	10	**5d**	85
5	**4e**	$PhCH_2$	12	**5e**	84

[a] The reaction conditions were the same as those for desulfonylation of **1**, see text.
[b] Isolated yields. All products are known compounds and were characterized by EI-MS, ^1H and ^{13}C NMR.

is advantageous in terms of nontoxicity and mild conditions. It is expected that more applications could be found for using ascorbic acid as a reducing agent in organic synthesis.

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