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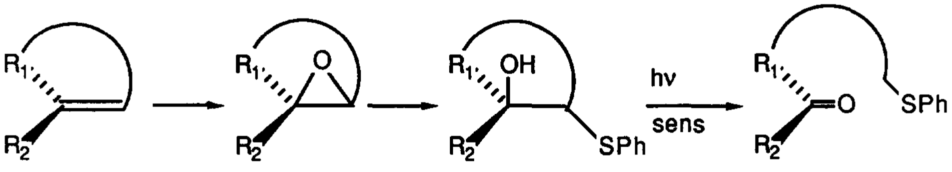
PHOTOSENSITIZED CLEAVAGE OF β-PHENYLTHIOALCOHOLS: A SYNTHETICALLY USEFUL INDIRECT REDOX CLEAVAGE OF THE OLEFINIC BOND

D. Gravel*, L. Farmer, C. Ayotte.
Département de Chimie, Université de Montréal.
Montréal, Québec, H3C 3J7, Canada.

Abstract : *This paper reports the preparative photosensitized redox cleavage of β-phenylthioalcohols derived from epoxides to give carbonyl and thioether functionalities in mostly fair to excellent yields. The method potentially represents the first synthetically viable methodology to effect, albeit indirectly, the redox cleavage of olefins.*

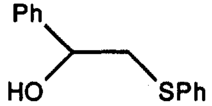
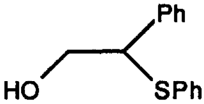
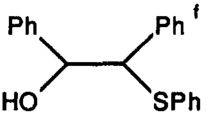
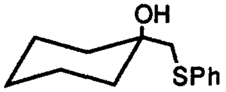
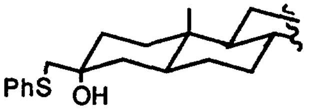
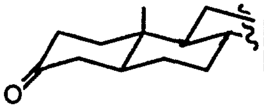
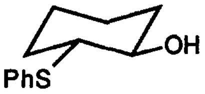
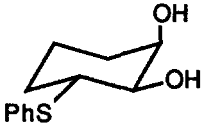
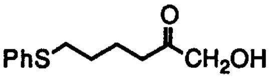
A number of preparative methods are available to cleave the olefinic bond, however, apparently all of these are oxidative at both carbon centers with exception of the retroaldol type reactions. To our knowledge, there is presently no viable methodology in the arsenal of synthetic organic chemistry to carry out the cleavage of an isolated double bond in a redox fashion. It occurred to us that such a method could be developed based on the known electron transfer quenching of excited acceptors by amines[1] and thioethers[2]and, more specifically, the photosensitized redox decarboxylation of heterosubstituted carboxylic acids[3] of the type $RXCH_2COOH$ (where X= O, S, NH) and redox fragmentation of 2-(N-aryl) aminoethanols[4]. This latter reaction, first reported by Davidson[4], constitutes an indirect redox cleavage of the olefinic bond which, however, was not developed as synthetic methodology probably because of the inherent limitations of the substituted amino group. The advantage of β-phenylthioalcohols proposed here should be twofold: 1) efficiency of preparation by formation [5] and ring opening [6] of epoxides and 2) versatility of the phenylthio auxiliary to give access to an array of functional groups due to its multifaceted reactivity and ease of hydrogenolysis.



Based on the above precedents, it was therefore anticipated that β-phenylthioalcohols could be cleaved in a redox fashion to yield carbonyl and thioether functionalities. In the case of terminal or exocyclic methylenes, the sequence should yield the corresponding ketones or aldehydes accompanied by thioanisole while, in the case of endocyclic olefins, a phenylthioalkyl aldehyde or ketone should be obtained.

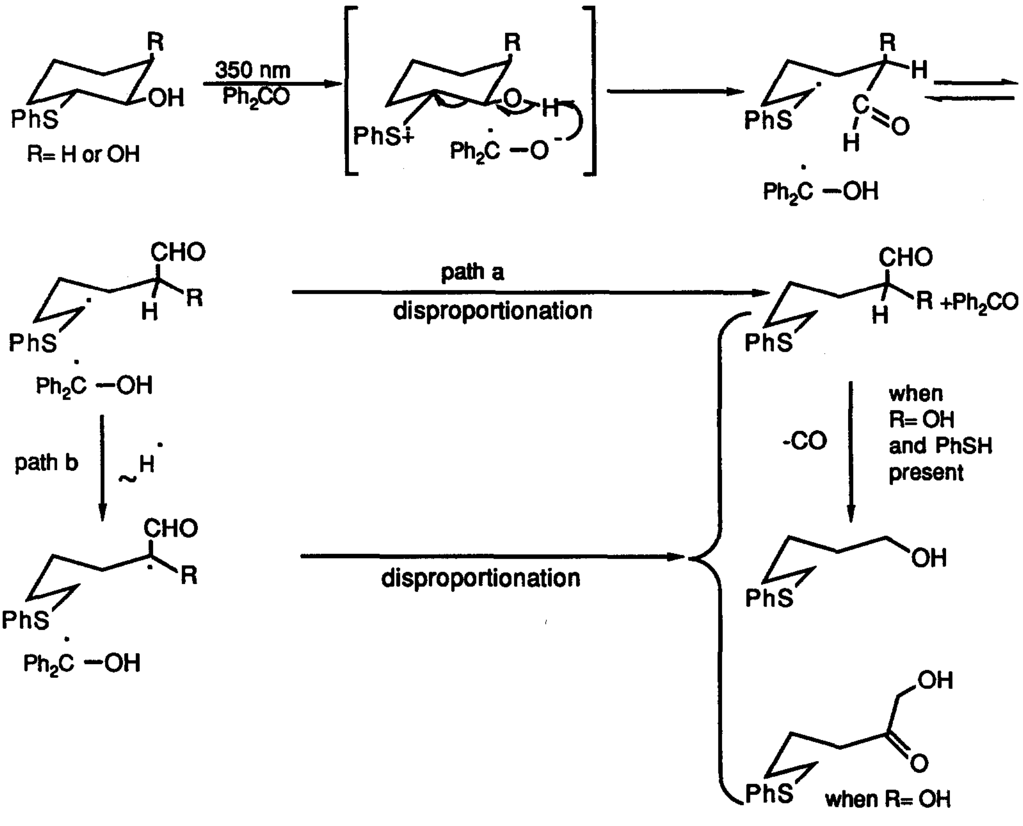
Consequently, a series of β-phenylthioalcohols (yields ranging from 72 to 90%) accessible from precursor epoxides (yields ranging from 78 to 95%) was generated to test this photochemical hypothesis and its applicability as a synthetic tool. As can be seen from the entries reported in Table 1, irradiation at 350 nm of acetonitrile solutions of the β-phenylthioalcohols containing one equivalent of benzophenone [7] as sensitizer gives from mostly fair to excellent yields of the cleaved compounds. In the case of terminal or exocyclic methylenes (entries 1-5), cleavage of the corresponding phenylthioalcohols gives excellent yields of carbonyl compounds (entries 1, 4, 5), taking into account the volatility of

Table 1. Benzophenone Sensitized Redox Cleavage of β-Phenylthioalcohols [a].

Entry	Starting Phenylthioalcohol[b]	Rxn. time(h)[c]	Carbonyl Compound	Yield (%)
1		6.5	PhCHO	80[d]
2		5.0	HCHO	0[e]
3		4.0	PhCHO	63[d]
4		5.0		73[d]
5		3.5		93[g]
6		.75 ; 1.75 [h]		40 [g]; 75[g,h]
7		0.5		50[g,i]

a) All compounds prepared and isolated in this work were fully characterized by mass spectrometry and high resolution NMR. b) 1.77 mmol in 160 mL of degassed acetonitrile ; benzophenone sensitizer (1.0 eq.), generally recuperated in 56 to 100% yield except entry 2 where 33% was recuperated. c)Careful monitoring of the reaction is important. d) Yield evaluated by NMR. e) Cleavage α to sulfur due to α phenyl group. f) Erythro-threo mixture. g) Isolated yield. h) Thiophenol (1.0 eq.) was added. i) Contains trace of α-hydroxy-aldehyde tautomer ; changing solvent to benzene and adding thiophenol or acetic acid did not enhance the yield of hydroxyketone.

some of the products, but diminished yields when a phenyl stabilizing group is present α to sulfur (compare entries 2 and 3). In the case of endocyclic double bonds, cleavage of the corresponding phenylthioalcohol leads to lesser yields of the redox product (entries 6, 7) possibly because of further reaction of the carbonyl compound bearing the phenylthio auxiliary. This situation can however be corrected to a large extent by adding one equivalent of thiophenol (entry 6) which is known to substantially increase the yields in the photosensitized decarboxylation of heterosubstituted carboxylic acids by aromatic ketones [8]. This effect is however apparently not general since yields, in the case of the more complex phenylthiodiol of entry 7, could not be raised by applying the same method. A plausible explanation for the failure of added thiophenol to enhance the yield of hydroxyketone product in entry 7 may however be found in the mechanistic scheme represented below. This mechanism is based, in part, on the analogy of the present reaction with the well established photosensitized decarboxylation of α-heterosubstituted carboxylic acids[3] and fragmentation of 2-aminoalcohols[4].



In analogy with literature precedents[3,4], photolysis of either the phenylthioalcohol or diol should yield a radical ion pair which should undergo proton transfer accompanied by fragmentation to yield a radical pair. In the case where R=H, path a or path b could be followed irrespectively to yield the observed phenylthioalkylaldehyde (entry 6). Also, in this case, one should observe thiophenol catalysis which is supported by experimental facts (entry 6). In the case where R=

OH, it appears that path b takes precedence, because of the added influence of the OH group, to yield an α-hydroxyaldehyde radical which, upon reduction, can yield an enediol functionality which should collapse to a mixture of α-hydroxyaldehyde and α-hydroxyketone. Experimental results, in this case, show a trace amount of α-hydroxyaldehyde in the product (entry 7) but more importantly, in the case of thiophenol catalysis, the presence of an important amount (18%) of decarbonylation product. Since it is known that mercaptans do catalyse the decarbonylation of certain aldehydes [9], the above scheme appears fully consistent with the observed results. Further optimization work will therefore be attempted with other sensitizers and extension of the scope of the reaction to substrates bearing functional groups adjacent to the reaction site will be examined.

The following is a typical procedure for the photosensitized redox cleavage of β-phenylthioalcohols: A solution of 1.77 mmol of β-phenylthioalcohol and 1.77 mmol of benzophenone in 160 mL of degassed acetonitrile is irradiated, under argon, in a Rayonet Photoreactor at 350 nm using 8 pyrex test tubes on a Merry-go-Round adaptor. The resulting reaction mixture is carefully concentrated, in vacuo, to a product which is purified by flash chromatography using ethyl acetate-hexane mixtures as eluent.

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5. Epoxidation of isolated double bonds is efficient and general with yields generally ranging from 70-95% for MCPBA (Fieser and Fieser, "Reagent for Organic Synthesis" 1, 135 (1967)).
6. For Sn2 type reactions at carbon, the following nucleophilic order, which shows thiolates as outstanding nucleophiles, has been compiled : $RS^- > PhS^- > S_2O_3^- > (H_2N)CS > I^- > CN^- > SCN^- > OH^- > N_3^- > Br^- > ArO^- > Cl^- > C_5H_5N > AcO^- > H_2O$ (J. O. Edwards and R. G. Pearson, J. Am. Chem. Soc., 84, 16 (1962)
7. Of the different sensitizers tested (benzophenone, xanthone, fluorenone, 1,4-dicyanobenzene and chloranil) on trans-2-phenylthiocyclohexanol (entry 6), benzophenone and xanthone gave comparable results and the others, < 10% expected product or no reaction at all.
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