Tetrahedron Letters No. 19, pp 1667 - 1670, 1978. 0040-4039/78/0501-1667. $02.00/0.

DEHYDROGENATIVE SULFENYLATION OF CYCLOHEXANONES

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(Received in USA 27 December 1977; received in UK for publication 23 March 1978)

The sulfenylation of carbonyl compounds has attracted attention as a result of the diversity of applications for the resultant α-thiocarbonyl compounds in structural elaboration and modification[1]. The use of disulfides for such reactions is normally thought to be restricted to strong bases under aprotic conditions because of the known ability to reduce α-thiocarbonyl compounds back to the parent by thiolates in alcohol solvents[2]. We reported the ability to cleave cyclobutanones by sulfenylation in methanolic methoxide in which the reversibly-formed α,α-bis-sulfenylatedcyclobutanone intermediate suffers nucleophilically triggered fragmentation[3]. As a result of this study, we examined other cycloalkanones and determined the inertness of norbornanone. On the other hand, cycloheptanone underwent sulfenylation but not fragmentation--a reaction which suggests the feasibility of alkoxide bases in alcohol solvents as a potential method for the direct sulfenylation of ketones. Cyclohexanones undergo a remarkably mild aromatization accompanying sulfenylation to give o-phenylthiophenols which forms the subject of this letter. The fact that few methods are available to convert cyclohexanones to phenols makes this reaction of special interest[4].

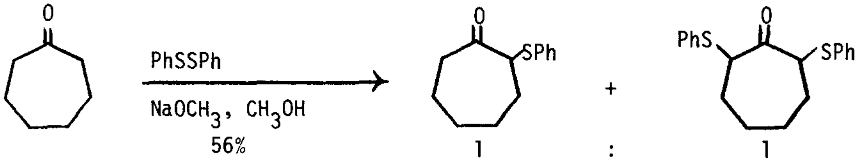
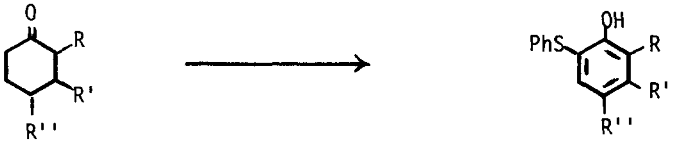


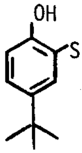
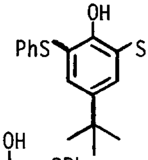
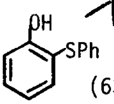
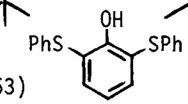
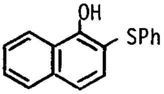
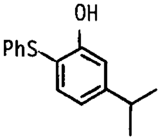
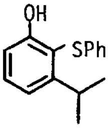
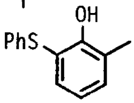
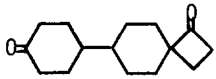
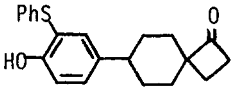
Table 1 and eq 1 summarize the examples of this new dehydrogenation procedure. The major



Eq 1

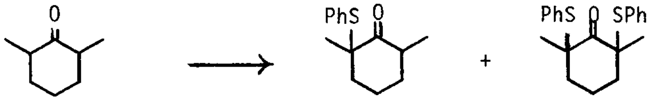
by-product observed is the bis-sulfenylated phenol. The ortho position of the phenylthio group was verified by 'H and ^{13}C nmr spectroscopy and, in some cases, comparison with data of known samples[5].

TABLE 1. Dehydrogenative Sulfenylation of Cyclohexanones[a]

Entry	Ketone	Time (hr)	Product	% Yield
1	4-t-butylcyclohexanone	72	**1**^{b,d}  (85)  (15)	74
2	cyclohexanone	40	**2**^{c}  (63)  (37)	56
3	tetralone	192	**3** 	42
4	3-isopropylcyclohexanone	18	 (80)  (20)	49
5	2-methylcyclohexanone	25		42
6		120	**4**^{e} 	67

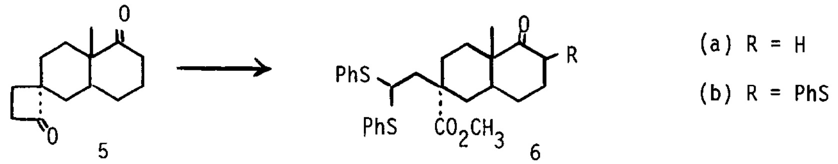
(a) A typical procedure involved refluxing a mixture of 1 mmol of ketone, 4 mmol of diphenyl disulfide and 6 mmol of sodium methoxide in 15 ml of methanol. (b) Mp 73-4°. (c) See ref 5a. (d) See ref 5b. (e) Mp 73-77.5°.

Only one alkyl group may be present at an alpha position. For example, 2,6-dimethylcyclohexanone led to a 4:3 mixture of mono- and bissulfenylated ketones, but no phenol. A 2,2-dialkylcycohexanone



Eq 2

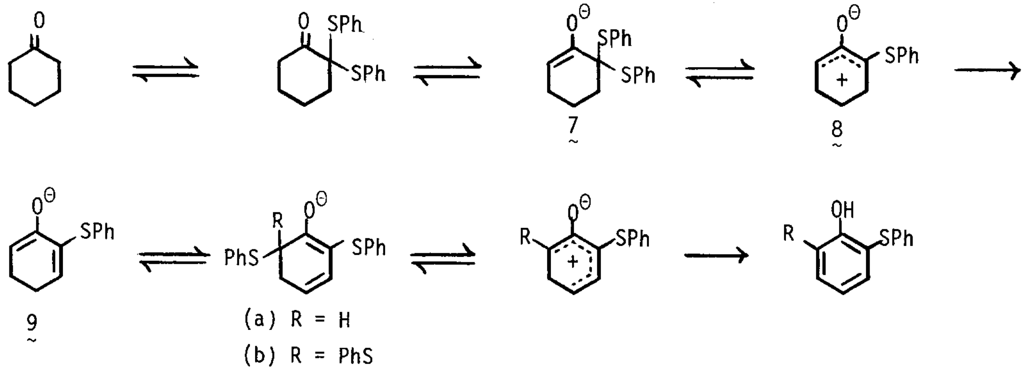
does not aromatize with dealkylation. Diketone **5** undergoes secosulfenylation unaccompanied by aromatization. On the other hand, dehydrogenative sulfenylation of cyclohexanones is normally much



5 6

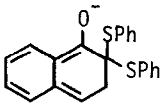
faster than secosulfenylation of cyclobutanones (see Table 1, entry 6).

Control experiments verify that the phenols related to the products do not undergo sulfenylation under these conditions in agreement with earlier observations[6]. In the case of tetralone, the intermediate mono- and bissulfenylated ketones were isolated and shown to convert to product. The extraordinarily long reaction times required in this case compared to the saturated cyclohexanones is noteworthy since normally monounsaturated systems aromatize more rapidly than their saturated analogs. A possible rationalization (eq 3) invokes a Favorskii-like reaction[7] which requires the



Eq 3

ability to form the bissulfenylated enolate 7 (or its enol) as a precursor to the zwitterion 8. This rationale nicely accommodates all of our observations especially the tetralone case since the generation of the equivalent of 7 (i.e. 10) requires loss of aromaticity. Support for this inter-



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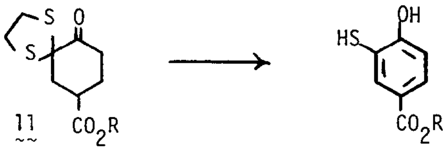

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pretation derives from the conversion of cyclopentanone to 2-phenylthiocyclopent-2-enone[8] which can be envisioned to involve the enol forms related to 7 - 9, the obtention of 2-arylthiocyclohex-2-enones by treating α-dialkylsulfonium cyclohexanones with sulfenimides[9], and the aromatization of ethylenedithiocyclohexanone 11 with base[10]--in the last case a Favorskii-like process was also invoked

This reaction provides access to ortho substituted phenols. The flexibility of the phenylthio group for further elaboration provides great opportunities. Desulfurization also provides entry to the parent phenols and thus would constitute one of the mildest methods for this transformation.

Acknowledgment. We wish to thank the National Science Foundation and the National Institutes of Health for their generous support of our programs.

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