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IODOMETHYL PHENYL SULFOXIDE: REACTIVITY AND SYNTHETIC APPLICATIONS

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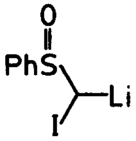
ABSTRACT: Lithio iodomethyl phenyl sulfoxides reacted with alkyl halides and carbonyl compounds to give adducts in good to moderate yields. Solvolysis of the carbonyl adducts led to sulfones or the ring expanded product.

We have recently demonstrated that α-chloro-, α-bromo- and α-fluoro-sulfinyl carbanions[1] could undergo alkylation and addition reactions to give synthetically useful intermediates. In this letter, we wish to report the result of our studies on the properties of the α-iodosulfinyl carbanion 1 and illustrates its potential in organic synthesis.

The lithio iodomethyl phenyl sulfoxide was successfully generated by the reaction of iodomethyl phenyl sulfoxide[2] with lithium diisopropylamide (LDA) in tetrahydrofuran (THF) at -78°C. The carbanion 1 was stable at -78°C for at least 3 hours but completely decomposed when left at -20°C for 2 hours. The anion reacted with electrophiles e.g. aldehydes, ketones and alkyl halides. The results are summarized in Table I.



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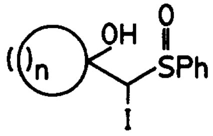

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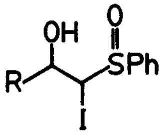

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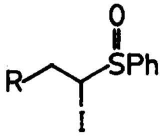

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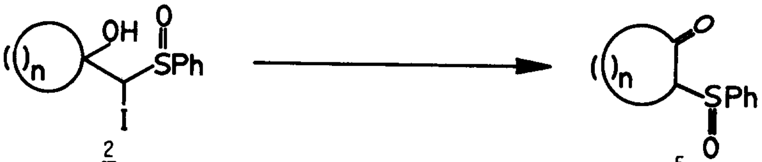
Table I

Electrophiles	Products, %
Cyclobutanone	2 (n = 3), 88
Cyclohexanone	2 (n = 5), 94
Cycloheptanone	2 (n = 6), 90
Ethyl methylketone	2 $(CH_2)_n$- = Me-, Et- , 83
n-hexanal	3 (R = C_5H_{11}-), 67
3,4-Dimethoxybenzaldehyde	3 R = 3,4-$(MeO)_2C_6H_3$- , 42
Methyl iodide	4 (R = H), 57
Benzyl bromide	4 (R = C_6H_5-), 24

The addition reaction between the carbanion 1 with carbonyl compounds was carried out at -78^{0}C in THF for 2 hours. The reaction was quenched with saturated ammonium chloride and the product β-hydroxy-α-iodomethyl phenyl sulfoxide 2 or 3 was isolated with chloroform. For the alkylation process, after much experimentation, it was found that the reaction could be effected by the addition of alkyl halides to the THF solution of 1 at -78^{0}C in the presence of hexamethylphosphotriamide. The mixture was stirred at this temperature for 20 minutes before being warmed to room temperature and then stirred overnight. The reaction was quenched with saturated ammonium chloride and the product was isolated with chloroform.

Solvolysis of the products[3] 2 (n = 3,5,6) derived from cyclic ketones was studied with the aim of effecting the one-carbon ring expansion reaction, equation (1).



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n = 3,5,6

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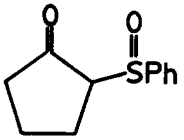
The reaction of 2 in silver nitrate/95% ethanol at 85^{0} for 3 hours gave compounds 6 (13% yield, from 2, n =3), 7 (21%) and 8 (18%) (from 2, n = 5), 10 (20%) and 11 (12%) (from 2, n = 6).



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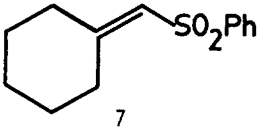

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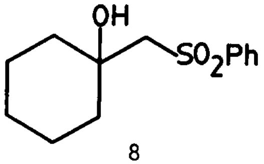

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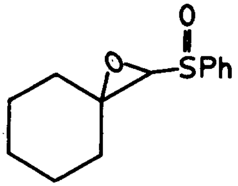

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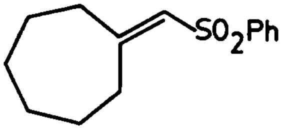

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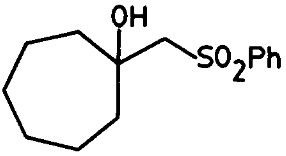

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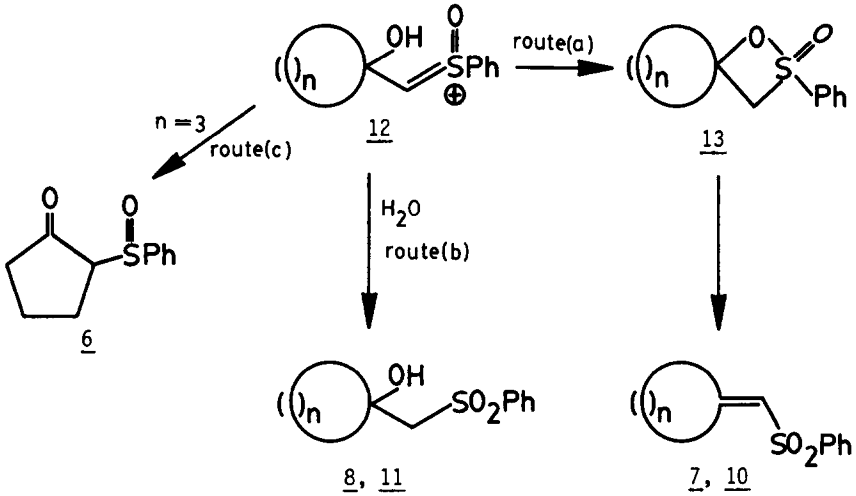
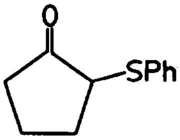
The formation of products 6, 7, 8, 10 and 11 could be accounted for by involving the intermediacy of phenylsulfinyl carbenium ion 12 during the solvolysis. Route (a) involves the formation of the cyclic sulfoxonium intermediate[4] which collapsed to give the vinyl sulfones 7 and 10. The competitive attack by water [route (b)] on the intermediate 12 gave the β-hydroxysulfones 8 and 11. The possibility that 7 and 10 were formed by simple dehydration of the corresponding 8 and 11 were ruled out by the fact that when 8 and 11 were subjected to the same solvolytic conditions, no vinyl sulfone 7 and 10 could be detected. Route (c), n = 3, gave the ring expanded



product exclusively. Our results give further supporting evidence for the formation of the phenylsulfinyl carbenium ion as first proposed by Venier *et al.*[3]. Additional evidence for the formation of 12 was obtained by carrying out the solvolysis in absolute ethanol-silver nitrate, in which case, the products obtained were 7 (43%) and 9 (19%) (from 2, n = 5), and 10 (53%) (from 2, n = 6). No β-hydroxysulfones 8 and 11 were detected.

The release of ring strain in the case of solvolysis of 2 (n = 3) led to the formation of compound 6 as the sole product[5]. However, the low yield of 6 (13%) was rather disappointing. The usefulness of iodomethyl phenyl sulfoxide as a one-carbon ring expansion reagent was greatly improved when we discovered that upon treating compound 2 (n = 3) with $TiCl_4$/Zn in ether/methylene chloride[6], α-phenylsulfenylcyclopentanone was isolated in 62% yield. Presumably, the reaction involves the intermediate thionium ion 15[6,7]. When the β-hydroxy-α-chloro compound[8] 16 was subjected to the same reaction conditions as 2 (n = 3), 14 was isolated in 52% yield. The process represents a potentially useful route to cyclopentanones.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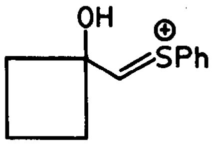
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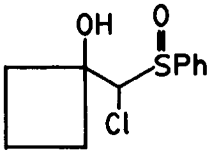
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Our result indicated the potential applications of iodomethyl phenyl sulfoxide in organic synthesis. It also revealed the novel chemistry of the derived intermediates.

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