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# α-Sulfinyl Carbenoid: One-Carbon Homologation of Ketones to α-Sulfinyl Ketones Using Chloromethyl Phenyl Sulfoxide

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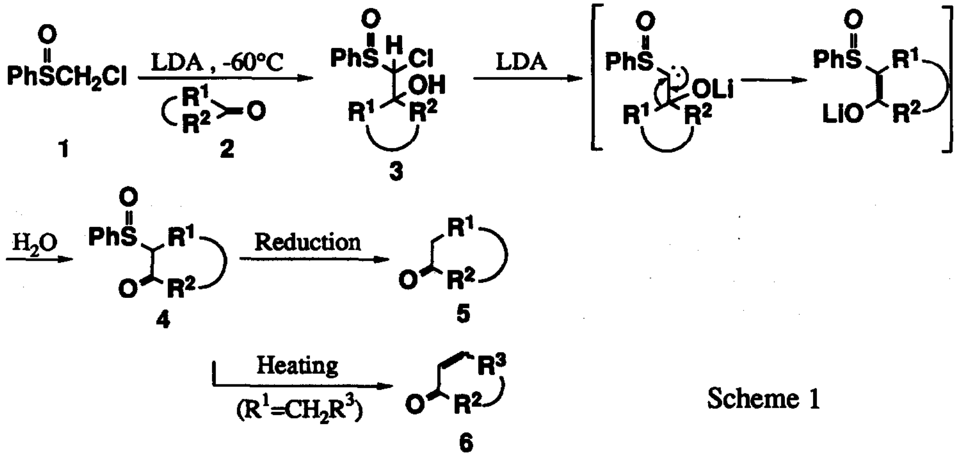
Key words: sulfoxide; chloromethyl phenyl sulfoxide; α-sulfinyl carbenoid; α-sulfinyl ketone; ring enlargement

*Abstract: Addition of the carbanion of chloromethyl phenyl sulfoxide to ketones gave the adducts, which were treated with lithium diisopropylamide to afford one-carbon homologated α-sulfinyl ketones via α-sulfinyl carbenoids in moderate to high yields.*

Carbenes and carbenoids have been recognized as useful intermediates in organic synthesis.[1] They are now frequently used in carbon-carbon bond forming reactions.[2] In the reaction of carbenoids, rearrangement of an alkyl group of β-oxido carbenoid is successfully used in ring expansion of cyclic ketones.[3]

Recently, we have reported some new methods for homologation of carbonyl compounds using 1-haloalkyl aryl sulfoxides.[4] In continuation of our studies on the use of 1-haloalkyl aryl sulfoxides in organic synthesis, here we report a new and versatile method for one-carbon homologation of ketones 2 to α-sulfinyl ketones 4 through α-sulfinyl β-oxido carbenoid (Scheme 1).

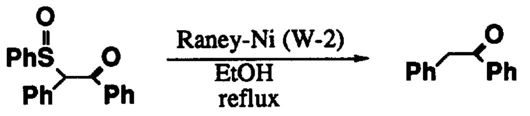


Scheme 1

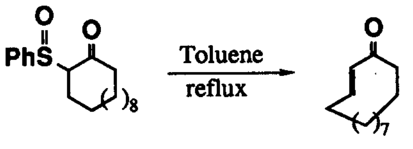
A typical experiment is reported for the synthesis of 2-(phenylsulfinyl)cyclopentanone (**4a**) (Table 1; entry a) from chloromethyl phenyl sulfoxide **1** and cyclobutanone. Treatment of **1** with 1.2 equivalents of lithium diisopropylamide (LDA) in THF at -60 °C gave a carbanion, which was reacted with cyclobutanone to give the adduct **3** ($R^1$, $R^2$= $-(CH_2)_3-$ ) as a single isomer (colorless crystals) in 92% yield. The adduct was again treated with 3 equivalents of LDA in THF at -60 to -50 °C for 1.5 h. Quite clean reaction took place and quenching the reaction with sat. aq. $NH_4Cl$ gave α-sulfinyl ketone **4a** in quantitative yield as a mixture of two inseparable diastereomers.

The results for the synthesis of α-sulfinyl ketones from ketones with one-carbon homologation are summarized in Table 1. This method is useful in the ring expansion of small ring compounds (entries a, b, h, and i). The method is also applicable to medium and large ring compounds; however, the yields are usually moderate (entries c-f). Acyclic ketones also gave α-sulfinyl ketones in moderate to good yields (entries j-l). When unsymmetrical ketones were used in this procedure, two regioisomers of the rearranged products were obtained (entries g, h, and k). As expected,[5] the phenyl group migrated faster than the alkyl group. By this method, 2-indanone gave 2-naphthol **7** in 61% yield (entry i). This product is thought to be produced by elimination of the sulfoxide from the ring expanded product, 3-phenylsulfinyl-2-tetralone, under these strong basic conditions.

The value of this method has been proved in the easy transformation of the produced α-sulfinyl ketones to ketones and α,β-unsaturated ketones under conventional conditions;[6] for example, reduction of the α-sulfinyl ketone **4l** with Raney-Ni (W-2) in ethanol afforded ketone **5** in good yield. Thermal elimination of the sulfinyl group of **4f** in refluxing toluene gave α,β-unsaturated ketone **6** in high yield.



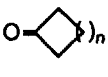
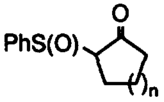
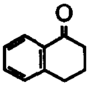
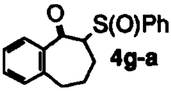
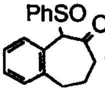
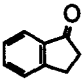
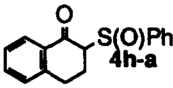
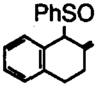
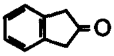
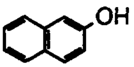
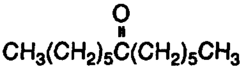
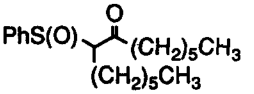
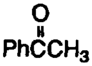
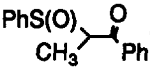
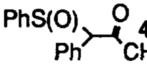
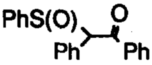
**4l** **5** (87%)



**4f** **6-E** (89%)

It is interesting to note that the intermediate of this rearrangement must be α-sulfinyl β-oxido carbenoid. A few examples of the ring expansion reaction through β-oxido carbenoid,[3] including α-sulfenyl carbenoid,[7] have been reported; however, to the best of our knowledge the α-sulfinyl β-oxido carbenoid reported in this paper is the first example of α-sulfinyl carbenoid[8] generated via α-elimination.

Table 1. One-Carbon Homologation of Ketones **2** to α-Sulfinyl Ketones **4** through Chloro Alcohols **3**

| Entry | **2** Ketone | | **3** Yield/%[a] | Condn.[b] | **4** Yield/%[a](%)[c] | |
|---|---|---|---|---|---|---|
| a |  | n=1 | 92 | A |  | **4a**(n=1) 95 |
| b | | n=2 | 82 | B | | **4b**(n=2) 81 |
| c | | n=3 | 91 | C | | **4c**(n=3) 47 |
| d | | n=4 | 76 | D | | **4d**(n=4) 38(47) |
| e | | n=7 | 85 | E | | **4e**(n=7) 52(73) |
| f | | n=9 | 83 | F | | **4f** (n=9) 51 |
| g |  | | quant.[d] | G |  **4g-a** 9 |  **4g-b** 68 |
| h |  | | 99[d] | H |  **4h-a** 21 |  **4h-b** 50 |
| i |  | | 88 | I |  **7** 61 | |
| j |  $CH_3(CH_2)_5\overset{\overset{O}{\|}}{C}(CH_2)_5CH_3$ | | 90 | J |  **4j** 61 | |
| k |  $Ph\overset{\overset{O}{\|}}{C}CH_3$ | | 88[d] | K |  **4k-a** 14 |  **4k-b** 61 |
| l |  $Ph\overset{\overset{O}{\|}}{C}Ph$ | | 87 | L |  **4l** 91 | |

a) Isolated yield. b) Unless otherwise noted, the reactions were carried out with 3.0 equiv. of LDA in THF: Conditions; A, -65 to -50 °C (1.5 h); B, -65 to -45 °C (2.5 h); C, -65 to 0 °C (2 h), then 0 °C (1 h); D, -65 to 0° C (2 h), then 0 °C (0.5 h); E, -60 to 10 °C (4 h); F, LDA (4.0 equiv.) was used and HMPA(4.0 equiv.) was added, -60 to -15 °C (3 h); G, -75 to -40 °C (1.5 h); H, -60 to -25 °C (1 h); I, HMPA(3.0 equiv.) was added, -60 to -30 °C (2 h); J, HMPA (3.0 equiv.) was added, -78 to -30 °C (3 h); K, -65 to -15 °C (3 h); L, HMPA(3.0 equiv.) was added, -70 to 0 °C (1.5 h), then 0 °C (0.5 h).

c) The yield in parenthesis was calculated based on the consumed starting material.

d) An inseparable mixture of two diastereomers. All other chloro alcohols **3** are single isomer.

The significant features of the presented procedure are as follows: a) the starting material **1** is easily obtainable from thioanisol in large quantity;[9] b) the yields of the addition of the carbanion of **1** to ketones are excellent; c) the method is applicable to both cyclic and acyclic ketones; d) the products, α-sulfinyl ketones, are easily transformed to ketones and α,β-unsaturated ketones. In conclusion, the method presented in this paper is very useful for one-carbon homologation of ketones.

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