Reactions of β-Heteroatom Substituted α,β-Unsaturated Ketones with Dimethylsulfonium Methylide

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β-Alkoxy- and β-alkylthio α,β-unsaturated ketones react with dimethylsulfonium methylide (DMSM) to give a furan, while β-anilino α,β-unsaturated ketones give the pyrrole. β,β-Bis(alkylthio) α,β-unsaturated ketones react with DMSM to afford the methylene inserted products, γ,γ-bis(alkylthio) β,γ-unsaturated ketones.

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Dimethylsulfonium methylide (DMSM) has received much attention for its reactivity towards several classes of electrophilic reagents (1). β-Heteroatom substituted α,β-unsaturated ketones (β-alkoxy, β-alkylthio and β-amino α,β-unsaturated ketones) are common synthetic intermediates used as protecting groups and for the introduction of functional groups (2). Also, there are many reports concerning the synthesis of several five-membered heterocycles from these compounds with nucleophilic reagents (3). We now report the reaction of β-heteroatom substituted α,β-unsaturated ketones with dimethylsulfonium methylide (DMSM).

Treatment of 1-phenyl-3-methoxy-2-buten-1-one (**1**) or 1-phenyl-3-ethylthio-2-buten-1-one (**2**) with DMSM in THF at 0° under an inert atmosphere gave 4-phenyl-2-methylfuran (**10**) in 26.5 and 28.5% yield, respectively (4). In the same manner, treatment of 1-phenyl-3-propylthio-2-propen-1-one (**3**) with DMSM gave 3-phenylfuran (**11**) (19%). On the other hand, reaction of 1-phenyl-3-anilino-2-propen-1-one (**4**) with DMSM afforded 1,3-diphenylpyrrole (**12**) (14%). The furans (**10** and **11**) were identified from ir and nmr spectra comparison with their authentic samples (5), and the pyrrole (**12**) was elucidated on the basis of spectral and elemental data.

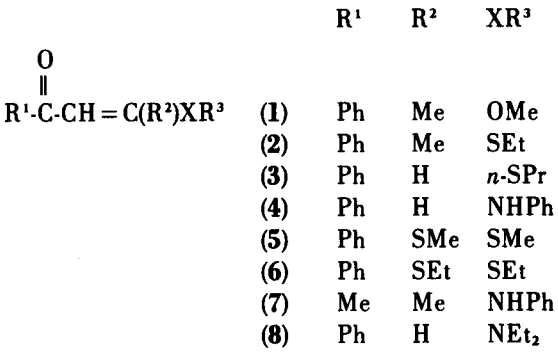
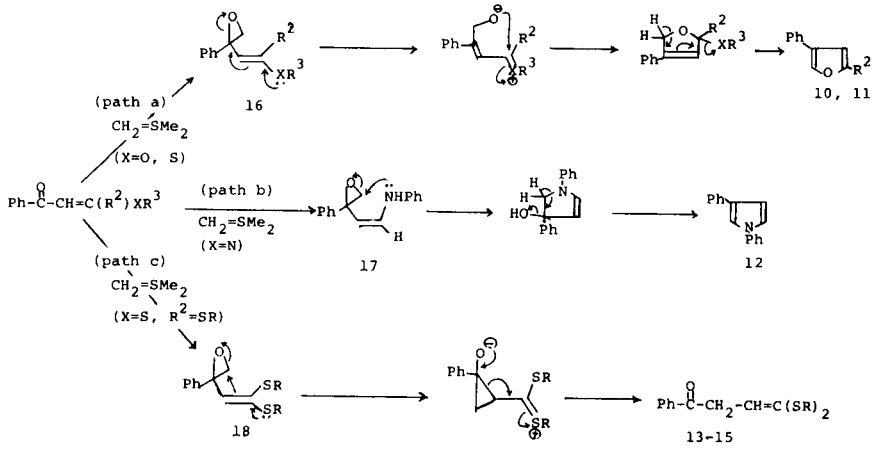


Fig.1



Scheme 1

0022-152X/79/040815-02$02.25

Furthermore, 1-phenyl-3,3-bis(alkylthio)-2-propen-1-ones (**5** and **6**) were treated with DMSM to give the methylene inserted products 1-phenyl-4,4-bis(alkylthio)-3-buten-1-one (**13** and **14**) (19 and 11%, respectively). These β,γ-unsaturated ketones were refluxed in methanol in the presence of sulfuric acid to give methyl 3-benzoylpropionate. A ring enlargement product, 3-[bis(methylthio)methylene]-1-cycloheptanone (**15**) (6%) was also obtained from the exocyclic β,β-bis(methylthio) α,β-unsaturated ketone (**9**) and DMSM. However, 4-anilino-3-penten-2-one (**7**) and 1-phenyl-3-diethylamino-2-propen-1-one (**8**) did not react with DMSM.

Possible reaction paths are shown in Scheme 1 for the formation of the furans (**10** and **11**), the pyrrole (**12**) and the methylene inserted products (**13-15**) from β-heteroatom substituted α,β-unsaturated ketones with DMSM. The initially formed epoxides (**16-18**) can rearrange by nucleophilic attack at either the tertiary or the primary epoxide carbons. The formation of the furans (**10** and **11**) can be explained by invoking the former mechanism, while the formation of the pyrrole (**12**) and the methylene inserted products (**13-15**) can be explained by invoking the latter mechanism.

EXPERIMENTAL

Materials.

β-Heteroatom substituted α,β-unsaturated ketones (**1-8**) were prepared according to previously reported procedures (6-9).

General Procecures.

To a stirred solution of 1.0 g. (4.9×10^{-2} mole) of trimethylsulfonium iodide in 20 ml. dry tetrahydrofuran under argon at 0° was added dropwise 8 ml. of a 10% solution of butyllithium in hexane. After stirring for 5 minutes at 0°, to this pale yellow mixture was added dropwise under atirring, 20 ml. of a solution ($1\text{-}2.5 \times 10^{-2}$ *M* solution) of the β-heteroatom substituted α,β-unsaturated ketone in dry tetrahydrofuran. Stirring was continued for 15 minutes at 0° and then for 30-60 minutes at room temperature. The reaction mixture was diluted with 30 ml. of water and extracted with ethyl acetate. The extract was dried over anhydrous magnesium sulfate, filtered and evaporated. The residual oil was chromatographed with benzene on a silica gel column to give the product.

4-Phenyl-2-methylfuran (**10**).

This compound was identical with the authentic material, m.p. 65-66° (lit. (5) m.p. 66-67°).

3- Phenylfuran (**11**).

This compound was also identical with the authentic material, m.p. 56-57° (lit. (5) m.p. 57-57.5°).

1,3-Diphenylpyrrole (**12**).

This compound was recrystallized from hexane, m.p. 84-85°; ir (potassium bromide): 3040, 1595,1490,760 and 700 cm^{-1}; nmr (deuteriochloroform): δ 6.38 (m, 1H), 6.91 (m, 1H), 7.1-7.6 (m, 11 H).

Anal. Calcd. for $C_{16}H_{13}N$: C, 87.63; H, 5.97; N, 6.38. Found: C, 87.98; H, 5.80; N, 5.95.

1-Phenyl-4,4-bis(methylthio)-3-buten-1-one (**13**).

This compound had b.p. 104°/5 mm dec. (Kugelrohr temperature); ir (film): 3050, 1685, 1595, 1450, 750 and 685 cm^{-1}; nmr (deuteriochloroform): δ 2.29 (s, 6H), 4.06 (d, 2H, J = 7 Hz), 6.15 (t, 1H, J = 7 Hz), 7.3-7.6 (m, 3H), 7.85-8.1 (m, 2H).

1-Phenyl-4,4-bis(ethylthio)-3-buten-1-one (**14**).

This compound had b.p. 105°/4 mm dec. (Kugelrohr temperature); ir (film): 3050, 1685, 1600, 1450, 755 and 690 cm^{-1}; nmr (deuteriochloroform): δ 1.21 (t, 3H), 1.25 (t, 3H), 2.75 (q, 2H), 2.81 (q, 2H), 4.09 (d, 2H, J = 7 Hz), 6.36 (t, 1H, J = 7 Hz), 7.25-7.6 (m, 3H), 7.9-8.1 (m, 2H).

3-[Bis(methythio)methylene]-1-cyclohentanone (**15**).

This compound was obtained as an oil; ir (film): 1700, 1655 and 1455 cm^{-1}; nmr (deuteriochloroform): δ 1.2-2.1 (m, 6H), 2.1-2.6 (m, 8H), 2.95 (t, 2H).

The results of the elemental analyses of the methylene inserted products (**13-15**) were not accurately in accord with the calculated values since these products decompose during purification by distillation.

Methyl 3-Benzoylpropionate.

(i).

A solution of 1-pheny-4,4-bis(alkylthio)-3-buten-1-one (**13** and **14**) (30 mg.) and a few drops of sulfuric acid in methanol (10 ml.) was stirred for 24 hours at room temperature. The reaction mixture was poured into water, extracted with ethyl acetate, and dried over anhydrous magnesium sulfate. After removal of the solvent, the residual oil was chromatographed with benzene to give methyl 3-benzoypropionate (20 mg.).

(ii).

A solution of 3-benzoylpropionic acid (1 g.) and a few drops of sulfuric acid in methanol (25 ml.) was refluxed for 20 hours. A usual work-up gave methyl 3-benzoylpropionate, quantitatively; ir (film): 3050, 1735, 1685, 1595, 1450, 760 and 690 cm^{-1}; nmr (deuteriochloroform): δ 3.00 (A_2B_2 type m, 4H), 3.65 (s, 3H), 7.2-7.6 (m, 3H), 7.85-8.1 (m, 2H).

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