Reactions of β-Sulfenyl α,β-Unsaturated Ketones with Guanidine, Amidines, and Diamines

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β-Sulfenyl α,β-unsaturated ketones **1a-c** reacted with guanidine or amidines to give pyrimidine derivatives **3** in 14-76% yields. Treatment of ketones **1** with diamines such as ethylenediamine and *o*-phenylenediamine afforded the seven-membered heterocycles, 2,3-dihydro-1,4-diazepine **5** and 2,3-benzo-1,4-diazepines **8a-c**.

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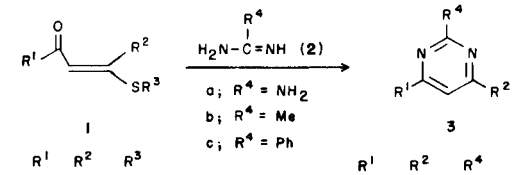
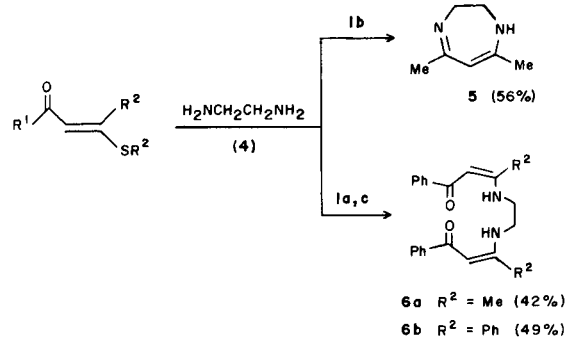
β-Sulfenyl α,β-unsaturated ketones **1** are useful intermediates for the synthesis of heterocycles [1] and for a variety of transformation [2] as ketones **1** possess reactive sites for nucleophilic attack at C-1 and C-3 and for electrophilic attack at the carbonyl *O*-atom, C-2, and the sulfur atom. We have previously reported the reaction of ketones **1** with sodium borohydride or lithium aluminium hydride leading to smooth reductive elimination of S-function to afford α,β-unsaturated ketones [3] and preparation of β-amino α,β-unsaturated ketones [4] and β-alkoxy α,β-unsaturated ketones [5] by the substitution reaction of ketones **1** with amines and alkoxides. We now report the reaction of β-sulfenyl α,β-unsaturated ketones **1** with guanidine (**2a**), amidines **2b-c** and diamines **4**, **7**.

When 1-phenyl-3-ethylsulfenyl-2-buten-1-one (**1a**) was heated with guanidine (**2a**) in ethanol in the presence of sodium hydroxide under reflux for 6 hours, 2-amino-4-methyl-6-phenylpyrimidine (**3aa**) was obtained in 68% isolated yield. In the same manner, treatment of ketone **1a** with acetamidine (**2b**) and benzamidine (**2c**) gave 2,4-dimethyl-6-phenylpyrimidine (**3ab**) and 2,4-diphenyl-6-methylpyrimidine (**3ac**) in 62, 56% yields, respectively. These pyrimidine derivatives **3aa-3ac** were identified from ir and nmr spectra comparison with their authentic samples [6-7]. Similarly, other β-sulfenyl α,β-unsaturated ketones **1b-c** were treated with guanidine (**2a**), acetamidine (**2b**) and benzamidine (**2c**) to give the corresponding pyrimidines **3ba-3cb** in 14-76% yields. The reaction described here would be the convenient method for the synthesis of pyrimidine derivatives, since all kinds of β-sulfenyl α,β-unsaturated ketones **1** can be readily prepared and are stable [3] and the pyrimidines are usually prepared by condensation of β-ketones with amidines, however, this method is restricted in some cases [7]. However, treatment of 1,3-diphenyl-3-ethylsulfenyl-2-propen-1-one (**1c**) with benzamidine (**2c**) did not give the pyrimidine and starting materials are recovered almost quantitatively. This might be due to the steric hindrance of phenyl group at β-position of the ketone **1c**. As the reaction of ethylenediamine with α,β-unsaturated ketones has been variously reported to give rise to tetrahydro 1,4-azepines [8], we have now investigated the reaction of β-sulfenyl α,β-unsaturated ketones **1** with ethylenediamine (**4**) and *o*-phenylenediamine (**7**). When 4-phenylsulfenyl-3-penten-2-one (**1b**) was treated with ethylenediamine (**4**) in the absence of solvent at 100°, 2,3-dihydro-5,7-dimethyl-1,4-diazepine (**5**) was obtained in 56% yield. The structure of diazepine (**5**) was confirmed by direct comparison of ir and nmr spectra with those of authentic material, which was prepared by condensation of acetylacetone with ethylenediamine (**4**) [9]. On the other hand, treatment of 1-phenyl-3-ethylsulfenyl-2-buten-1-one (**1a**) and 1,3-diphenyl-3-ethylsulfenyl-2-propen-1-one (**1c**) with ethylenediamine (**4**) gave bisenaminones **6a** and **6b** in 42 and 49% yields, respectively. β-Sulfenyl α,β-unsaturated ketones **1a-c** also reacted with *o*-phenylenediamine (**7**) to yield 2,3-benzo-1,4-diazepines **8a-c**. The double bond structure of seven-membered ring of diazepines **8** is not certain (**8** or **9**). The ir spectra of 5-methyl-7-phenyl-2,3-

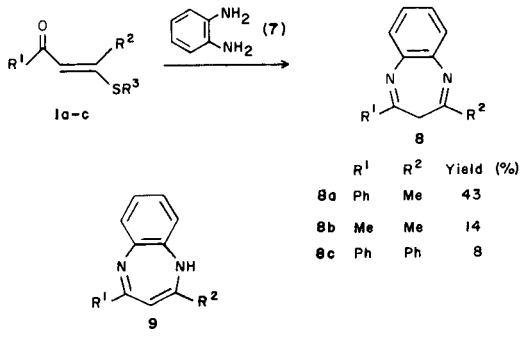


	R¹	R²	R³
1a	Ph	Me	Et
1b	Me	Me	Ph
1c	Ph	Ph	Et

	R¹	R²	R⁴	Yield (%)
3aa	Ph	Me	NH_2	68
3ab	Ph	Me	Me	62
3ac	Ph	Me	Ph	56
3ba	Me	Me	NH_2	73
3bb	Me	Me	Me	76
3bc	Me	Me	Ph	57
3ca	Ph	Ph	NH_2	23
3cb	Ph	Ph	Me	14



benzo-1,4-diazepine (**8a**) showed an absorption band at 1620 cm^{-1} due to the C=N stretching and absence of NH stretching band. The nmr spectra of diazepine **8a** exhibited the presence of methylene protons at δ 3.16 (s, 2H). The benzoazepine appears to be type **8**.



	R^1	R^2	Yield (%)
8a	Ph	Me	43
8b	Me	Me	14
8c	Ph	Ph	8

EXPERIMENTAL

β-Sulfenyl α,β-unsaturated ketones **1a-c** were prepared according to previously reported procedures [3].

The Reaction of β-Sulfenyl α,β-Unsaturated Ketones **1a-c** with Guanidine (**2a**) or Amidines **2b-c**.

A mixture of ketone **1** (1 mmole), guanidine (**2a**) or amidine **2b,c** (1.2 mmoles) and sodium hydroxide (2.4 mmoles) in absolute ethanol (10 ml) was refluxed for 6 hours. The reaction mixture was poured into water, extracted with dichloromethane, and the extract was dried over anhydrous magnesium sulfate. After removal of the solvent, the residual oil was chromatographed on a silica gel column with benzene-ethyl acetate (10:1) to yield the pyrimidines **3**.

2-Amino-4-methyl-6-phenylpyrimidine (**3aa**).

This compound had mp 174-175° (lit [6] 175°); ir (potassium bromide): 3320, 3200, 1635, 1580, 1545, 1355, 763, 703 cm^{-1}; nmr (deuteriochloroform): δ 2.35 (s, 3H), 5.65 (br s, 2H), 6.90 (s, 1H), 7.4-7.60 (m, 3H), 7.9-8.1 (m, 2H).

2,4-Dimethyl-6-phenylpyrimidine (**3ab**).

This compound had bp 125°/2 mm Hg (lit [7] 124°/4 mm Hg); ir (film): 3070, 1595, 1580, 1545, 1440, 745, 685 cm^{-1}; nmr (deuteriochloroform): δ 2.45 (s, 3H), 2.73 (s, 2H), 7.25 (s, 1H), 7.3-7.5 (m, 3H), 7.95-8.2 (m, 2H).

2,6-Diphenyl-4-methylpyrimidine (**3ac**).

This compound had mp 92-94° (lit [7] 93.5-95°); ir (potassium bromide): 3060, 1590, 1570, 1530, 1365, 760, 685 cm^{-1}; nmr (deuteriochloroform): δ 2.54 (s, 3H), 7.25-7.65 (m, 7H), 8.05-8.3 (m, 2H), 8.55-8.75 (m, 2H).

2-Amino-4,6-dimethylpyrimidine (**3ba**).

This compound had mp 152-153° (lit [9] 152-154°); ir (potassium bromide): 3410, 3300, 3190, 1620, 1590, 1460, 1385, 805, 785 cm^{-1}; nmr (deuteriochloroform): δ 2.24 (s, 6H), 5.7 (br s, 2H), 6.37 (s, 1H).

2,4,6-Trimethylpyrimidine (**3bb**).

This compound had mp 46-47° (lit [10] 47-48°); ir (potassium bromide): 3060, 1580, 1478, 1460, 735, 685 cm^{-1}; nmr (deuteriochloroform): δ 2.44 (s, 6H), 2.66 (s, 3H), 6.89 (s, 1H).

4,6-Dimethyl-2-phenylpyrimidine (**3bc**).

This compound had mp 81-82° (lit [7] 81-83°); ir (potassium bromide): 3055, 1600, 1580,1 440, 745, 705 cm^{-1}; nmr (deuteriochloroform): δ 2.40 (s, 6H), 6.73 (s, 1H), 7.35-7.5 (m, 3H), 8.4-8.6 (m, 2H).

2-Amino-4,6-diphenylpyrimidine (**3ca**).

This compound had mp 135-137.5° (lit [11] 135-137°); ir (potassium bromide): 3470, 3300, 3180, 1620, 1580, 1560, 1445, 1360, 755, 700, 685 cm^{-1}; nmr (deuteriochloroform): δ 5.79 (br s, 2H), 7.35-7.6 (m, 6H), 7.95-8.2 (m, 4H).

2-Methyl-4,6-diphenylpyrimidine (**3cb**).

This compound had mp 95.5-96.5° (lit [7] 96-97°); ir (potassium bromide): 3040, 1578, 1560, 1520, 1435, 750, 735, 680 cm^{-1}; nmr (deuteriochloroform): δ 2.88 (s, 3H), 7.2-7.7 (m, 6H), 7.90 (s, 1H), 8.05-8.3 (m, 4H).

The Reaction of β-Sulfenyl α,β-Unsaturated Ketones **1a-c** with Ethylenediamine.

A mixture of ketones **1** (1 mmole) and ethylenediamine (0.6 mmole) was heated at 100° under argon for 2 hours. The reaction mixture (for **1a**) was dissolved in acetic acid (5 ml), then perchloric acid (2 ml) was added and the precipitate was filtered. The solid was recrystallized from ethanol. The reaction mixture (for **1b-c**) was chromatographed on a silica gel column with ethyl acetate-hexane (1:1) to give the bisenaminones **6a-b**.

2,3-Dihydro-5,7-dimethyl-1,4-diazepine (**5**).

This compound had mp 139-140° (perchlorate) (lit [12] 140°); ir (potassium bromide): 3230, 3150, 2930, 1625, 1510, 1445, 1315 cm^{-1}; nmr (deuteriochloroform): δ 2.28 (s, 6H), 3.66 (s, 4H), 4.77 (s, 1H), 7.80 (br s, 1H).

1,2-Di-(2-benzoyl-1-methylvinylamino)ethane (**6a**).

This compound had mp 180-180.5° (lit [13] 180.5°); ir (potassium bromide): 3060, 1600, 1580, 1540, 1340, 1290, 750, 700 cm^{-1}; nmr (deuteriochloroform): δ 2.05 (s, 6H), 3.56 (m, 4H), 5.70 (s, 2H), 7.2-7.5 (m, 6H), 7.75-7.95 (m, 4H).

1,2-Di-(2-benzoyl-1-phenylvinylamino)ethane (**6b**).

This compound had mp 245-246°; ir (potassium bromide): 3050, 1600, 1565, 1480, 1330, 740, 690, 685 cm^{-1}; nmr (deuteriochloroform): δ 3.25-3.40 (m, 4H), 5.79 (s, 2H), 7.15-7.55 (m, 6H), 7.7-8.05 (m, 4H).

Anal. Calcd. for $C_{32}H_{28}N_2O_2$: C, 81.33; H, 5.97; N, 5.93. Found: C, 81.52; H, 5.89; N, 5.90.

The Reaction of β-Sulfenyl α,β-Unsaturated Ketones **1a-c** with *o*-Phenylenediamine (**7**).

A solution of ketone (**1**) (1 mmole) and *o*-phenylenediamine (1.2 mmoles) in benzene (5 ml) was heated at 120° in a sealed tube for 12-15 hours. After removal of the solvent, the residue was chromatographed on a silica gel column with benzene-ethyl acetate (10:1) to yield the benzodiazepines (**8**).

5,7-Dimethyl-2,3-benzo-1,4-diazepine (**8a**).

This compound had mp 130-132° (lit [14] 131-132°); ir (potassium bromide): 1625, 1415, 1260, 875, 775, 755 cm^{-1}; nmr (deuteriochloroform): δ 2.30 (s, 6H), 2.78 (s, 2H), 7.1-7.55 (m, 4H).

5-Methyl-7-phenyl-2,3-benzo-1,4-diazepine (**8b**).

This compound had mp 86-87° (lit [14] 87-88°); ir (potassium bromide): 3060, 1620, 1600, 1565, 1320, 775, 760, 680 cm^{-1}; nmr (deuteriochloroform): δ 2.22 (s, 3H), 3.16 (s, 2H), 7.3-7.55 (m, 7H), 7.95-8.15 (m, 2H).

5,7-Diphenyl-2,3-benzo-1,4-diazepine (**8c**).

This compound had mp 140-141° (lit [9] 140-141°); ir (potassium bromide): 3050, 1585, 1565, 1440, 1250, 770, 758, 680 cm^{-1}; nmr (deuteriochloroform): δ 3.58 (br s, 2H), 7.25-7.7 (m, 10H), 7.9-8.1 (m, 4H).

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