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THE SULFENYLATION OF THE ACTIVE METHYLENE COMPOUNDS BY THE USE OF SULFENAMIDES

Teruaki Mukaiyama, Susumu Kobayashi and Takanobu Kumamoto
Laboratory of Organic Chemistry, Tokyo Institute of Technology
Ookayama, Meguro-ku, Tokyo, Japan

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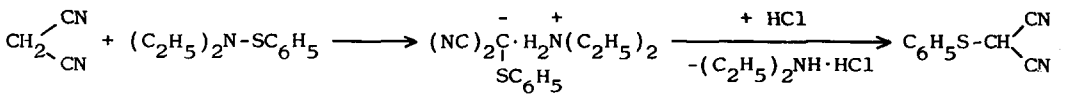
Recently, it has been found in our laboratory that α-phenylthioalkylidene-triphenylphosphorane was obtained in high yield by the reaction of alkylidene-triphenylphosphorane with a sulfenamide, such as N-methyl-N-phenylthio-acetamide[1].

In the present studies, the sulfenylation of active methylene compounds by the use of sulfenamides was attempted with the expectation that the reaction would afford a convenient method for the preparation of mono- or di-sulfenylated compounds which are considered valuable as synthetic intermediates. When equimolar amounts of N,N-diethylbenzenesulfenamide (I) and malononitrile were stirred in methylene chloride at room temperature for 5 hr, the diethylammonium salt of phenylthiomalononitrile (II) was obtained in 55% yield. The structure of this salt was established by the IR spectrum and elemental analysis. The salt (II) was converted to phenylthiomalononitrile (III), mp 84-87°C, in quantitative yield by acid hydrolysis.



I II III

Further, it was found that in the case of the reaction of N,N-diethylbenzenesulfenamide with dibenzoylmethane, α-phenylthio-β-N,N-diethylaminochalcone was obtained in 66% yield instead of the salt. By acid hydrolysis of

the enamine, phenylthiodibenzoylmethane, mp 93-94°C, was obtained in quantitative yield.

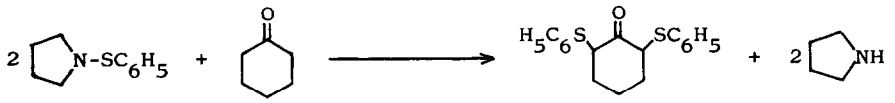
The reactions of N,N-diethylbenzenesulfenamide with acetylacetone, ethyl acetoacetate or diethyl malonate were also examined under similar conditions without isolation of the intermediates, enamines or salts, and the corresponding mono-sulfenylated products were obtained in good yields (See Table 1).

Table 1

$CH_2^{X}_{Y}$	Product*	Yield (%)	bp °C (mmHg) or [mp °C]
$CH_2(COC_6H_5)_2$	$C_6H_5S\text{-}CH(COC_6H_5)_2$	66	[93-94]
$CH_2(COCH_3)_2$	$C_6H_5S\text{-}CH(COCH_3)_2$	77	152-153 (22)
$CH_2(CN)_2$	$C_6H_5S\text{-}CH(CN)_2$	55	[84-87]
$CH_3COCH_2CO_2C_2H_5$	$CH_3COCH(SC_6H_5)CO_2C_2H_5$ [2]	37	125-127 (4.5)
$CH_2(CO_2C_2H_5)_2$	$C_6H_5S\text{-}CH(CO_2C_2H_5)_2$ [3]	48	148 (1.7)

* Satisfactory elemental analyses were obtained for all new compounds.

In the case of the reaction of N,N-diethylbenzenesulfenamide with cyclohexanone, the sulfenylated product was not obtained and only starting materials were recovered quantitatively. However, the reaction of 2 moles of N-phenylthiopyrrolidine (IV) and 1 mole of cyclohexanone in methylene chloride at room temperature for 20 hr, followed by the hydrolysis gave 2,5-bis(phenylthio)cyclohexanone (V) in 67% yield, which was separated by Silica Gel column chromato-



IV V

graphy. The product V was confirmed by converting it to the 2,4-dinitrophenylhydrazone, mp 197-198°C.

Next, the reactions of N-phenylthiopyrrolidine with ethyl acetoacetate or diethyl malonate were examined (See Table 2). The results show that the yields of the mono-sulfenylated products are higher as compared with those of the reac-

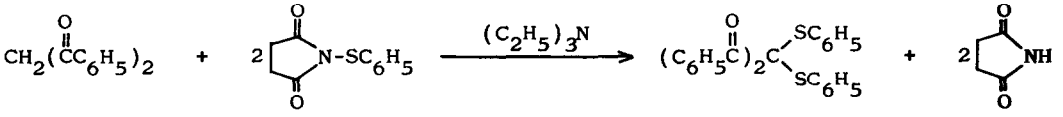
tions of active methylene compounds with N,N-diethylbenzenesulfenamide.

On the other hand, it was found that disulfenylated products were obtained by the reactions of N-phenylthiosuccinimide (VI) with active methylene compounds in the presence of a base. For example, when 2 moles of N-phenylthiosuccinimide, 1 mole of dibenzoylmethane and 2 moles of triethylamine as a base in methylene chloride were stirred overnight at room temperature, a white syrup was obtained after removal of the solvent. Crystallization by addition of isopropyl alcohol gave bis(phenylthio)dibenzoylmethane (VII), mp 184.5-185.5°C. The structure of this product was established by the IR spectrum and elemental analysis.

Table 2

$CH_2^{X}_{Y}$	Yield (%)
$CH_3COCH_2CO_2C_2H_5$ *	60
$CH_2(CO_2C_2H_5)_2$ *	52
	67

* The products were the same listed in Table 1.



VI VII

In a similar way, the reactions of N-phenylthiosuccinimide with acetylacetone, malononitrile, ethyl acetoacetate or diethyl malonate afforded the

Table 3

$CH_2^{X}_{Y}$	Product *	Yield (%)	mp °C
$CH_2(COC_6H_5)_2$	$(H_5C_6S)_2C(COC_6H_5)_2$	50	184.5-185.5
$CH_2(COCH_3)_2$	$(H_5C_6S)_2C(COCH_3)_2$	73	117-118
$CH_2(CN)_2$	$(H_5C_6S)_2C(CN)_2$	54	58-59
$CH_3COCH_2CO_2C_2H_5$	$CH_3COC(SC_6H_5)_2CO_2C_2H_5$ [a]	64	122-124
$CH_2(CO_2C_2H_5)_2$	$(H_5C_6S)_2C(CO_2C_2H_5)_2$	93	74-75

a This compound was isolated as its 2,4-dinitrophenylhydrazone.

* Satisfactory elemental analyses were obtained for all new compounds.

corresponding di-sulfenylated products (See Table 3).

Further, it was found that when 1 mole of cyclohexanone, 2 moles of N-phenylthiophthalimide and 2 moles of Triton B were stirred in benzene at room temperature, 2,2-bis(phenylthio)cyclohexanone, mp 120-122°C, was obtained in 12% yield. Similarly, when 1 mole of acetophenone, 3 moles of N-phenylthio-succinimide and 3 moles of Triton B were stirred in dioxane at room temperature, α,α-bis(phenylthio)acetophenone[4], mp 99.5-100.0°C, was obtained in 41% yield.

The sulfenylation of active methylene compounds with the sulfenamides derived from the secondary alkylamines would proceed through the activation of sulfur-nitrogen bond by the protonation to the nitrogen atom, followed by the reaction on the sulfur atom with active methylene compounds to give the mono-sulfenylated products. These would be converted rapidly to the enamines or the salts by the subsequent reactions with the secondary alkylamines formed at the same time. Since the enamines or the salts can not participate in the activation of the sulfenamides, di-sulfenylated products would not be produced in these reactions. On the other hand, in the case of the sulfenylation with the sulfenamides derived from the imides, the sulfenamides can react with active methylene compounds in basic media to produce sulfenylated products owing to a labile elimination of stable imide anions from the sulfenamides. Therefore, the initially formed triethylammonium salts of mono-sulfenylated products further react with sulfenamides to give di-sulfenylated products.

In conclusion, it was established that mono- or di-sulfenylated compounds are prepared by the choice of two types of the sulfenamides derived from the secondary alkylamines or derived from the imides.

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