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Smiles-Type Rearrangement of *N*-(*trans*-Styrylsulfonyl) and *N*-(4-Phenyl-1,3-butadienylsulfonyl)thioureas and Isothioureas

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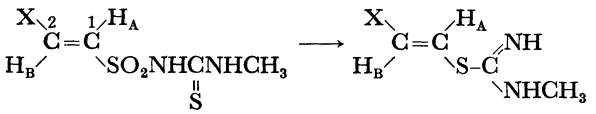
Synopsis. Treatment of *N*-(*trans*-styrylsulfonyl)- (**1**) and *N*-(4-phenyl-1,3-butadienylsulfonyl)-*N'*-methylthiourea (**2**), and the corresponding *S*-methylisothioureas (**6** and **7**), with strong base afforded the Smiles-type and Michael-type products. Effects of substituents at C-2 and nucleophiles on the products are discussed.

We recently reported that treatment of *N*-(2,2-diarylvinylsulfonyl)thioureas,[1] isoureas,[2] isothioureas[2] and *N*-(*trans*-*p*-nitrostyrylsulfonyl)thiourea[1] with base affords Smiles-type products. Matier and Comer[3] described that base-treatment of *N*-(*trans*-styrylsulfonyl)-amidines yields Michael-type and Smiles-type products. These rearrangements are facilitated by electron-withdrawing *para* substituents on the aromatic rings. However, effects of substituents at C-2 and nucleophiles on the products are not well known. This paper describes these effects by base-treatment of 2-substituted vinylsulfonylthioureas **1**—**3** and isothioureas **6** and **7**.

Results and Discussion

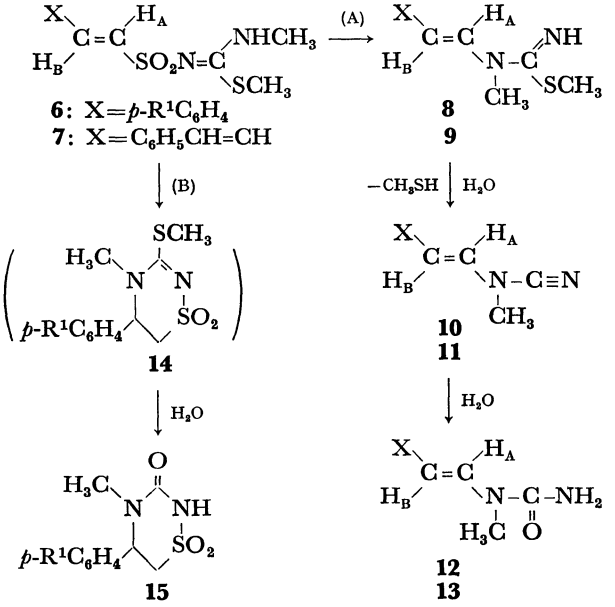
In contrast to known base-catalyzed Michael cycloaddition of *N*-(*trans*-styrylsulfonyl)thioureas[4] (**1**), -isothioureas[5] (**6**) and *N*-(4-phenyl-1,3-butadienylsulfonyl)-thioureas[6] (**2**), treatment of **1** and **2** with strong base (ten equiv. of 10M NaOH) in some solvents for 3 hr at 80 °C gave Smiles-type products, *N*-methyl-*S*-(*trans*-styryl)- (**4**) and *N*-methyl-*S*-(4-phenyl-1,3-butadienyl)-isothioureas (**5**), respectively (Table 1). No Michael cycloadducts were obtained because



1: X=*p*-R¹C₆H₄ **4**: X=*p*-R¹C₆H₄
2: X=C₆H₅CH=CH **5**: X=C₆H₅CH=CH

they were split into **1** and **2** in the strongly basic media (pH>13.30).[4] Similar treatment of *N*-(2-methyl-*trans*-styrylsulfonyl)-*N'*-methylthiourea (**3**) and *N*-(*trans*-styrylsulfonyl)-*N'*-methylurea afforded no rearranged products. The IR spectra of **4** and **5** exhibited absorption bands at 3450—3150 (NH) and 1615 (C=N) cm⁻¹.

Smiles-type rearrangement of **6** requires more vigorous reaction conditions than those of *N*-(2,2-diarylvinylsulfonyl)- and *N*-(4-phenyl-1,3-butadienylsulfonyl)-*N'*, *S*-dimethylisothioureas (**7**). Treatment of **6** with ten equiv. of aqueous 10M NaOH in DMF for 3 hr at 75 °C gave *N*-(*trans*-styryl)-*N*-methylureas (**12**) and 4-methyl-5-aryl-2,3,5,6-tetrahydro-3-oxo-1,2,4-thiadiazine-1,1-dioxides[5] (**15**) (Tables 1 and 2). Similar treatment of **7** gave the corresponding urea (**13**) and *N*-(4-phenyl-1,3-butadienylsulfonyl)-*N'*-methyurea (**16**). The Michael cycloadduct of



6: X=*p*-R¹C₆H₄ **8**
7: X=C₆H₅CH=CH **9**
14 **10**
11
15 **12**
13

7 was not obtained because of stabilization of Smiles-type intermediary carbanion.[1-3] The structures of **12**, **13**, **15**, and **16** were determined on the basis of analytical and spectral data (1650 and 1600 (C=O) cm⁻¹).

The formation of **12** and **13** would proceed through a Smiles rearrangement path (**A**) and that of **15** through a Michael cycloaddition path (**B**). Rearrangement path (A) is similar to that of *N*-(2,2-diarylvinylsulfonyl)-*N'*,*S*-dimethylisothioureas.[2] Attempts to obtain the intermediary new isothioureas **8** and **9**, and the new cyanamides **10** and **11** were unsuccessful due to their easy hydrolysis to **12** and **13** under the reaction conditions used. Under moderate reaction conditions (1N NaOH, 45 °C, 4 hr), **7** gave **9** (3%, IR: 1615 (C=N) cm⁻¹) and **11** (7%, IR: 2220 (C≡N) cm⁻¹) as yellow oils after column chromatography on silica gel, but, satisfactory analytical data were not obtained.

Tables 1 and 2 show that the rearrangements of the thioureas and isothioureas are favored by electron-withdrawing substituents on the aromatic ring, by the styryl group at C-2 and by solvents of high polarity.

Possible mechanisms for the formation of the isothioureas, **4**, **5**, **8**, and **9**, are analogous to those for the rearrangements of *N*-(2,2-diarylvinylsulfonyl)thioureas,[1] isothioureas[2] and *N*-(*trans*-styrylsulfonyl)amidines.[3] The presence of the styryl group at C-2 would stabilize the cinnamyl carbanion by resonance more than the

Table 1. List of rearranged products

Compd.	X	Yield (%) solvent			Mp (°C)	Found (%)				Calcd (%)			
		DMF	Acetone	Dioxane		C	H	N	S	C	H	N	S
4a[a]	*p*-$NO_2C_6H_4$	>95[b]			181—182	50.73	4.52	17.75	13.69	50.63	4.67	17.72	13.49
4b	*p*-BrC_6H_4	91	90	79	174—175	44.48	3.79	10.50		44.31	4.09	10.33	
4c	*p*-ClC_6H_4	70	67	39	171—172	53.10	4.87	12.39	13.89	52.97	4.89	12.36	14.14
4d	C_6H_5	21	7	0	149—150	62.76	6.24	14.52	16.61	62.48	6.29	14.58	16.65
4e	*p*-$CH_3C_6H_4$	6	2	0	161—162	64.29	7.09	13.83		64.06	6.84	13.58	
5	C_6H_5CH=CH	67			180—181	66.15	6.71	12.73		66.03	6.94	12.83	
12a	*p*-BrC_6H_4	65			209—211	47.24	4.57	11.02		47.08	4.35	10.98	
12b	*p*-ClC_6H_4	46			197—198	57.22	5.36	13.15		57.01	5.26	13.30	
12c	C_6H_5	18			191—193	67.87	6.72	15.81		68.16	6.86	15.90	
13	C_6H_5CH=CH	42			193—195	71.26	6.72	14.03		71.26	6.98	13.85	

a) Mp and analytical data were already given in the previous paper.[1] b) Compound **4a** was obtained in a yield more than 95% after 30 min.

Table 2. Product distribution from the base treatment of **6** and **7**

X	Yield (%)		Yield (%)	
	12	**13**	**15**	**16**
p-BrC_6H_4	65		trace	
p-ClC_6H_4	46		4	
C_6H_5	18		56	
p-$CH_3C_6H_4$	trace		68	
C_6H_5CH=CH		42		10

phenyl group. Introduction of electron-releasing methyl group at C-2 would descrease benzyl carbanion, stability, and no rearrangement could occur.

Experimental

Spectral data are given only for a representative of each class.

*Base-treatment of **1** and **2**.* The isothioureas **4** and **5** were prepared by a method similar to the base-treatment of *N*-(2,2-diarylvinylsulfonyl)thioureas[1] and recrystallized from methanol. **4d**: IR (KBr); 3420, 3280, and 3170 (NH), 1615 (C=N) cm^{-1}. NMR (DMSO-d_6) δ: 3.50 (s, 3, CH_3), 6.25 (d, 1, H_A), 8.53 (d, 1, H_B), J_{AB}=15.0 Hz, 7.30—7.70 (m, 5, C_6H_5), 7.90 (broad, 1, NHCH$_3$) and 8.34 (broad, 1, NH). MS *m/e*: 192 (M^+). **5**: IR (KBr); 3400, 3260, and 3140 (NH), 1610 (C=N) and 1580 (C=C) cm^{-1}. MS *m/e*: 218 (M^+).

*Base-treatment of **6** and **7**.* The sulfonylthioureas **6** and **7** were treated with ten equiv. of aqueous 10M NaOH in DMF for 3 hr at 75 °C and the mixtures were poured into water and filtered to give **12** and **13**, respectively, which were recrystallized from chloroform. **12b**: IR (KBr): 3360 and 3180 (NH), 1650 and 1600 (C=O) cm^{-1}. NMR (DMSO-d_6) δ: 3.07 (s, 3, CH_3), 5.70 (d, 1, H_A), 7.72 (d, 1, H_B), J_{AB}=15.0 Hz, 6.65 (s, 2, NH_2) and 7.30 (s, 4, C_6H_4). MS *m/e*: 210 (M^+). Acidification of the filtrate gave **15b** (4%, R^1=Cl), which was recrystallized from methanol, mp 235—237 °C (236—238 °C[5]).

13: IR (KBr): 3350 and 3170 (NH), 1650 and 1600 (C=O) cm^{-1}. MS *m/e*: 202 (M^+). Acidification of the filtrate gave **16** which was recrystallized from benzene–petroleum ether, mp 188—190 °C. IR (KBr): 3340 (NH), 1655 (C=O), 1335 and 1145 (SO_2) cm^{-1}. MS *m/e*: 266 (M^+). Found: C, 54.14; H, 5.38; N, 10.41%. Calcd for $C_{12}H_{14}N_2O_3S$: C, 54.13; H, 5.30; N, 10.52%.

References

1) K. Hasegawa, S. Hirooka, and T. Sasaki, This Bulletin, **48**, 1513 (1975).
2) K. Hasegawa, S. Hirooka, T. Sasaki, Y. Mizukami, T. Yamamoto, J. Ishikawa, and H. Shinno, *Nippon Kagaku Kaishi*, **1975**, 1035.
3) W. L. Matier and W. T. Comer, *J. Org. Chem.*, **39**, 3080 (1974).
4) K. Hasegawa and S. Hirooka, This Bulletin, **45**, 525 (1972).
5) K. Hasegawa and S. Hirooka, *ibid.*, **45**, 1893 (1972).
6) K. Hasegawa, S. Hirooka, T. Sasaki, S. Ikeda, and K. Hashimoto, *Nippon Kagaku Kaishi*, **1975**, 1028.