

The Synthesis of Some *N*-Aryl- and *N*-Benzyl-*N'*-furfurylthioureas

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This paper refers to the preparation and infrared spectra of some *N*-aryl- and *N*-benzyl-*N'*-furfurylthioureas. The title compounds were synthesized by addition of 2-aminomethylfuran and ethyl-5-aminomethylfuroate to phenyl-, benzyl-, 4-tolyl-, 4-chlorophenyl-, 4-bromophenyl- and 4-dimethylaminophenylisothiocyanate.

As reported in previous papers [1, 2], differently substituted derivatives of thiourea are antioxidants and many of them are used as stabilizers of some polymolecular compounds, *e.g.* polyvinylchloride, polyurethanes and others. There are also papers reporting a tuberculostatic effect of various derivatives of thiourea [3, 4].

We have been interested in such thiourea derivatives which possess a substituted furan ring in its molecule; this ring easily undergoes oxidation and, as a result, enhanced antioxidation properties of the synthesized thioureas can be anticipated. The introduction of a furan ring into the molecule of substituted thioureas can be reflected in the increase of the tuberculostatic effect since a wide spectrum of biological activity of furan derivatives has been described [5, 6]. Thus, *Nazarova and Gach* [7, 8] reported a more intense biological activity of thioureas with a substituted furan ring, the substituent in α -position being also of importance.

We synthesized some *N*-aryl- and *N*-benzyl derivatives of *N'*-furfurylthiourea when reacting *p*-substituted phenyl- and benzylisothiocyanates with 2-aminomethylfuran and ethyl-5-aminomethylfuroate.

Isothiocyanates were prepared from the proper amines by thiophosgene method [9, 10], ethyl-5-aminomethylfuroate from ethyl-5-chloromethylfuroate and hexamethylenetetramine in absolute ethanol according to Delephine method [11].

From the results listed in Table 1 it follows that the highest yields of thiourea derivatives were obtained when using aromatic isothiocyanates with desactivating substituents (chloro derivative 81%, bromo derivative 82%) what is in accordance with the nucleophilic addition of amine to isothiocyanate. Yields are lower when an activating substituent is present (dimethylamino derivative 65%). Dimethylamino group increases the electron density of the $-NCS$ group by its strong activation effect, thereby lowering its reactivity in nucleophilic addition to an amine.

Derivatives 5 and 11 were used to stabilize wool towards thermooxidation; the latter was found to be of better, the former of weaker antioxidation effect when compared with that of thiourea [12].

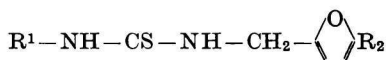
The examined derivatives of thiourea are characterized in their infrared spectra by $\nu(\text{N}-\text{H})$ at 3400 cm^{-1} these being associated to a considerable extent, further by the band of pulsation vibration of the furan ring at $1017-1021\text{ cm}^{-1}$ and substances 7-12 also by a very strong band $\nu(\text{C}=\text{O})$ at $1730-1720\text{ cm}^{-1}$.

Experimental

Infrared spectra of substances under investigation were recorded with a double-beam UR-10 spectrophotometer (Zeiss, Jena), in the $3600-700\text{ cm}^{-1}$ region in NaCl cells of 0.41 mm thickness as 0.025 M solutions in carbon tetrachloride. Melting points were determined on a Kofler micro hot-stage.

Table 1


Characteristics of the synthesized thiourea derivatives



No.	R ¹	Molecular formula	M	Calculated/found			Yield [%]	M.p. [°C]
				% C	% H	% N		
R ² = H								
1	phenyl	C ₁₂ H ₁₂ N ₂ OS	232.3	62.04	5.20	12.06	73	131 ^a
				62.12	5.08	12.38		
2	benzyl	C ₁₃ H ₁₄ N ₂ OS	246.3	63.38	5.17	11.37	68	80 ^a
				63.51	5.23	11.35		
3	4-chlorophenyl	C ₁₂ H ₁₁ ClN ₂ OS	266.7	54.02	4.15	10.50	81	119 ^a
				53.76	4.08	10.38		
4	4-bromophenyl	C ₁₂ H ₁₁ BrN ₂ OS	311.1	46.31	3.56	9.00	82	120 ^a
				46.05	4.05	8.95		
5	4-tolyl	C ₁₃ H ₁₄ N ₂ OS	246.3	63.38	5.17	11.37	70	172 ^a
				63.41	4.94	11.60		
6	4-dimethylaminophenyl	C ₁₄ H ₁₇ N ₃ OS	275.4	61.06	6.22	15.26	65	140 ^a
				59.70	6.39	15.31		
R ² = COOC ₂ H ₅								
7	phenyl	C ₁₅ H ₁₆ N ₂ O ₃ S	304.4	59.18	5.29	9.20	71	116 ^b
				59.40	5.33	9.38		
8	benzyl	C ₁₆ H ₁₈ N ₂ O ₃ S	318.4	60.35	5.69	8.79	79	89 ^c
				60.12	5.73	9.08		
9	4-chlorophenyl	C ₁₅ H ₁₅ ClN ₂ O ₃ S	338.8	53.17	4.46	8.26	85	125 ^b
				53.29	4.18	7.98		
10	4-bromophenyl	C ₁₅ H ₁₅ BrN ₂ O ₃ S	383.6	47.00	3.94	7.30	85	126 ^b
				46.62	4.05	7.29		
11	4-tolyl	C ₁₆ H ₁₈ N ₂ O ₃ S	318.4	60.35	5.69	8.79	75	101 ^c
				59.91	5.47	8.66		
12	4-dimethylaminophenyl	C ₁₇ H ₂₁ N ₃ O ₃ S	347.4	58.76	6.09	12.09	67	136 ^d
				58.53	6.17	11.81		

Crystallized from a) methanol, b) ethanol, c) ether, d) chloroform.

Table 1 (Continued)

No.	Infrared spectra [cm ⁻¹]						
	$\nu(N-H)$	$\nu_{arom.}(C-H)$	$\nu_{aliph.}(C-H)$	$\nu(C=O)$	$\nu(C=C)$	$\nu(C=S)$	
1	3423 m	3180 vw 3071 vw	2933 w	—	1602 w 1534 s	1458 m	1017 m
	3409 m	3039 vw	2960 w		1504 vs 1605 w 1580 vs	1077 m	
	3418 s	3070 s	2930 m		1540 vs	1470 s	
2	3410 infl	3050 s 3190 m 3160 m	2880 m	—	1515 vs	1085 s	1017 s
	3	3412 s	3100 w		2945 w	1540 vs	1465 vw
3000 m			2880 w	1510 vs	1085 vs		
4	3412 s	3050 w	2930 w	—	1605 w 1540 vs	1465 vw	1019 s
		3000 w	2880 w		1510 vs	1085 s	
5	3430 m	3190 vw	2930 m	—	1495 s 1605 vw	1465 w	1019 s
	3410 m	3140 vw	2860 w		1535 vs	1085 m	
6	3435 vw	3190 vw	2930 vw 2865 vw	—	1540 vs	1455 vw	1018 s
	3405 m	2990 vw	2815 m		1490 vs	1085 m	
7	3422 m	2989 w	2946 vw	1727 s	1603 w 1529 vs	1456 w	1020 m
	3410 m	2985 w 3070 vw 3039 vw			1504 s 1603 w 1537 vs		
8	3380 m	2989 w	2941 w	1710 vs	1503 w 1601 vw	1080 w	1019 m
		9	3414 m	2990 w	2942 vw	1731 vs	1453 vw
1499 vs 1600 vw 1532 s	1094 m 1456 w 1098 w						
10	3414 vw	2993 vw	2941 vw	1730 s	1498 s 1603 w	1076 s	1020 s
	3338 w		2912 vw		1484 m	1452 w 1098 vw 1450 w 1096 w	1021 m
11	3424 m	3040 vw	2940 w	1727 vs	1523 vs	1452 w	1021 m
	3409 m	2989 w	2875 vw		1484 m	1098 vw	
12	3425 m	3185 w	2945 w	1724 s	1615 w	1450 w	1069 vw
	3400 m		2910 w			1096 w	
	3360 m		2816 w			1069 vw	

vs — very strong, s — strong, m — medium, w — weak, vw — very weak.

The preparation of N,N'-disubstituted thioureas

A 0.02 mole of phenyl-, benzyl-, 4-chlorophenyl-, 4-bromophenyl-, 4-tolyl- and 4-dimethylaminophenylisothiocyanate, respectively, in ethanol (50 ml) was placed into a three-necked flask provided with a reflux condenser. During 5 minutes a 0.02 mole solution of 2-aminomethylfuran, or ethyl-5-aminomethylfuroate in ethanol (50 ml) was added from a dropping funnel while stirring and the reaction mixture was then

heated on a steam bath for 1/2—1 hour. Ethanol was distilled off under diminished pressure and the precipitate was purified by crystallization from methanol, ethanol, ether or chloroform (Table 1).

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