

Isothiocyanates. XXVII.

The Synthesis of Substituted 2-Naphthylisothiocyanates

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This paper deals with the preparation, infrared and ultraviolet spectra of some substituted 2-naphthylisothiocyanates. Thiophosgene method was used to synthesize 2-naphthylisothiocyanates.

Relationships between carcinogenic, carcinostatic and mutagenic properties of isothiocyanates were reported in one of our previous papers [1]. The first substance of the isothiocyanate series having a carcinostatic effect against Ehrlich ascetic carcinoma was found to be 2-naphthylisothiocyanate [2] prepared from the carcinogenic active 2-naphthylamine.

Coming back to the preparation of 2-naphthylisothiocyanates we wish to report the effect of substituents in position 1 or 8 on the character and properties of derivatives synthesized.

Thiophosgene method was used to prepare the mentioned derivatives and in the case of 2-naphthylisothiocyanate thiourea method [3] was also employed.

So far, 2-naphthylisothiocyanate has been prepared by two methods: either by decomposition of the appropriate thiourea derivative by boiling in a suitable solvent for a longer time [3, 4], or by the modified Kaluz synthesis (*via* dithiocarbamate and its decomposition with ethyl chlorocarbonate) [5]. The thiophosgene method was reported to be improper [6] when preparing 2-naphthylisothiocyanate.

Experimental

Isothiocyanates were synthesized starting from the proper amines: 2-naphthylamine was commercially available, 1-bromo-2-naphthylamine was prepared according to [7], 8-acetyl-2-naphthylamine according to [8] and 1-(4-X-phenylthiomethyl)-2-naphthylamines (X = H, Cl, NO₂) were prepared by condensation of the respective thiophenols with formaldehyde and 2-naphthylamine in acidic medium [9]. Unsubstituted thiophenol was a commercial product, *p*-chlorothiophenol and *p*-nitrothiophenol were obtained as described in [10, 11], respectively.

Infrared spectra of the isothiocyanates were measured with a double-beam UR-10 (Zeiss, Jena) apparatus in the 700–3600 cm⁻¹ range in NaCl cells of 0.4 mm thickness; concentration 0.025 mole l⁻¹ CHCl₃. Reading accuracy ±1 cm⁻¹ with the exception of NCS group peaks where the frequency reading was accurate to ±3 cm⁻¹.

Ultraviolet spectra were recorded with a VSU-1 universal spectrophotometer (Zeiss, Jena) in the 220–400 nm range. Concentration 1 × 10⁻⁵ M in methanol, cell width 1 cm.

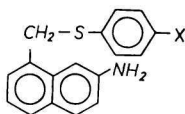
Modified method for preparation of 1-(4-X-phenylthiomethyl)-2-naphthylamines

In a 250-ml three-necked flask provided with a mechanical stirrer, reflux condenser and dropping funnel 0.1 mole of the proper thiophenol and 0.1 mole of 37% formaldehyde in ethanol (50 ml) were allowed to react under stirring with a solution consisting of 0.1 mole of 2-naphthylamine and 8.6 ml of concentrated hydrochloric acid in ethanol (50 ml) added dropwise from the dropping funnel. The addition being finished, the reaction mixture was stirred while heating on a steam bath for two hours, then cooled to the room temperature and finally a cold, 10% sodium hydroxide solution was added to slight alkaline reaction. (The light green colour of the precipitate formed turned to brown.) The crude product was filtered off with suction, washed with water, dried and crystallized either from toluene, or tetrachloromethane, or acetone.

Data characterizing the amines prepared in this way are listed in Table 1.

Table 1

1-(4-X-Phenylthiomethyl)-2-naphthylamines synthesized



X	Molecular formula	M	Calculated/found			Yield [%]	M.p. [°C]
			% N	% S	% Cl		
H	C ₁₇ H ₁₅ NS	265.36	—	—	—	62.2	120 ^a
Cl	C ₁₇ H ₁₄ ClNS	299.83	4.69	10.69	11.82	73.3	145–147
			4.71	10.82	11.99		
NO ₂	C ₁₇ H ₁₄ N ₂ O ₂ S	310.36	9.02	10.30	—	64.5	207–210
			8.81	9.82	—		

a) Ref. [9] 121–122.5°C.

Preparation of substituted 2-naphthylisothiocyanates

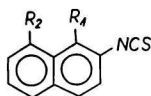
The proper amine (0.01 mole) dissolved in chloroform (50 ml) was dropped into a well stirred emulsion of thiophosgene (0.013 mole) in water (50 ml) within half an hour at room temperature. Either NaHCO₃ or CaCO₃ was added during the reaction in the mixture in order hydrogen chloride to be neutralized. After addition of amine, the mixture was kept stirred for additional one hour, then the chloroform layer was separated, dried over calcium chloride and evaporated at room temperature. Isothiocyanates thus prepared were crystallized from light petroleum or acetone and characterized by data given in Table 2.

Results and Discussion

The condensation of 2-naphthylamine with formaldehyde and the proper thiophenol requires a strong acidic medium because *N*-2-naphthylaminomethylarylsulfides are formed.

Table 2

Substituted 2-naphthylisothiocyanates prepared



R ₁	R ₂	Molecular formula	M	Calculated/found				Yield [%]	M.p. [°C]
				% N	% S	% Br	% Cl		
H	H	C ₁₁ H ₇ NS	185.24	—	—	—	—	61.2 ^a	56—58
Br	H	C ₁₁ H ₆ BrNS	263.14	5.33	12.18	30.42	—	51.3	130—133 ^b
				5.60	12.52	29.95	—		
H	CH ₃ CO	C ₁₃ H ₉ NOS	227.29	6.16	14.11	—	—	62.5	84.5 ^b
				6.20	14.35	—	—		
C ₆ H ₅ SCH ₂	H	C ₁₈ H ₁₃ NS ₂	307.42	4.57	20.85	—	—	44.2	69—69.5 ^b
				4.77	20.79	—	—		
4-ClC ₆ H ₄ SCH ₂	H	C ₁₈ H ₁₂ ClNS ₂	341.88	4.10	18.72	—	10.37	55.5	76—77 ^b
				4.14	18.71	—	10.56		
				7.95	18.20	—	—		
4-NO ₂ C ₆ H ₄ SCH ₂	H	C ₁₈ H ₁₂ N ₂ O ₂ S ₂	352.44	7.91	17.85	—	—	34.3	171—174 ^c
				7.91	17.85	—	—		

a) Ref. [3]; b) recrystallized from light petroleum; c) recrystallized from acetone.

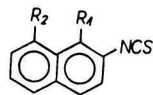
When applying thiourea method to prepare 2-naphthylisothiocyanate 20-hour decomposition of the substituted thiourea and almost the same time for extraction in the Soxhlet apparatus are so far reported; 7 days are needed to obtain the substituted dithiocarbamate using the dithiocarbamate method when preparing isothiocyanates. The thiophosgene method affording 2-naphthylisothiocyanate in 78% yield is quite advantageous for its simplicity and relatively short preparation time.

All isothiocyanates are crystalline substances; they were crystallized from light petroleum or acetone in 34—78% yield. As seen from Table 2, yields of derivatives with a bulkier substituent in position 1 are lower and the effect of the bulky bromine is greater than that of the more remote acetyl group.

Characteristic group frequencies in the infrared region of the synthesized isothiocyanates are listed in Table 3. The symmetric vibrations of the NCS group at about 940 cm⁻¹ are mostly of lower intensity like those described in our previous paper [13]. The position of bands attributed to aromatic C=C vibrations is approximately the same (~1602 cm⁻¹) for all isothiocyanates. The C=O vibration of 8-acetyl-2-naphthylisothiocyanate is located at 1687 cm⁻¹ and the $\nu_s(\text{NO}_2)$ and $\nu_{as}(\text{NO}_2)$ of 1-(4-nitrophenylthiomethyl)-2-naphthylisothiocyanate appear at 1347 and 1528 cm⁻¹, respectively.

Ultraviolet absorption spectra of the above-mentioned isothiocyanates are shown in Fig. 1; their absorption maxima and log ϵ values are summarized in Table 3. These derivatives are characterized by three absorption maxima in the 232—240, 252—274 and 292—337 nm range. The absorption band intensity indicates that a $\pi-\pi^*$ transition is involved. Absorption bands in the 232—240 and 252—274 nm

Table 3



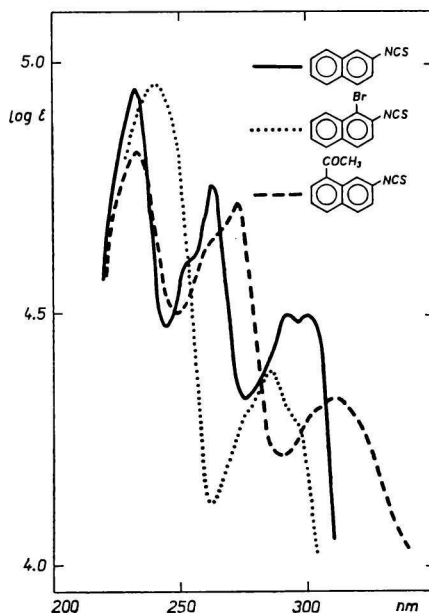
R_1	R_2	$\nu_s(\text{NCS})$ [cm^{-1}]	$\nu_{\text{arom}}(\text{C}=\text{C})$ [cm^{-1}]	$\nu_{\text{asym}}(\text{NCS})$ [cm^{-1}]	$\lambda_1 \text{ max}$ [nm] $\log \epsilon$	$\lambda_2 \text{ max}$ [nm] $\log \epsilon$	$\lambda_3 \text{ max}$ [nm] $\log \epsilon$
H	H	935 m	1602 m	1967 w, 2060 vw 2105 w, 2125 m 2170 m, 2205 w	232 4.95	262 4.75 252 <i>i</i> 4.60	292 4.50 300 4.45
Br	H	949 m	1602 m	2050 vw 2100 w 2120 vw, 2165 vw	240 4.95	274 <i>i</i> 4.29 4.60	286 4.38 296 <i>i</i> 4.28
H	CH_3CO^a	942 m	1602 m	1955 w, 2069 w 2125 m, 2200 w	232 4.83	272 4.72 262 <i>i</i> 4.65	310 4.33 302 4.31
$\text{C}_6\text{H}_5\text{SCH}_2$	H	934 w	1609 m	2059 m, 2100 m	232 4.95	268 4.75 257 <i>i</i> 4.63	301 <i>i</i> 4.35
4- $\text{ClC}_6\text{H}_4\text{SCH}_2$	H	935 vw	1602 m	2065 w, 2105 m	234 4.97	268 4.81 258 <i>i</i> 4.67	300 4.36
4- $\text{NO}_2\text{C}_6\text{H}_4\text{SCH}_2^b$	H	—	1603 m	2065 w, 2095 w	236 5.03	268 4.86 257 <i>i</i> 4.84	308 <i>i</i> 4.53 337 <i>i</i> 4.39

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

a) Additional bands of $\nu(\text{C}=\text{O})$ at 1687 cm^{-1} (s); *b*) $\nu_s(\text{NO}_2) = 1347 \text{ cm}^{-1}$ (vs) and $\nu_{\text{as}}(\text{NO}_2) = 1528 \text{ cm}^{-1}$ (s).

i) Inflexion.

Fig. 1. Ultraviolet spectra of substituted 2-naphthylisothiocyanates in ethanol.



range are characteristic of naphthalene skeleton [12]. The absorption band in the 292–337 nm range is possibly due to the $\pi-\pi^*$ transition of the entire conjugated system.

Various substituents attached to the naphthalene ring influence both the shape and the position of the absorption maximum (Fig. 1).

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