

REACTIONS OF BENZOYL ISOTHIOCYANATES WITH AZOMETHINES

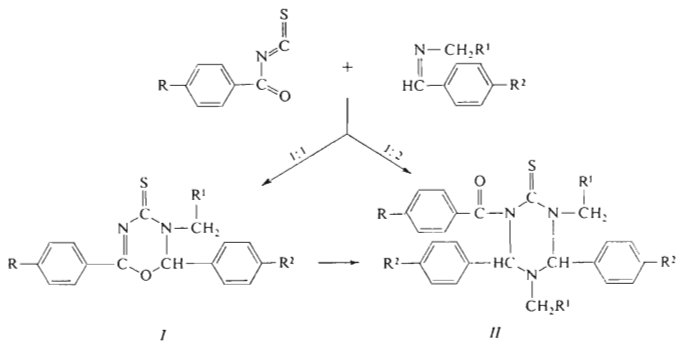
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Preparation of substituted 1,3,5-oxadiazine-4-thiones and s-triazines by reacting benzoyl isothiocyanates with azomethines, and hydrolysis of the obtained oxadiazinethiones is described. The observed, IR, Raman, UV and $^1\text{H-NMR}$ spectral characteristics of the prepared substances are discussed.

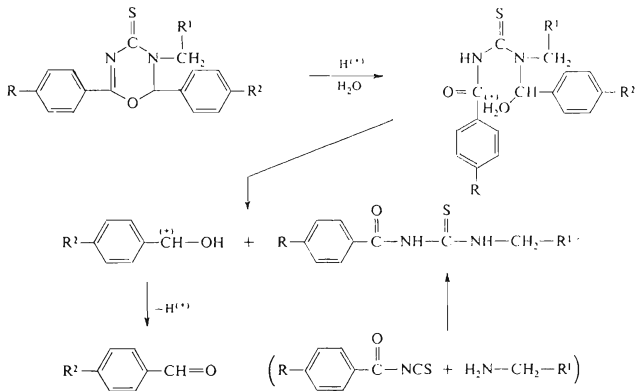
Huisgen and coworkers¹ have studied [4 + 2] cycloaddition reactions by means of the reaction of benzoyl isothiocyanate with benzylidenemethylamine. They obtained a thermally unstable 1 : 1 cycloadduct which decomposed to starting materials. Milzner and Seckinger² have found that in addition to 1 : 1 adduct 1 : 2 cycloadducts are also formed, and that the reaction depends primarily upon electronic effects of C-aryl substituents present in the molecule of azomethine. It is known that these reactions occur on the C=N linkage of the corresponding isothiocyanates³.



SCHEME 1

In pursuing our works on cycloaddition reactions of isothiocyanates with diazoalkanes⁴, azoimide and trimethylsilyl azide⁵ we decided to study the reaction of benzoyl isothiocyanate with azomethine using benzoyl and *p*-nitrobenzoyl isothiocyanates, and *p*-substituted benzylidenebenzyl- and furfurylamines as substrates. The substituents on the C-aryl residue of azomethines were chosen in such a way that they differed in their electron effects upon the reaction center. Cycloaddition reactions of benzyl isothiocyanates with azomethines were performed in an inert atmosphere using dichloromethane and tetrahydrofuran as solvents.

The studied reactions afforded good yields of substituted 1,3,5-oxadiazine-4-thiones (Scheme 1). Reactions with benzoyl isothiocyanates bearing electron-withdrawing substituents and with azomethines bearing electron-attracting substituents gave higher yield of the desired products. On the other hand, substituting furyl for phenyl (R^1) group resulted in lower yields. When the reaction time was prolonged, as well as by reacting 1,3,5-oxadiazine-4-thiones with azomethine, *s*-triazines were formed. All prepared derivatives were found to be unstable in common atmosphere and to decompose at the temperature of melting. The acid hydrolysis of *Ia* and *Ij* afforded the corresponding thiourea derivatives and an aldehyde (Scheme 2). The formation of thiourea was confirmed also by synthesis from the corresponding isothiocyanate and an amine.



SCHEME 2

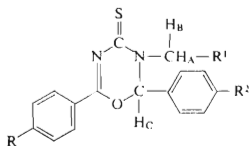
The UV spectra of the prepared substances show two absorption bands at 237 to 245 and 277–293 nm (Table I). The first band slightly depends upon the nature of the substituent, whereas the one at the longest wave-length is affected by the substituent

TABLE I

2-(4-R²-Phenyl)-3-(R¹-methylene)-6-4-R-phenyl)-2,3-dihydro-4H-1,3,5-oxadiazine-4-thiones

Compound R	R ¹ R ²	Molecular formula (m.w.)	M.p., °C (yield, %)	Calculated/Found				λ_1 max (log ϵ)	λ_2 max (log ϵ)
				% C	% H	% N	% S		
<i>Ia</i> H	phenyl H	C ₂₂ H ₁₅ N ₂ OS (358.4)	82—83 (84)	73.71 73.64	5.14 5.03	7.82 8.15	8.94 9.16	245 (4.22)	280 (4.07)
<i>Ib</i> NO ₂	phenyl H	C ₂₂ H ₁₇ N ₃ O ₃ S (403.4)	140—141 (52)	65.49 65.66	4.24 4.20	10.41 10.13	7.94 8.12	245 s —	293 (4.37)
<i>Ic</i> H	furyl H	C ₂₀ H ₁₆ N ₂ O ₂ S (348.4)	69—70 (71)	68.94 68.76	4.62 4.65	8.04 8.34	9.20 9.63	— —	— —
<i>Id</i> NO ₂	phenyl NO ₂	C ₂₂ H ₁₆ N ₄ O ₃ S (448.3)	198—199 (22)	58.91 58.65	3.59 3.56	12.49 12.67	7.15 7.31	240 s —	291 (4.59)
<i>Ie</i> H	phenyl CH ₃ O	C ₂₃ H ₂₀ N ₂ O ₂ S (388.5)	111—113 (76)	71.10 71.11	5.18 5.14	7.21 6.93	8.25 8.13	243 (4.48)	278 (4.53)
<i>If</i> H	furyl CH ₃ O	C ₂₁ H ₁₈ N ₂ O ₃ S (378.5)	89—90 (71)	66.64 66.81	4.79 4.77	7.40 7.30	8.47 8.58	242 (4.31)	277 (4.38)
<i>Ig</i> NO ₂	phenyl CH ₃ O	C ₂₃ H ₁₉ N ₃ O ₄ S (433.5)	119—121 (82)	63.72 63.46	4.41 4.43	9.69 9.79	7.39 7.52	239 (4.39)	289 (4.37)
<i>Ih</i> NO ₂	furyl CH ₃ O	C ₂₁ H ₁₇ N ₃ O ₅ S (423.4)	115—116 (84)	59.57 59.63	4.04 4.10	9.92 9.68	7.58 7.32	238 (4.44)	288 (4.43)
<i>Ii</i> H	phenyl (CH ₃) ₂ N	C ₂₄ H ₂₃ N ₃ OS (401.4)	105—107 (78)	71.80 72.10	5.75 5.83	10.46 10.56	7.98 8.19	240 s —	288 (4.48)
<i>Ij</i> NO ₂	phenyl (CH ₃) ₂ N	C ₂₄ H ₂₂ N ₄ O ₃ S (446.5)	134—136 (98)	64.55 64.35	4.96 4.81	12.54 12.31	7.18 7.19	241 s —	298 (4.56)
<i>Ik</i> H	phenyl CH ₃ CONH	C ₂₄ H ₂₁ N ₃ O ₂ S (416.0)	128—130 (97)	69.37 69.09	5.09 5.09	10.11 10.22	7.71 7.82	245 s —	278 (4.64)
<i>Il</i> H	furyl CH ₃ CONH	C ₂₂ H ₁₉ N ₃ O ₃ S (405.3)	143—145 (76)	65.16 64.83	4.72 4.70	10.36 10.47	7.91 7.83	240 s —	276 (4.66)
<i>Im</i> NO ₂	phenyl CH ₃ CONH	C ₂₄ H ₂₀ N ₄ O ₄ S (460.5)	167—168 (87)	62.59 62.39	4.57 4.44	12.16 12.19	6.96 6.78	242 s —	284 (4.59)
<i>In</i> H	furyl HO	C ₂₀ H ₂₆ U ₂ O ₃ S (364.4)	105—106 (86)	65.91 65.97	4.42 4.54	7.68 7.45	8.80 8.98	242 (4.44)	277 (4.44)
<i>Io</i> NO ₂	furyl HO	C ₂₀ H ₁₅ N ₃ O ₅ S (409.4)	146—147 (93)	58.67 58.95	3.69 3.77	10.26 10.07	7.83 8.06	237 (4.44)	287 (4.44)

s Shoulder; ¹H-NMR data (ppm) for *Ie*—H_A 3.86 (d), H_B 5.07 (d), H_C 5.72 (d), R₂ 3.72 (s) J_{AB} 15 Hz; *If*—H_A 4.06 (d), H_B 4.96 (d), H_C 5.83 (s), R₂ 3.75 (s), J_{AB} 15 Hz; *Ii*—H_A 3.86 (d), H_B 5.11 (d), H_C 5.74 (s), R₂ 2.92 (s), J_{AB} 14.8 Hz; *Ij*—H_A 3.91 (d), H_B 5.08 (d), H_C 5.75 (s), R₂ 2.93 (s), J_{AB} 15 Hz.



R; these bands can be assigned to $\pi-\pi^*$ transition⁶. The IR spectra of 1,3,5-oxadiazine-4-thione derivatives show bands at 3020–3105, 1647–1654, 1500–1606, 1274–1322, 1152–1183 and 1065–1088 cm^{-1} . In the region of deformation vibrations $\delta(\text{CH})$ of aromatic rings containing two substituents at positions 1 and 4 intense bands at 817–856 cm^{-1} are present (except for compounds *Ia* and *Ic*). Pronounced bands at 1274–1291 and 1298–1322 cm^{-1} can be assigned to linkage vibrations in the $-\text{N}-\text{C}=\text{S}$ groups.

Previous authors⁷ assigned bands at $\sim 1280 \text{ cm}^{-1}$ to vibrations of $\text{C}=\text{S}$ bonds; unambiguous assignment is not possible in the present case since the bands are much stronger than would be expected considering the nature of $\text{C}=\text{S}$ groups. Raman spectra of these substances show strong bands at 1644–1665 ($\text{C}=\text{N}$), 1595–1605 ($\text{C}=\text{C}$), and 1290–1305 cm^{-1} ($\text{C}=\text{S}$).

In order to confirm structures of the prepared substances ¹H-NMR spectra (Table II) of selected compounds have been measured. The presence of two doublets at 3.86–5.11 ppm is indicative of the presence of two non-equivalent methylene protons: proton A, directed towards the benzene ring bearing the R^2 substituent, and proton B directed to the sulphur atom of the $\text{C}=\text{S}$ group. As a consequence, proton B is more deshielded than proton A. This orientation of A and B protons is possible only when the aromatic ring bearing the R^2 substituent is directed below the plane of the 6-membered ring; otherwise, the A and B protons would be both chemically and magnetically equivalent.

EXPERIMENTAL

Benzoyl isothiocyanates were prepared^{8,9} from the corresponding acyl chlorides. Reactions^{10,11} of equimolar amounts of the aldehyde and an amine with the solvent afforded benzylidene- and 4-dimethylaminobenzylidenebenzylamines, and benzylidene-furfurylamine. Similar reaction in the absence of solvent gave 3-acetylaminobenzylidenebenzylamine. 4-Hydroxybenzylidene-furfurylamine (63%), no solvent, m.p. 157°C. For $\text{C}_{12}\text{H}_{11}\text{NO}_2$ (201.1) calculated: 6.95% N; found 7.03% N. 4-Acetylaminobenzylidene-furfurylamine (82%), no solvent, m.p. 185°C. For $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_2$ (242.1) calculated: 11.62% N; found: 11.56% N. Removal of water by azeotropic distillation gave 4-nitrobenzylidene-, 4-methoxybenzylidenebenzylamines and 4-methoxybenzylidene-furfurylamine (63%), b.p. 150°C/63 Pa. For $\text{C}_{13}\text{H}_{13}\text{NO}_2$ (216.1) calculated: 6.65% N; found: 6.73% N.

The IR spectra (KBr technique, 2 mg/g KBr) were recorded with UR-20 (Zeiss) spectrometer. The UV spectra for $5 \cdot 10^{-5}$ M solutions in dioxane were measured with a Specord UV VIS spectrometer using 10 mm cells. Raman spectra were obtained with Spex Ramalog 4 instrument using a Spectra Physic 164 argon ion laser, without solvents. Excitation of molecules was achieved by applying a green line ($\lambda = 514$ nm). $^1\text{H-NMR}$ spectra for solutions in CDCl_3 were recorded with a Tesla BS-487C, 80 MHz spectrometer.

Reactions of Benzoyl Isothiocyanates with Azomethines

These reactions were performed in sealed vials in an argon atmosphere *a*) According to the procedure described¹², to a solution of isothiocyanate (0.01 mol) in dichloromethane or tetrahydrofuran (8 ml) contained in a vial, a solution of the respective azomethine (0.01 mol) in dichloromethane or tetrahydrofuran (4 ml) was added with the aid of a syringe. The vial was sealed and shaken for 24 h. When the product crystallized the mother liquor was withdrawn, otherwise crystallization was induced by an addition of light petroleum. The crude product was recrystallized from a light petroleum-dichloromethane mixture. Reactions with dichloromethane yielded *Ia-Ii* and *Io*, those carried out with tetrahydrofuran gave *Ij-In* (Table I).

b) Following the procedure described in *a*), a solution of benzyl isothiocyanate (0.01 mol) in dichloromethane (12 ml) was allowed to react with benzylidenebenzylamine (0.02 ml) in dichloromethane (10 ml) for 5 days to give 1,5-dibenzyl-3-benzoyl-4,6-diphenyl-perhydro-*s*-triazine-2-thione *II* (2.76 g, 49%). For $\text{C}_{36}\text{H}_{31}\text{N}_3\text{O}_3$ (553.7) calculated: 77.96% C, 5.54% H, 7.96% N, 5.89% S; found: 78.11% C, 5.64% H, 7.58% N, 5.97% S. $^1\text{H-NMR}$ data (ppm): 5.24 (s, 1 H, $-\text{HC}-\text{N}-\text{C}=\text{O}$), 5.75 (s, 1 H, $-\text{HC}-\text{N}-\text{C}=\text{S}$), 3.14 (d, 1 H, CH_2), 3.64 (d, 1 H, CH_2), 8.3–8.4 and 7.5–6.3 (m, phenyl protons); λ_{max} nm ($\log \epsilon$) = 216 (4.53), 247 (4.23), 273 (4.32).

Reaction of *Ia* with Benzylidenebenzylamine

A solution of *Ia* (0.01 mol) in dichloromethane (10 ml) was allowed to react for 3 days with a solution of benzylidenebenzylamine (0.01 mol) in dichloromethane. The product crystallized on addition of ether. The crude product was recrystallized from dichloromethane and *II* was identical with the substance obtained as described in *b*.

Hydrolysis of *Ia* and *Ij*

Concentrated hydrochloric acid (2 ml) was added to a solution of *Ia* (0.001 mol) in dioxane (5 ml) and the mixture was refluxed for 20 min. After concentration, the residue was washed with ether, filtered and the crude product was recrystallized from methanol. The obtained N-benzoyl-N'-benzylthiourea (50%) melted at 124–125°C.

Similar hydrolysis of *Ij* afforded N-(4-nitrobenzoyl)-N'-benzylthiourea (70%), m.p. 150–151°C. The filtrate, when reacted with 2,4-dinitrophenylhydrazine, showed the presence of an aldehyde.

N-(4-Nitrobenzoyl)-N'-benzylthiourea

A solution of 4-nitrobenzoyl isothiocyanate (0.01 mol) in benzene (17 ml) was added slowly (30 min) with stirring to a boiling solution of benzylamine (0.01 mol) in benzene (14 ml). The mixture was refluxed for 1 h, cooled, the precipitate was filtered and washed with benzene (25 ml), to give after two recrystallizations from ethanol the title substance (2.55 g, 80.7%), m.p. 149 to 150°C. For $\text{C}_{15}\text{H}_{13}\text{N}_3\text{O}_3\text{S}$ (315.3) calculated: 13.21% N, 9.90% S; found: 13.32% N, 10.10% S.

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