Reactions of benzoyl isothiocyanate with some carbodiimides and sulfinylamines

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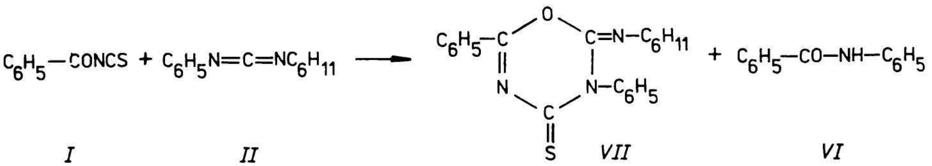
Benzoyl isothiocyanate enters the reaction with *N*-cyclohexyl-*N*′-phenylcarbodiimide under the formation of benzoylanilide and the appropriate (4 + 2) cycloadduct on the phenyl—N = C bond of carbodiimide. On the other hand, the reactions of benzoyl isothiocyanate with *N*-methyl-*N*′-phenylcarbodiimide, *N*-sulfinylaniline, and *N*-sulfinylcyclohexylamine, respectively, result in differently substituted ureas and thioureas as well as in one unknown compound.

Бензоилизотиоцианат реагирует с *N*-циклогексил-*N*′-фенилкарбодиимидом с образованием бензоиланилида и соответственного (4 + 2) циклического продукта присоединения к связи фенил—N = C у карбодиимида. Напротив этого, при реакции бензоилизотиоцианата с *N*-метил-*N*′-фенилкарбодиимидом, *N*-сульфиниланилином и *N*-сульфинилциклогексиламином образуются различно замещенные тиомочевины и мочевины и также одно неизвестное вещество.

Recently the reactions of benzoyl isothiocyanates with different types of dienophiles have received considerable attention. Relatively little attention has been paid to the study of isothiocyanates with carbodiimides and sulfinylamines. The reactions of benzoyl and thiobenzoyl isocyanates, respectively, with *N*,*N*′-dicyclohexylcarbodiimide [1—5], giving (2 + 2) and (4 + 2) cycloadducts, respectively, have been studied in detail. *N*-Cyclohexyl-*N*′-phenylcarbodiimide reacted with benzoyl isocyanate selectively only with the double cyclohexyl—N = C bond, while thiobenzoyl isocyanate reacted with both —N = C bonds of carbodiimide under the formation of the appropriate (4 + 2) cycloadducts. Since the cycloaddition reactions of acyl isothiocyanates with carbodiimides have not been studied so far, in our previous work [6], we followed the reactions of 4-substituted benzoyl isothiocyanates with symmetrical carbodiimides, *i.e.* with *N*,*N*′-dicyclohexyl- and *N*,*N*′-diphenylcarbodiimide. While *N*,*N*′-dicyclohexylcarbodiimide afforded (4 + 2) and (2 + 2) cycloadducts, from the reaction mixture with *N*,*N*′-diphenylcarbodiimide only the appropriate 4-substituted benzoylanilides could be isolated. *Kresze* [7] as well as other authors [8—15] emphasized in their works the ability of *N*-sulfinyl compounds to undergo cycloaddition reactions through the N = S bond. Reactions of these compounds with acyl isothiocyanates have not been investigated so far.

In the present work we have focused our attention to cycloaddition reactions of unsymmetrical carbodiimides and sulfinylamines with benzoyl isothiocyanates. In the reaction of benzoyl isothiocyanate (*I*) with *N*-cyclohexyl-*N*′-phenylcarbodiimide (*II*) in benzene we isolated from the reaction mixture two products, *i.e.* benzoylanilide (*VI*) and a (4 + 2) cycloadduct, namely, 2-cyclohexylimino-3,6,-diphenyl-1,3,5-oxadiazine-4-thione (*VII*) (Scheme 1).



Scheme 1

The structure of the formed cycloadduct was proved by i.r., ^{1}H-n.m.r., and mass spectra. In the i.r. spectrum an absorption band at 1650 cm^{-1}, characteristic of exocyclic C = N bond, and an absorption band at 1575 cm^{-1} belonging to stretching vibrations of ν(C = N) bond in the ring were observed. The latter band can be overlapped by the band ν(C = C) of the aromatic system. The mass spectrum of this cyclization product displayed the molecular mass $M = 363$. The base peak was that of the fragmentation ion *m/z* 105 $[C_6H_5—CO)^{\cdot +}$. Contrary to benzoyl isocyanate [4], benzoyl isothiocyanate reacted with *N*-cyclohexyl-*N*′-phenylcarbodiimide on the phenyl—N = C bond only as evidenced by the appearance of the intensive fragmentation ion *m/z* 135 $[C_7H_5NS]^{\cdot +}$ in the mass spectrum and of a multiplet of the methine proton of the *N*-cyclohexyl ring at δ 3.8—4.3 p.p.m. (= N—C_6H_{11}) in the ^{1}H-n.m.r. spectrum. The melting point and the i.r. spectrum of benzoylanilide were in accordance with the literature data [16].

As different reactivity of C = N bonds in unsymmetrical carbodiimides causes the formation of different cycloadducts, we carried out also the reactions of benzoyl isothiocyanate with an aliphatic-aromatic carbodiimide, namely, *N*-methyl-*N*′-phenylcarbodiimide in benzene—ether (3 : 1) at 0°C. Instead of the expected cycloaddition products, we succeeded in isolation of *N*-benzoyl-*N*-phenyl-*N*′-methylurea only, as evidenced by elemental analysis, i.r., ^{1}H-n.m.r., and mass spectra. The mother liquors obtained after isolation of the reaction products contained the unreacted starting compounds.

In the reaction of benzoyl isothiocyanate with *N*-sulfinylaniline we isolated *N*-benzoyl-*N*′-phenylurea and *N*-benzoyl-*N*′-phenylthiourea from the reaction mixture. The structures of both compounds were proved on the basis of i.r. and mass spectra. The melting points were compared with the literature data [17, 18]. The formation of *N*-benzoyl-*N'*-phenylthiourea can probably be explained by decomposition of *N*-sulfinylaniline to the starting compounds at higher temperature. The formed aniline readily reacted with benzoyl isothiocyanate under the formation of the appropriate thiourea. *N*-Benzoyl-*N'*-phenylurea was probably formed by decomposition of the (2 + 2) cycloadduct. Similarly, we carried out the reaction of benzoyl isothiocyanate with *N*-sulfinylcyclohexylamine under the formation of *N*-benzoyl-*N'*-cyclohexylcarbonylurea, the structure of which was determined by elemental analysis as well as i.r. and mass spectra. In addition, we isolated another compound from the supernatant, however, we failed to determine its structure on the basis of its chemical and spectral properties.

Experimental

Infrared spectra in the region of 800—3600 cm^{-1} were recorded with a Specord 75 IR spectrophotometer in NaCl cells; concentration of chloroform solutions was 0.05—0.08 mol dm^{-3}. The apparatus was calibrated with polystyrene foil. ^{1}H-NMR spectra were measured in deuteriochloroform on a Tesla BS-487 A (80 MHz) spectrometer using tetramethylsilane as standard. Mass spectra were run with an MS 902 S (AEI Manchester) apparatus at 70 eV (direct inlet system) and ionization temperature 90—120°C.

In this work we used the following starting compounds: Benzoyl isothiocyanate (*I*) [19, 20], *N*-cyclohexyl-*N'*-phenylcarbodiimide (*I*) [4], *N*-methyl-*N'*-phenylcarbodiimide (*III*) [21, 22], *N*-sulfinylaniline (*IV*) [23], and *N*-sulfinylcyclohexylamine (*V*) [24].

Reaction of benzoyl isothiocyanate (I) with N-cyclohexyl-N'-phenylcarbodiimide (II)

To the solution of *I* (2.28 g; 13.9 mmol) in benzene (35 cm^3) *II* (2.96 g; 14.8 mmol) was added dropwise and the mixture was refluxed for 7 h. The solvent was distilled off *in vacuo* and n-heptane was added to the oily residue. Crystalline benzoylanilide (*VI*) [6] of m.p. 161—163°C (n-heptane) was obtained in 4.72% (0.130 g) yield. Addition of further amount of n-heptane to the supernatant resulted in precipitation of white crystals of 2-cyclohexylimino-3,6-diphenyl-1,3,5-oxadiazine-4-thione (*VII*), m.p. 104—106°C (n-heptane), in 10.3% (0.560 g) yield.

For $C_{21}H_{21}N_3OS$ (363) calculated: 69.42% C, 5.78% H, 11.57% N; found: 69.85% C, 5.62% H, 11.78% N.

IR spectrum ($CHCl_3$): $\nu(C=N)_{\text{exocyclic}}$ 1650 cm^{-1}, $\nu(C=N)_{\text{cyclic}}$ 1575 cm^{-1}. ^{1}H-NMR data (δ): 3.1—3.5 (m, 1H, $=N—C_6H_{11}$). Mass spectrum (70 eV) *m/z* (relative intensity %): 363 (9.8), 228 (0.48), 135 (28.6), 119 (5.24), 109 (3.1), 105 (100), 97 (3.33), 91 (4.3), 83 (5.5), 77 (11.9).

Reaction of benzoyl isothiocyanate (I) with N-methyl-N′-phenylcarbodiimide (III)

To the solution of *I* (1.62 g; 0.01 mol) in benzene (10 cm^3) *III* (1.32 g; 0.01 mol) in the mixture of benzene—ether (1 : 1) (10 cm^3) was added dropwise at 0°C. The reaction mixture was then stirred at this temperature for 3 h. The solvents were distilled off *in vacuo* and petroleum ether was added to the formed oily residue. Light-yellow crystals of *N*-benzoyl-*N*-phenyl-*N*′-methylurea, m.p. 135—137°C (n-heptane) precipitated in 26% (0.62 g) yield.

For $C_{15}H_{14}N_2O_2$ (254) calculated: 73.4% C, 5.7% H, 11.4% N; found: 72.9% C, 5.69% H, 11.39% N.

IR spectrum ($CHCl_3$): ν(NH) 3330 cm^{-1}, ν(C=O) 1710 cm^{-1}, $\nu(C=C)_{ar}$ 1600 cm^{-1}, δ(NH) 1540 cm^{-1}, 1270 cm^{-1}. ^{1}H-NMR data (δ): 2.9 (d, 3H, CH_3), 7.1 (10H, aromatic H), 8.9 (1H, NH). Mass spectrum (70 eV) *m/z* (relative intensity %): 254 (3.7), 197 (22), 135 (3.7), 121 (37), 119 (7.4), 105 (100), 77 (81), 57 (7).

Reaction of benzoyl isothiocyanate (I) with N-sulfinylaniline (IV)

To the solution of *IV* (2.7 g; 0.019 mol) in benzene (30 cm^3) *I* (3.1 g; 0.019 mol) in benzene (20 cm^3) was added dropwise and the reaction mixture was refluxed for 46 h under stirring. After cooling the solvent was distilled off *in vacuo* and n-heptane was added to the oily residue. White crystals of *N*-benzoyl-*N*′-phenylurea [17], m.p. 204—206°C (methanol), precipitated in 4.4% (0.2 g) yield. The supernatant was evaporated *in vacuo* and ethanol was added to the residue. Light-yellow crystals of *N*-benzoyl-*N*′-phenylthiourea [18], m.p. 146—148°C (ethanol), were obtained in 68% (3.3 g) yield.

Reaction of benzoyl isothiocyanate (I) with N-sulfinylcyclohexylamine (V)

The solution containing *V* (2 g; 0.014 mol) in benzene (15 cm^3) and *I* (2.25 g; 0.014 mol) in benzene (10 cm^3) was worked up similarly as in the previous case (38 h reflux). Crystals of *N*-benzoyl-*N*′-cyclohexylcarbonylurea, m.p. 218—220°C (ethanol), were obtained in 18.2% (0.2 g) yield.

For $C_{15}H_{18}N_2O_3$ (274) calculated: 65.69% C, 6.62% H, 10.2% N; found: 64.9% C, 6.56% H, 10.12% N.

IR spectrum ($CHCl_3$): ν(NH) 3430 cm^{-1}, ν(C=O) 1750 cm^{-1}, 1660 cm^{-1}, $\nu(C=C)_{ar}$ 1595 cm^{-1}. Mass spectrum (70 eV) *m/z* (relative intensity %): 274 (5.8), 245 (8.3), 229 (6.3), 209 (14.6), 203 (10.4), 181 (4.2), 165 (8.3), 122 (29.2), 105 (100), 99 (4.2), 98 (8.3), 77 (50), 43 (10.4). The supernatant was evaporated and the mixture of ether—petroleum ether (3 : 1) was added to the oily residue. A second product of m.p. 137—139°C (ethanol—ether) was obtained in 0.45 g yield; its structure is unknown.

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