

REACTION OF 4-SUBSTITUTED BENZOYL ISOTHIOCYANATES
WITH N,N' -DICYCLOHEXYLCARBODIIMIDE
AND N,N' -DIPHENYLCARBODIIMIDE

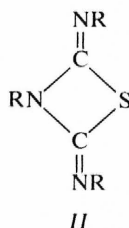
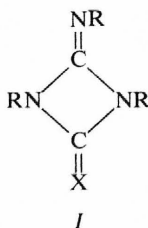
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Benzoyl isothiocyanates enter 4 + 2 cycloaddition reactions with N,N' -dicyclohexylcarbodiimide to give 1,3,5-oxadiazine-4-thiones. In the case of benzoyl isothiocyanate it is possible after a shorter reaction time to isolate also the 2 + 2 cycloadduct, *i.e.* 2-benzoylimino-3-cyclohexyl-4-cyclohexylimino-1,3-thiazetidine. With N,N' -diphenylcarbodiimide, benzoyl isothiocyanates afford corresponding substituted benzoylanilides.

In accord with the polarisation of the NCS group, isothiocyanates can enter 2 + 2 cycloaddition reactions by reaction of the C=S as well as of the C=N bond. In this connection the reaction of isothiocyanates with carbodiimides has drawn considerable attention. Ulrich and collaborators¹⁻³ found that, whereas alkyl and aryl isothiocyanates react with carbodiimides very sluggishly, reactive isothiocyanates, such as 4-nitrophenyl, alkylsulfonyl or arylsulfonyl isothiocyanates, afford 2 + 2 cycloadducts with carbodiimide already at room temperature. On the basis of analogy with isocyanates which react exclusively at the C=N bond⁴, the authors assigned to the resulting cycloadduct the 1,3-diazetidine structure *I*. Structure of the cycloadduct was studied later by several authors. It was proved that thermolysis of cycloadducts of *N*-methyl-*N'*-tert-butylcarbodiimide with 4-nitrophenyl or tosyl isothiocyanate, as well as with ethyl isothiocyanatoformate, leads to the 1,3-thiazetidine derivative⁵ *II*. Similar results were obtained by Ojima and coworkers⁶ who in the



X = O, S

strong peaks, m/e 206 ($[\text{C}_{13}\text{H}_{22}\text{N}_2]^{\bullet+}$) and m/e 163 ($[\text{C}_8\text{H}_5\text{NOS}]^{\bullet+}$), correspond to species arising by fission of the bonds c and d of the 1,3-thiazetidine ring (Scheme 1, V). The absence of a free $\text{C}=\text{S}$ bond in the molecule of V was confirmed also by the negative Feigl test.

Heating benzoyl isothiocyanate with $\text{N,N}'$ -dicyclohexylcarbodiimide in more polar solvents (methanol, acetonitrile) afforded already after 1/2 h the oxadiazine derivative IV and a small amount of dicyclohexylurea VI whereas the 4-membered thiazetidine derivative V was not isolated. Also 4-methylbenzoyl, 4-chlorobenzoyl and 4-biphenylcarbonyl isothiocyanates VII – IX react with $\text{N,N}'$ -dicyclohexylcarbodiimide under formation of 1,5-oxadiazine-4-thione derivatives X – XII as the products. Yields of the cyclisation products depend mainly on the ease of their isolation from the reaction mixture.

Reaction of benzoyl isothiocyanates III , VII and $VIII$ with $\text{N,N}'$ -diphenylcarbodiimide proceeds completely differently. Instead of the expected 4-membered thiazetidine or 6-membered oxadiazine derivatives we isolated only the corresponding 4-substituted benzoylanilides $XIII$ – XV . Mother liquors from isolation of the reaction products contained only the unreacted starting isothiocyanates and diphenylcarbodiimide.

EXPERIMENTAL

Compounds: Benzoyl isothiocyanate^{10,11} (III), b.p. 77–78°C/45.33 Pa; 4-methylbenzoyl isothiocyanate^{12,13} (VII), b.p. 99–100°C/39.99 Pa; 4-chlorobenzoyl isothiocyanate^{14,15} ($VIII$), m.p. 46–47°C; 4-biphenylcarbonyl isothiocyanate¹⁶ (IX), m.p. 51–53°C; $\text{N,N}'$ -dicyclohexylcarbodiimide, m.p. 33–35°C; $\text{N,N}'$ -diphenylcarbodiimide¹⁷, b.p. 107 to 109°C/55.99 Pa.

Reaction of 4-Substituted Benzoyl Isothiocyanates with $\text{N,N}'$ -Dicyclohexylcarbodiimide

To a stirred solution of carbodiimide (0.012 mol) in cyclohexane (40 ml) the corresponding acyl isothiocyanate (0.012 mol) was added, the mixture was refluxed for 1–2 h, cooled and the separated $\text{N,N}'$ -dicyclohexylurea filtered. The solvent was driven off *in vacuo* and the residue crystallized several times from a suitable solvent. Following compounds were prepared in this manner:

2-Cyclohexylimino-3-cyclohexyl-6-phenyl-1,3,5-oxadiazine-4-thione (IV): yield 33%, m.p. 84 to 85.5°C (n-heptane–light petroleum). For $\text{C}_{21}\text{H}_{27}\text{N}_3\text{OS}$ (369.5) calculated: 68.29% C, 7.32% H, 11.38% N, 8.67% S; found: 68.58% C, 7.56% H, 11.68% N, 8.52% S. IR spectrum (CHCl_3): $\nu(\text{C}=\text{N})_{\text{exocyclic}}$ 1658 cm^{-1} , $\nu(\text{C}=\text{N})_{\text{cyclic}}$ 1587 cm^{-1} . Mass spectrum (70 eV) m/e (rel. intensity, %): 369 (1.3), 222 (3), 206 (26), 177 (29), 163 (78), 149 (38), 147 (1.6), 141 (29), 125 (73), 105 (100), 97 (13), 83 (99), 77 (99).

2-Cyclohexylimino-3-cyclohexyl-6-(4-methylphenyl)-1,3,5-oxadiazine-4-thione (X): yield 69.9%, m.p. 109–110.5°C (light petroleum). For $\text{C}_{22}\text{H}_{29}\text{N}_3\text{OS}$ (383.5) calculated: 68.89% C, 7.62% H, 10.95% N; found: 68.61% C, 7.76% H, 10.84% N. IR spectrum (CHCl_3): $\nu(\text{C}=\text{N})_{\text{exocyclic}}$ 1657 cm^{-1} , $\nu(\text{C}=\text{N})_{\text{cyclic}}$ 1587 cm^{-1} .

2-Cyclohexylimino-3-cyclohexyl-6-(4-chlorophenyl)-1,3,5-oxadiazine-4-thione (XI): yield 35.5%, m.p. 101–102°C (n-heptane). For $C_{21}H_{26}ClN_3OS$ (403.9) calculated: 62.48% C, 6.49% H, 10.40% N; found: 62.79% C, 6.60% H, 10.56% N. IR spectrum ($CHCl_3$): $\nu(C=N)_{\text{exocyclic}}$ 1661 cm^{-1} , $\nu(C=N)_{\text{cyclic}}$ 1587 cm^{-1} .

2-Cyclohexylimino-3-cyclohexyl-6-(4-biphenyl)-1,3,5-oxadiazine-4-thione (XII): yield 51.2%, m.p. 123.5–125°C (ether–light petroleum). For $C_{27}H_{31}N_3OS$ (445.6) calculated: 72.74% C, 7.01% H, 9.42% N; found: 73.22% C, 6.98% H, 9.18% N. IR spectrum ($CHCl_3$): $\nu(C=N)_{\text{exocyclic}}$ 1660 cm^{-1} , $\nu(C=N)_{\text{cyclic}}$ 1587 cm^{-1} .

When benzoyl isothiocyanate was refluxed with N,N'-dicyclohexylcarbodiimide for only 1/2 h under the same conditions, the following work-up procedure was employed: the reaction mixture was cooled, the separated N,N'-dicyclohexylurea (0.080 g) filtered and the filtrate taken down *in vacuo*. Light petroleum was added to the oily residue and the mixture was chilled. The separated orange crystals were crystallized from an ether–light petroleum mixture, yielding 2-benzoylimino-3-cyclohexyl-4-cyclohexylimino-1,3-thiazetidone (V), m.p. 144–145.5°C, in 15% yield. For $C_{21}H_{27}N_3OS$ (369.5) calculated: 68.29% C, 7.32% H, 11.38% N, 8.67% S; found: 68.58% C, 7.58% H, 11.65% N, 8.47% S. IR spectrum ($CHCl_3$): $\nu(C=O)$ 1710 cm^{-1} , $\nu(C=N)_{\text{exocyclic}}$ 1612 cm^{-1} . Mass spectrum (70 eV): *m/e* (rel. intensity, %): 369 (1.3), 228 (1.6), 206 (48), 177 (61), 163 (99), 149 (44), 147 (1.6), 141 (3), 109 (22), 105 (100), 97 (16), 83 (99), 77 (99). Concentration of the mother liquors afforded the thione IV in 25% yield.

Reaction of 4-Substituted Benzoyl Isothiocyanates with N,N'-Diphenylcarbodiimide

The corresponding benzoyl isothiocyanate III, VII or VIII (0.012 mol) was added dropwise to a stirred solution of carbodiimide (0.012 mol) in cyclohexane (50 ml), the mixture was refluxed for 0.5–2 h, cooled and the separated crystals crystallized from an appropriate solvent. Following products were obtained according to this procedure: Benzoylanilide¹⁸ (XIII), m.p. 161–163°C (n-heptane); yield 41.6%. 4-Methylbenzoylanilide¹⁹ (XIV), m.p. 140–141°C (methanol); yield 52.1%. 4-Chlorobenzoylanilide¹⁸ (XV), m.p. 201–202°C (methanol); yield 63%.

Spectral Measurements

The IR absorption spectra in the region 800–3600 cm^{-1} were measured on a double-beam UR-20 (Zeiss, Jena) spectrophotometer in NaCl cells; concentration of the chloroform solutions was 0.033M. The instrument was calibrated using a polystyrene foil. Mass spectra of the obtained cycloadducts were taken on an MS 902 S (AEI Manchester) spectrometer (direct inlet, 70 eV, temperature of the ionisation chamber 120°C).

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