Synthesis and Transformations of 3-Benzoylimino-5,6-dihydro-3*H*-⟨imidazo[2,1-*c*][1,2,4]dithiazole⟩

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1-(N-benzoylthiocarbamoyl)-2-imidazolidinethione (**3**), obtained from 2-imidazolidinethione (**1**) and benzoyl isothiocyanate (**2**), was oxidized with hydrogen peroxide in acid solution to give the title compound (**6A**). Some transformations of **6A** are reported.

1,3,5-Trisubstituted dithiobiurets are known to react with two equivalents of oxidizing agents to yield dithiazolidines incorporating disulfide linkages[1]. On the other hand, Beer and coworkers have shown that 1-(*N*-methylthiocarbamoyl)-2-imidazolidinethione is oxidized with bromine affording 2,3,5,6-tetrahydro-2-methyl-3-thioxo-⟨imidazo[1,2-*d*][1,2,4] thiadiazole⟩[2]. The latter product was transformed by reaction with phenyl isothiocyanate into 2,7-bis-[phenylimino]-⟨imidazolino-[1,2,3-*c*,*d*]-2,3,4,5-tetrahydro-1,6,6aλ^4-trithia-3,4-diazapentalene⟩ (**12**).

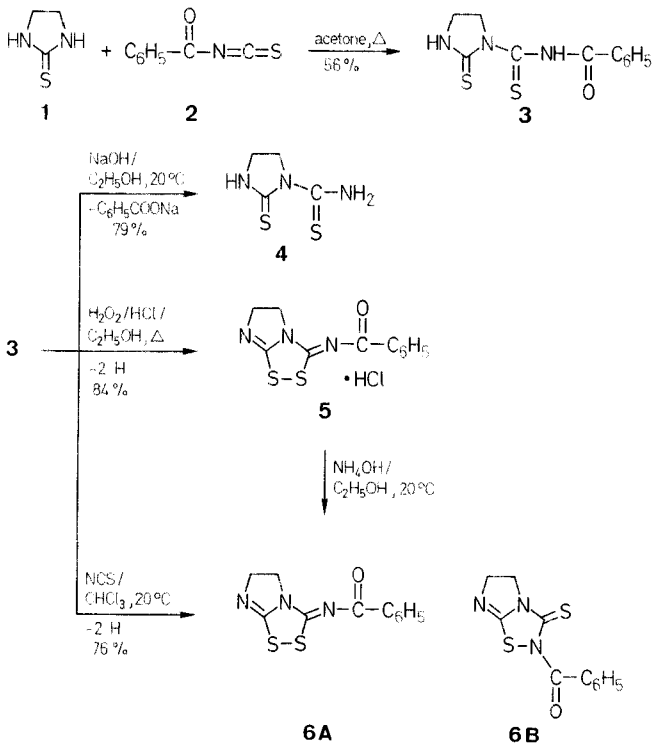
We wish to report here the synthesis and oxidation of 1-(*N*-benzoylthiocarbamoyl)-2-imidazolidinethione (**3**) leading to 3-benzoylimino-5,6-dihydro-3*H*⟨imidazo[2,1-*c*][1,2,4] dithiazole⟩ (**6A**) which proved to be of synthetic importance and shows a remarkable reactivity towards a variety of nucleophilic reagents.

Compound (**3**) is obtained in good yield by reaction of 2-imidazolidinethione **1** with benzoyl isothiocyanate **2** in boiling acetone and appeared to be a labile derivative which afforded 1-thiocarbamoyl-2-imidazolidinethione (**4**) on alkaline hydrolysis.

The oxidation of the compound **3** is performed by a standard method employing hydrogen peroxide in acid solution to yield the colorless hydrochloride **5**. The free base **6A** is liberated by treatment of **5** with ammonium hydroxide in ethanolic solution. The same product, **6A**, can be obtained from the reaction of **3** with *N*-chlorosuccinimide (NCS) in chloroform.

Two plausible, significantly different products **6A** and **6B** are envisioned for the oxidation of **3**. The dithiazole **6A** formed in the first stage of the reaction may become a by-product which undergo Dimroth rearrangement[3] to give thiadiazole **6B**.

The ^{13}C-NMR spectrum of the product **6** exhibits resonances at δ = 177.1, 165.6 and 159.5 ppm indicating that the molecule contains three heterosubstituted sp^2-C-atoms. The structure **6A** is supported by the IR spectrum which revealed strong absorptions at ν = 1590 and 1560 cm^{-1} characteristic of exocyclic benzoylimino group[4,5], and related to C=O and C=N vibrations respectively. Although

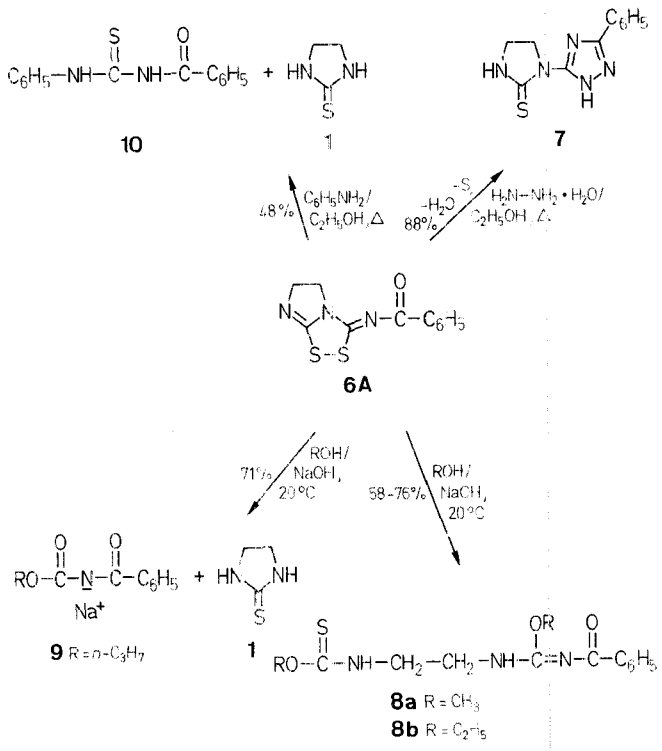


Scheme A

the structure **6B** can not be excluded, the weight of the available evidence supports the cyclic disulfide structure **6A**.

Compound **6A** possesses the marked reactivity expected of compounds containing disulfide linkages flanked by double bonds[1] and exemplified by its reactions with hydrazine hydrate, alcohols in the presence of sodium hydroxide and aromatic amines. Thus, refluxing the compound **6A** with hydrazine hydrate in ethanol gives 5-phenyl-3-(2-thioxo-1-imidazolidinyl)-2*H*-1,2,4-triazole (**7**). When the compound **6A** is treated with methanol or ethanol in the presence of sodium hydroxide, *O*-alkyl-N-[2-(2-alkyl-1-benzoyl-3-isoureido)ethyl] thiocarbamates **8a,b** (alkyl = CH_3, C_2H_5) are formed as a result of the opening of imidazoline and dithiazole rings.

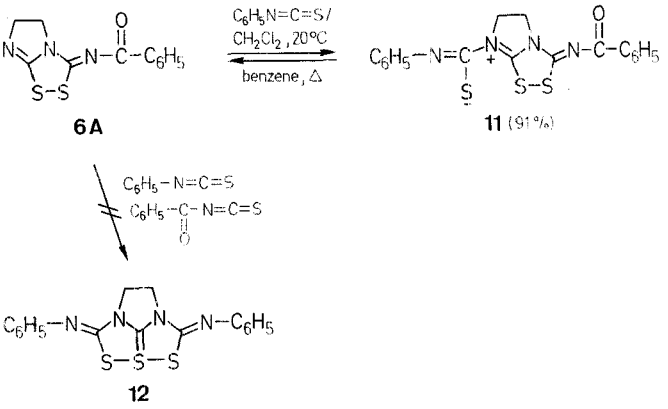
The structural elucidation of **8** was accomplished on the basis of IR, ^{1}H-NMR and mass spectra as well as microanalysis. The reaction of **6A** with two alcohol molecules takes place with elimination of sulfur leading to the linear products containing both thiocarbamate and isourea functionalities. On the other hand, less polar alcohols, such as *n*-propanol, under analogous conditions react with **6A** affording the sodium salt of *N*-benzoyl-*O*-propyl-carbamate **9**.



Scheme **B**

The reaction of **6A** with aniline in boiling ethanol led to the formation of complex mixture of products from which only 1-benzoyl-3-phenylthiourea (**10**) (48% yield) and **1** were isolated in pure form.

It is noteworthy that compound **6A** possessing a nucleophilic nitrogen atom at position 7 failed to give heteropentalene of type **12** in the reaction with heterocumulenes such as phenyl- and benzoyl isothiocyanates. It reacts, however, with phenyl isothiocyanate in dichloromethane or benzene to give the yellow adduct **11**, which is extremely insoluble at room temperature in most solvents and which is thermally unstable: on heating in boiling benzene, it reverts to compound **6A**.



Scheme **C**

Melting points are uncorrected. The mass spectra were recorded on a LKB 9000 spectrometer, the IR spectra on a Specord 75 IR spectrophotometer, ^{1}H-NMR spectra on a BS-487 Tesla Brno spectrometer at 80 MHz, and ^{13}C-NMR spectra on a Jeol SX 90Q spectrometer at 22,5 MHz.

1-(*N*-Benzoylthiocarbamoyl)-2-imidazolidinethione (3):
A suspension of **1** (10.2 g, 0.1 mol) and **2** (13.5 ml, 0.1 mol) in acetone (400 ml) is refluxed for 4 h. The excess solvent is evaporated under reduced pressure to give **3** which is purified by crystallization from dimethylformamide/water; yield 14.8 g (56%); yellow prisms; m.p. 179–181 °C.

$C_{11}H_{11}N_3OS_2$	calc.	C 49.78	H 4.18	N 15.84
(265.3)	found	49.65	4.37	15.89

IR (KBr): ν = 3160, 2770, 1700, 1540, 1460, 1170, 830, 715 cm^{-1}.

^{1}H-NMR (DMSO-d_6/HMDSO$_{int}$): δ = 3.4–4.0 (dd, 2H, J = 7.5 Hz); 4.55–4.95 (t, 2H, J = 7.5 Hz); 7.6–8.0 (m, 3H); 8.1–8.45 (m, 2H); 10.8 ppm (br. s, 1H).

1-Thiocarbamoyl-2-imidazolidinethione (4):
To a suspension of **3** (1.3 g, 5 mmol) in ethanol (20 ml) is added 10% aqueous sodium hydroxide (3 ml). The mixture is kept at 20 °C for 12 h and then the solvent is evaporated under reduced pressure. The solid residue is treated with cold water (5 ml), the unsoluble product is separated by suction, washed with cold water and recrystallized from water; yield 0.7 g (79%); m.p. 195–196 °C (Lit.[6], m.p. 192–194 °C).

$C_4H_7N_3S_2$	calc.	C 29.79	H 4.37	N 26.06
(161.2)	found	29.56	4.21	26.33

IR (KBr): ν = 3150, 1595, 1540, 1455, 1350, 1060, 865 cm^{-1}.

^{1}H-NMR (DMSO-d_6/TMS$_{int}$): δ = 3.3–3.8 (dd, 2H, J = 7 Hz); 4.15–4.65 (dd, 2H, J = 7 Hz); 9.3 (br. s, 1H); 9.85 (br. s, 1H); 11.1 ppm (br. s, 1H).

MS (70 eV): m/e = 161 (M^+, 100%); 102 (17.9); 101 (7.9); 86 (7.0); 74 (11.7); 73 (10.2); 60 (20.2); 59 (7.6); 45 (16.5); 42 (10.3).

3-Benzoylimino-5,6-dihydro-3*H*⟨imidazo[2,1-*c*][1,2,4]dithiazole⟩ (6A):
Method A: To a suspension of **3** (5.3 g, 0.02 mol) in ethanol (60 ml) is added concentrated hydrochloric acid (2 ml) and 30% hydrogen peroxide (5 ml). The reaction mixture is refluxed for 5 min and the colourless hydrochloride **5** obtained is separated by suction and washed with ethanol; yield 5 g (84%); m.p. 226–228 °C (from dimethylformamide).

$C_{11}H_{10}ClN_3OS_2$	calc.	C 44.07	H 3.36	N 14.02
(299.8)	found	44.40	3.12	14.30

IR (KBr): ν = 1585, 1540, 1340, 1315, 1250, 920, 715 cm^{-1}.

^{1}H-NMR (CF_3SO_3H/TMS$_{ext}$): δ = 4.25–5.1 (m, 4H); 7.15–8.1 (m, 5H); 9.1 ppm (br. s, 1H).

The free base **6A** is obtained on treatment of the suspension of **5** in ethanol (30 ml) with 25% ammonium hydroxide solution (2 ml) at 20 °C; yield 4.2 g (80%); m.p. 166–168 °C (benzene).

$C_{11}H_9N_3OS_2$ (263.3) calc. C 50.17 H 3.44 N 15.96 found 50.29 3.67 15.69

IR (KBr): ν = 3060, 2880, 1590, 1560, 1500, 1365, 1310, 1210, 1100, 970, 710 cm^{-1}.

^{1}H-NMR (DMSO-d_6/TMS_{int}): δ = 4.1 (m, 4H); 7.4–7.8 (m, 3H); 8.0–8.25 ppm (m, 2H).

^{13}C-NMR (DMSO-d_6/TMS_{int}): δ = 177.1 (7-C=N); 165.6 (C=O); 159.5 (3-C=N); 133.3; 133.1; 129.4; 128.6 (C_6H_5); 60.1; 47.5 (4-C, 5-C).

MS (15 eV): m/e = 263 (M^+, 34.7%); 105 (100); 102 (15.8); 77 (6.3).

Method B: Compound **3** (0.26 g, 1 mmol) is dissolved in chloroform (150 ml) and treated with *N*-chlorosuccinimide at 20°C. The mixture is stirred for 0.5 h and concentrated under vacuum to a volume of 30 ml. The crude precipitate is separated by suction and recrystallized from benzene; yield 0.2 g (76%) of the compound **6A** which is identical with those obtained according to the Method A.

5-Phenyl-3-(2-thioxo-1-imidazolidinyl)-2*H*-1,2,4-triazole (7):

Compound **6A** (1.3 g, 5 mmol) in ethanol (5 ml) is treated with 80% hydrazine hydrate (0.3 ml) and the mixture is heated under reflux for 10 min. After cooling the product is separated by suction and recrystallized from dimethylformamide/water; yield: 1 g (88%); m.p. 309–311°C.

$C_{11}H_{11}N_5S$ (245.3) calc. C 53.85 H 4.52 N 28.55 found 53.66 4.19 28.78

IR (KBr): ν = 3270, 3040, 2940, 1570, 1525, 1440, 1410, 1245, 715, 690 cm^{-1}.

^{1}H-NMR (DMSO-d_6/$HMDSO_{int}$): δ = 3.75–4.2 (m, 2H); 4.35–4.8 (m, 2H); 7.6–8.1 (m, 3H); 8.15–8.5 (m, 2H); 9.7 ppm (br. s, 1H).

MS (15 eV): m/e = 245 (M^+, 100%); 174 (10.2); 173 (93.4); 160 (33.6); 144 (8.9); 118 (8.2); 104 (18.8); 103 (16.1); 91 (6.2); 86 (11.9); 77 (25.7); 76 (8.3); 59 (13.8); 51 (9.8).

***o*-Methyl-*N*-[2-(2-methyl-1-benzoyl-3-isoureido)ethyl]-thiocarbamate (8a):**

Sodium hydroxide (1 g, 25 mmol) is added to the suspension of **6A** (1.3 g, 5 mmol) in methanol (10 ml) and the mixture is stirred vigorously at 20°C for 1 h. Then, the product is extracted with benzene (3 × 30 ml), the organic layer is washed with water (15 ml) and dried with magnesium sulfate. Evaporation of the solvent gives compound **8a** which is purified by crystallization from acetone/water; yield 1.1 g (76%); m.p. 121–123°C.

$C_{13}H_{17}N_3O_3S$ (295.3) calc. C 52.86 H 5.80 N 14.23 found 52.64 5.51 14.56

IR (KBr): ν = 3320, 3275, 3070, 2965, 1625, 1585, 1380, 1330, 1255, 1210, 1110, 1060, 880 cm^{-1}.

^{1}H-NMR (DMSO-d_6/TMS_{int}): δ = 3.0–3.6 (m, 4H); 3.7 (s, 3H); 3.8 (s, 3H); 6.95–7.45 (m, 3H); 7.8–8.1 (m, 2H); 9.0 (br. s, 1H); 9.55 ppm (br. s, 1H).

***o*-Ethyl-*N*-[2-(2-ethyl-1-benzoyl-3-isoureido)ethyl]thiocarbamate (8b):**

The reaction of **6A** with ethanol is performed as described above. **8b**; yield: 58%; m.p. 90–92°C (acetone/water).

$C_{15}H_{21}N_3O_3S$ (323.4) calc. C 55.70 H 6.54 N 12.99 found 55.48 6.28 12.81

IR (KBr): ν = 3220, 3070, 2985, 1615, 1540, 1420, 1320, 1245, 1185, 1090, 1045, 715 cm^{-1}.

^{1}H-NMR (DMSO-d_6/$HMDSO_{int}$): δ = 1.25–1.75 (q, 6H, J = 7 Hz); 3.5–3.85 (m, 4H); 4.35–4.95 (m, 4H); 7.55–7.95 (m, 3H); 8.3–8.7 (m, 2H); 9.55 (br. s, 1H); 10.25 ppm (br. s, 1H).

MS (15 eV): m/e = 323 (M^+, 17.9%); 295 (10.3); 294 (52.1); 219 (23.6); 218 (56.0); 205 (8.3); 194 (12.0); 193 (100); 191 (6.5); 122 (10.8); 113 (17.5); 105 (52.2); 85 (6.3).

Reaction of 6A with *n*-Propyl Alcohol in the Presence of Sodium Hydroxide:

Compound **6A** (1.3 g, 5 mmol) suspended in *n*-propanol (10 ml) is treated with sodium hydroxide (1 g, 25 mmol) and the mixture is stirred vigorously at 20°C for 2 h. The solid that precipitates is collected by filtration and washed with water to give the sodium salt **9**; yield: 0.8 g (71%); m.p. 293–296°C.

IR (KBr): ν = 3070, 2970, 1690, 1660, 1540, 1365, 1260, 1125, 1015, 705 cm^{-1}.

The filtrate is evaporated to dryness and the residue is treated with water to give **1**; yield: 0.16 g (32%).

Sodium salt **9** treated with 50% aqueous acetic acid affords *O*-propyl-*N*-benzoylcarbamate; yield: 0.65 g (65%); m.p. 119–120°C (*Lit.*[7], m.p. 118–120°C).

Reaction of 6A with Aniline:

Equimolar amounts of **6A** and aniline (5 mmol) are heated under reflux in ethanol (5 ml) for 1 h. After cooling to 0°C, compound **10** has precipitated and is separated by suction; yield: 0.6 g (48%); m.p. 147–149°C (Lit.[8], m.p. 148–149°C). The filtrate is concentrated under reduced pressure and treated with water to give **1**; yield: 0.1 g (20%).

Reaction of 6A with Phenyl Isothiocyanate:

Compound **6A** (0.5 g, 2 mmol) in dichloromethane (10 ml) is treated with phenyl isothiocyanate (0.54 g, 4 mmol) and the mixture is stirred at 20°C for 2 h. The yellow 1:1 adduct **11** is separated by suction and washed with dichloromethane; yield: 0.7 g (91%); m.p. 141–144°C (decomp.).

$C_{18}H_{14}N_4OS$ (398.5) calc. C 54.25 H 3.54 N 14.06 found 54.01 3.37 14.28

IR (KBr): ν = 1610, 1565, 1530, 1465, 1370, 1310, 1260, 1195 cm^{-1}.

The reverse reaction is accomplished by refluxing the compound **11** (0.5 g, 1.25 mmol) in benzene (15 ml) until yellow color has discharged (10 min). Treatment of the colorless solution with petroleum ether affords compound **6A**; yield: 0.3 g (91%); m.p. 166–168°C.

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