

A Convenient Synthesis of 2-Alkyliminocyclopentanedithiocarboxylic Acids by Reaction of Cyclopentanone with Carbon Disulfide in an Aqueous Amine Medium

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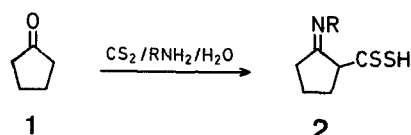
Bordás et al.¹ have previously reported the preparation of 2-methyliminocyclopentanedithiocarboxylic acid (**2a**) from cyclopentanone (**1**) and carbon disulfide in the presence of

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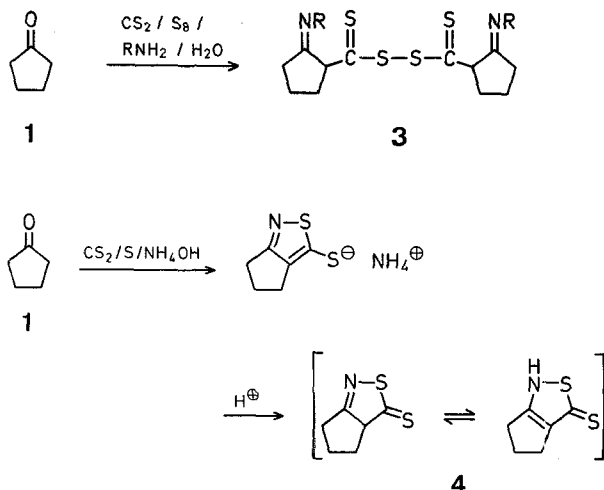
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an aqueous methylamine solution. However, the preparation of other 2-alkyliminocyclopentanethiocarboxylic acids by this method has not been reported and these acids were prepared from 2-iminocyclopentanethiocarboxylic acid² (**2**, R = H) by an amine exchange reaction. An earlier report³ described the synthesis of the several 2-alkylimino acids by treatment of *N*-alkylimino compounds, prepared from *gem*-dithiols, with carbon disulfide. Later, we reported a simple method⁴ of preparing the acids, involving addition of carbon disulfide to the product obtained by refluxing a mixture of the carbonyl compound and a primary amine with anhydrous potassium fluoride.

We now report a convenient, general, one-step preparation of 2-alkyliminocyclopentanethiocarboxylic acids **2**. The reaction of cyclopentanone (**1**) with carbon disulfide in an aqueous alkylamine medium is carried out below 10 °C for 0.5–2 h. It is significant to note that this method requires a large amount of water. When the reaction was conducted without water, the alkylamine reacted readily to give the corresponding alkylammonium *N*-alkyldithiocarbamate. The reaction mechanism may be explained in that the presence of water brings about protonation of the lone pair of electrons of the amine nitrogen atom, which suppresses the ability of the alkylamine to react with carbon disulfide.



The oxidatively coupled products **3**⁵ of **2** were also directly obtained by the above reaction involving addition of sulfur to the starting materials. We have recently reported⁶ that on using aqueous ammonia in place of alkylamine, the reaction leads to the cyclo-oxidation of 2-iminocyclopentanethiocarboxylic acid to give 3*H*-1,4,5,6-tetrahydrocyclopent[*c*]isothiazole-3-thione (**4**). In the case of the latter reaction, the intermediate 2-iminocyclopentanethiocarboxylic acid contains an *N*-hydrogen atom which is subject to reduction, and perhaps the oxidation reaction occurs between the hydrogen and thiol hydrogen close to the imino group to give the intramolecular cyclization product.



In the case of cyclohexanone, unstable 2-alkyliminocyclohexanedithiocarboxylic acids (**5**) were similarly obtained in

Table 1. 2-Alkyliminocyclopentanethiocarboxylic Acids (**2**) and 2-Alkyliminocyclohexanedithiocarboxylic Acids (**5**)

Compound	R	Yield [%]	m.p. [°C] (solvent)	Molecular formula ^a or Lit. m.p. [°C]
2a	CH ₃	65	125–126° (acetone)	125.5° ¹
2b	C ₂ H ₅	54	110–111° (acetone)	111° ¹
2c	<i>n</i> -C ₃ H ₇	40	114–115° (acetone)	117° ³
2d	<i>i</i> -C ₃ H ₇	31	110–111° (acetone)	106° ³
2e	<i>s</i> -C ₄ H ₉	38	103–104° ^b	101–102° ⁴
2f	<i>c</i> -C ₅ H ₉	77	107–109° ^{b,c}	C ₁₁ H ₁₇ NS ₂ (227.3)
2g	<i>c</i> -C ₆ H ₁₁	80	105–107° ^b	107° ³
5a	CH ₃	15	69–70° ^d (ethanol)	C ₈ H ₁₃ NS ₂ (187.2)
5b	C ₂ H ₅	8	68–69° ^e (ethanol)	C ₉ H ₁₅ NS ₂ (201.2)
5c	<i>n</i> -C ₃ H ₇	6	66–67° ^f (ethanol)	C ₁₀ H ₁₇ NS ₂ (215.2)

^a The microanalyses were in satisfactory agreement with the calculated values (C ± 0.14, H ± 0.13, N ± 0.13, S ± 0.33); M⁺ peak observed in the mass spectra.

^b Purified by reprecipitation from ethanol/2 normal hydrochloric acid; acetone/2 normal hydrochloric acid for **2f**.

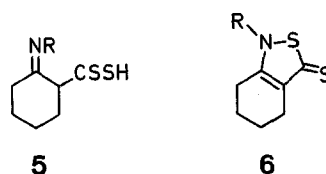
^c I.R. (KBr): ν = 2450 (s, SH); 1585 cm⁻¹ (vs. C=N). U.V. (C₂H₅OH): λ_{max} = 304 (ε = 11 400); 398 nm (24 600).

^d I.R. (KBr): ν = 2460 (s, SH); 1585 cm⁻¹ (vs. C=N). U.V. (C₂H₅OH): λ_{max} = 305 (ε = 8700); 393 nm (18 800).

^e I.R. (KBr): ν = 2470 (m, SH); 1585 cm⁻¹ (vs. C=N). U.V. (C₂H₅OH): λ_{max} = 305 (ε = 5400); 393 nm (11 500).

^f I.R. (KBr): ν = 2470 (m, SH); 1585 cm⁻¹ (vs. C=N). U.V. (C₂H₅OH): λ_{max} = 306 (ε = 12 100); 396 nm (25 800).

low yields (Table 1). The reaction with sulfur did not give the oxidatively coupled products but a small amount of the *N*-alkyl-1*H*,3*H*-4,5,6,7-tetrahydrobenzo[*c*]isothiazole-3-thiones (**6**). Treatment⁷ of the free acid **5** with iodine in dimethylformamide gave **6** in 30–40% yield.



All the imino acids reported here were exceedingly sensitive to Ni(II) ion, giving a pink-red precipitate. In the mass spectrum the molecular ion peak of the coupled products was not observed.

2-Alkyliminocyclopentanethiocarboxylic Acids **2** (Table 1); General Procedure:

To a mixture of cyclopentanone (**1**; 3 g, 0.036 mol) and carbon disulfide (4 g, 0.053 mol) is added a solution of alkylamine (0.05–0.07 mol) in water (25–30 ml) with cooling in ice. The mixture is stirred for 0.5–2 h below 10 °C and then 2 normal hydrochloric acid (20 ml) is added. The yellow precipitate is collected, washed with water, dried, and recrystallized or reprecipitated. When a yellow oil is

Table 2. Bis[2-alkyliminocyclopentylthiocarbonyl] Disulfides (**3**)

Compound	R	Yield [%]	m.p. [°C] (dec.) (solvent)	Molecular formula ^a or Lit. m.p. [°C]	I.R. (KBr) $\nu_{C=S}$ [cm ⁻¹]	U.V. (CHCl ₃) λ [nm] (ϵ)
3a	CH ₃	48	179–180° (C ₆ H ₅ NH ₂ /C ₂ H ₅ OH)	C ₁₄ H ₂₀ N ₂ S ₄ (344.5)	1598 (vs)	312 (8300); 407 (29500)
3b	C ₂ H ₅	42	174–176° (C ₆ H ₅ NH ₂ /C ₂ H ₅ OH)	C ₁₆ H ₂₄ N ₂ S ₄ (372.5)	1580 (vs)	312 (3000); 412 (15200)
3c	<i>n</i> -C ₃ H ₇	45	157–158° (C ₆ H ₆ /C ₂ H ₅ OH)	C ₁₈ H ₂₈ N ₂ S ₄ (400.4)	1580 (vs)	315 (5800); 416 (24800)
3d	<i>i</i> -C ₃ H ₇	33	150–151° (acetone)	149–150 ⁵	—	—
3e	<i>s</i> -C ₄ H ₉	35	146–147° (CHCl ₃)	146–147 ⁵	—	—
3f	<i>c</i> -C ₄ H ₉	72	177–178° (C ₆ H ₅ NH ₂ /C ₂ H ₅ OH)	C ₂₂ H ₃₂ N ₂ S ₄ (452.5)	1570 (vs)	312 (10400); 415 (49800)
3g	<i>c</i> -C ₆ H ₁₁	65	188–189° (CHCl ₃)	187–188 ⁵	—	—

^a The microanalyses were in satisfactory agreement with the calculated values (C \pm 0.27, H \pm 0.05, N \pm 0.27, S \pm 0.29).

Table 3. *N*-Alkyl-4,5,6,7-tetrahydrobenzo[*c*]isothiazole-3-thiones (**6**) from Acids **5**

Compound	R	Yield [%]	m.p. [°C] (solvent)	Molecular formula ^a or Lit. m.p. [°C]	I.R. (KBr) $\nu_{C=S}$ [cm ⁻¹]	U.V. (C ₂ H ₅ OH) λ_{max} [nm] (ϵ)
6a	CH ₃	37 (6) ^b	172–173° (C ₂ H ₅ OH)	C ₈ H ₁₁ NS ₂ (185.2)	1512 (s)	260 (9900); 365 (25800)
6b	C ₂ H ₅	34	128–129° (C ₂ H ₅ OH)	C ₉ H ₁₃ NS ₂ (199.2)	1505 (s)	261 (6400); 367 (16600)
6c	<i>n</i> -C ₃ H ₇	32	127–128° (C ₂ H ₅ OH)	125–126 ⁷	—	—
6d	<i>i</i> -C ₃ H ₇	(2) ^b	165–167° (CH ₃ OH)	167–168 ⁷	—	—

^a The microanalyses were in satisfactory agreement with the calculated values (C \pm 0.04, H \pm 0.16, N \pm 0.16, S \pm 0.3); M⁺ peak observed in mass spectra.

^b One-step reaction with addition of sulfur.

obtained instead of the crude precipitate, the oil is separated, dried under reduced pressure, and cooled to induce crystallization.

Bis[2-alkyliminocyclopentylthiocarbonyl] Disulfides **3** (Table 2); General Procedure:

To a mixture of cyclopentanone (**1**; 3 g, 0.036 mol), carbon disulfide (4 g, 0.053 mol), and sulfur (0.2 g, 0.0063 mol) is added a solution of alkylamine (0.05–0.07 mol) in water (20–25 ml) with cooling in ice. The mixture is stirred for 3–8 h below 10 °C, kept overnight at room temperature, and worked up as described for the preparation of **2**.

2-Alkyliminocyclohexanedithiocarboxylic Acids **5** (Table 1); General Procedure:

To a mixture of cyclohexanone (3 g, 0.031 mol) and carbon disulfide (4.5 g, 0.059 mol) is added a solution of alkylamine (0.1 mol) in water (12–20 ml) with cooling in ice. The mixture is stirred for 1–2 h below 3 °C. In the case of **5c**, 2 normal hydrochloric acid is added to pH 6. The yellow precipitate is collected, dried, and recrystallized. The acid **5** is stored in a refrigerator.

N-Alkyl-4,5,6,7-tetrahydrobenzo[*c*]isothiazole-3-thiones (**6**) from Acids **5**; General Procedure:

To a suspension of acid **5** (0.001 mol) in ethanol (5 ml) is added a solution of iodine (0.1 g) in dimethylformamide (2 ml) and the

mixture is kept overnight at room temperature. Water (40 ml) is then added and the aqueous mixture is extracted with benzene (15 \times 2 ml). After removal of solvents, the yellow solid product is recrystallized.

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