

Addition Reaction of 2-Iminocyclopentanedithiocarboxylic Acid with Schiff's Bases: A Novel Route to the Synthesis of 1,3-Thiazine Derivatives

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2-Iminocyclopentanedithiocarboxylic acid (1) reacted with Schiff's bases to give the adduct esters (2). The esters were easily converted into the corresponding thiazines (3a), (3e), and (3f) with accompanying elimination of anilines. In the case of cyclopentylideneanilines, the esters could not be isolated, instead the thiazine (4) was directly obtained.

THE present investigation was directed towards exploring the addition reaction of β -iminodithiocarboxylic acids with Schiff's bases. 2-Iminocyclopentanedithiocarboxylic acid (1) was chosen as a model acid, because it is easily accessible as a crystalline free acid.¹ Schiff's bases were prepared by the dehydration reaction of ketones and anilines with potassium fluoride. The addition reaction of the acid (1) with cyclohexylideneanilines proceeded as expected to give the adduct esters (2) (Scheme 1).

The esters (2), when heated in a solvent, easily underwent elimination of 1 mol equivalent of the aniline function to yield the 1,3-thiazine derivatives (3a),¹ (3e), and (3f) (Scheme 2). The u.v. spectra of the 1,3-thiazines resembled those of the esters (2). This may

be due to the fact that these 1,3-thiazines are cyclic β -iminodithiocarboxylic acid esters (see Table). The reaction of the acid (1) with cyclopentylideneanilines resulted in direct formation of the 1,3-thiazine (4),¹ the intermediate adduct esters being not stable enough to be isolated (Scheme 3).

The addition reaction was influenced by a steric effect. 2-Methylcyclohexylideneaniline and 3-pentylideneaniline did not enter into the reaction, instead the imino-group of the acid (1) was displaced by a phenylimino-group (Scheme 4). Thus, the 1,3-thiazine (3g) was made from the acid (1) and 2-methylcyclohexanone *via* the alternative route² (Scheme 2). The 1,3-thiazines (3e) and (3f) could also be obtained by this method.

¹ T. Takeshima, M. Yokoyama, T. Imamoto, M. Akano, and H. Asaba, *J. Org. Chem.*, 1969, **34**, 730.

² M. Muraoka, M. Yokoyama, K. Yamamoto, and T. Takeshima, *Bull. Chem. Soc. Japan*, 1970, **43**, 2134.

EXPERIMENTAL

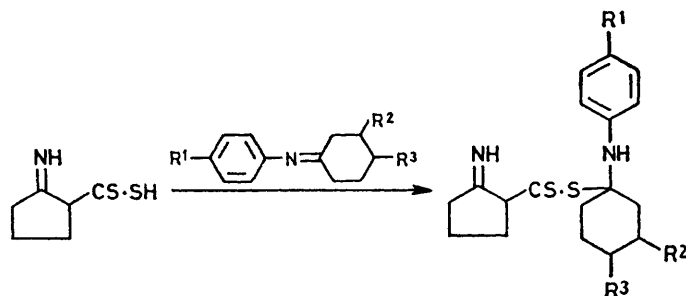
N-Alkylideneanilines.—A mixture of aniline (or *p*-substituted aniline) (0.1 mol) and ketone (0.12 mol) was refluxed with anhydrous potassium fluoride (0.1 mol) for 3–6 h. The potassium fluoride was filtered off and the filtrate was distilled under reduced pressure. The following Schiff's bases with the b.p.s stated were obtained as oils in

cyclopentylidene-p-chloroaniline, 157–159 °C at 17 mmHg; *N-cyclopentylidene-p-anisidine*, 162–166 °C at 18 mmHg; *N-3-pentylideneaniline*, 102–105 °C at 17 mmHg.

Addition Reaction of 2-Iminocyclopentanedithiocarboxylic Acid (1) with N-Cyclohexylideneanilines.—A mixture of the acid (1)¹ (0.4 g, 0.0025 mol), *N-cyclohexylideneaniline* (0.011 mol), and ethanol (0.5–1 ml) was kept overnight in

Compound	Yield (%)	M.p. (°C) ^a	$\lambda_{\max.}/\text{nm}$ (log ϵ) ^b	$\nu_{\max.}/\text{cm}^{-1}$ ^c	Formula	Found (%)				Required (%)			
						C	H	N	S	C	H	N	S
(2a)	71	111–114	235 (4.01) 336 (3.72) 410 (4.26)	3 290s 3 150s	$\text{C}_{18}\text{H}_{24}\text{N}_2\text{S}_2$	64.7	7.25	8.3	19.1	65.0	7.3	8.4	19.25
(2b)	39	98–101	236 (4.26) 336 (3.83) 408 (4.36)	3 285s 3 150s	$\text{C}_{19}\text{H}_{26}\text{N}_2\text{S}_2$	66.1	7.7	8.05	18.2	65.9	7.6	8.1	18.5
(2c)	37	98–100	245 (4.10) 338 (3.80) 408 (4.32)	3 295s 3 150s	$\text{C}_{18}\text{H}_{23}\text{N}_2\text{S}_2\text{Cl}$	60.0	6.3	7.8	17.4	58.9	6.3	7.6	17.5
(2d)	69	108–111	236 (4.08) 336 (3.76) 408 (4.30)	3 340vs 3 160vs	$\text{C}_{19}\text{H}_{26}\text{N}_2\text{OS}_2$	63.0	7.3	7.7	17.4	63.0	7.2	7.7	17.7
(2e)	36	119–120	234 (4.12) 337 (3.80) 408 (4.33)	3 290s 3 150s	$\text{C}_{19}\text{H}_{26}\text{N}_2\text{S}_2$	65.8	7.7	8.1	18.9	65.9	7.6	8.1	18.5
(2f)	52	106–107	234 (4.16) 337 (3.84) 408 (4.35)	3 300s 3 170s	$\text{C}_{19}\text{H}_{26}\text{N}_2\text{S}_2$	65.8	7.5	8.4	18.3	65.9	7.6	8.1	18.5
(3e)	63 ^d	170	240sh (3.66) 337 (3.86) 407 (4.37)	3 190vs	$\text{C}_{13}\text{H}_{19}\text{NS}_2$	61.45	7.6	5.55	25.0	61.6	7.6	5.5	25.3
(3f)	85 ^e 70 ^d	147–149	240sh (3.52) 336 (3.70) 408 (4.20)	3 150s	$\text{C}_{13}\text{H}_{19}\text{NS}_2$	61.5	7.5	5.45	25.1	61.6	7.6	5.5	25.3
(3g)	81 ^e 50 ^d	192	245sh (3.64) 337 (3.81) 407 (4.33)	3 165s	$\text{C}_{13}\text{H}_{19}\text{NS}_2$	61.6	7.55	5.5	25.8	61.6	7.6	5.5	25.3

^a Rapid heating. ^b In EtOH. ^c NH stretching absorption. ^d From the ester (2). ^e From the acid (1) and methylcyclohexanone.



(1)

(2)

a; $\text{R}^1 = \text{R}^2 = \text{R}^3 = \text{H}$ b; $\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{R}^3 = \text{H}$ c; $\text{R}^1 = \text{Cl}$, $\text{R}^2 = \text{R}^3 = \text{H}$ d; $\text{R}^1 = \text{OMe}$, $\text{R}^2 = \text{R}^3 = \text{H}$ e; $\text{R}^1 = \text{R}^3 = \text{H}$, $\text{R}^2 = \text{Me}$ f; $\text{R}^1 = \text{R}^2 = \text{H}$, $\text{R}^3 = \text{Me}$

SCHEME 1

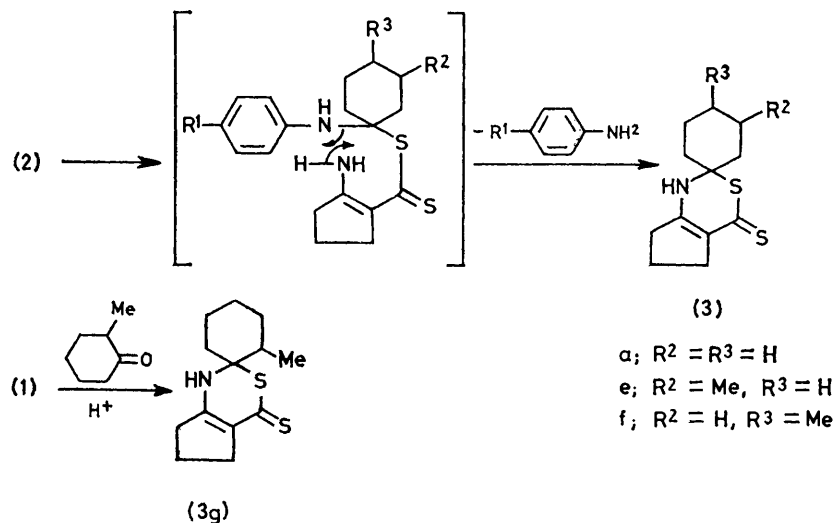
yields of ca. 20–50%; *N-cyclohexylideneaniline*, 137–141 °C at 16 mmHg; *N-cyclohexylidene-p-toluidine*, 155–157 °C at 18 mmHg; *N-cyclohexylidene-p-chloroaniline*, 167–168 °C at 15 mmHg; *N-cyclohexylidene-p-anisidine*, 170–174 °C at 15 mmHg; *N-2-methylcyclohexylideneaniline*, 142–146 °C at 16 mmHg; *N-3-methylcyclohexylideneaniline*, 137–141 °C at 15 mmHg; *N-4-methylcyclohexylideneaniline*, 135–140 °C at 15 mmHg; *N-cyclopentylideneaniline*, 132–136 °C at 18 mmHg; *N-cyclopentylidene-p-toluidine*, 142–146 °C at 18 mmHg; *N-*

a refrigerator. The solid product was collected, washed with ethanol, and dried. The following adduct esters were obtained: 1-anilinocyclohexyl (2a), 1-p-toluidinocyclohexyl (2b), 1-p-chloroanilinocyclohexyl (2c), 1-p-anisidinocyclohexyl (2d), 1-anilino-3-methylcyclohexyl (2e), and 1-anilino-4-methylcyclohexyl (2f) 2-iminocyclopentanedithiocarboxylates (see Table). These esters were not recrystallised because they were easily converted into the corresponding stable 1,3-thiazines (3) when warmed in a solvent.

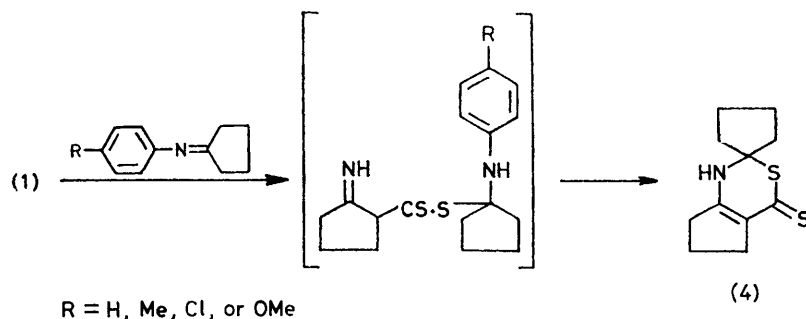
1,3-Thiazines (3).—(a) From the esters (2). The ester

(2) (0.0012 mol) was dissolved in ethanol (*ca.* 10 ml) and the solution was reduced in volume at *ca.* 80 °C by one half. The solid product was collected, washed with ethanol, and

paste was collected, dissolved in acetone, and water was added to it. The orange solid product was collected, washed with ethanol-water, and recrystallised from methanol.

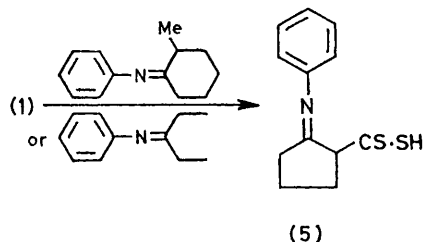


SCHEME 2



SCHEME 3

recrystallised from methanol or methanol-water. The known 1,3-thiazine (3a)¹ was obtained from (2a)—(2d). The esters (2e) and (2f) afforded 1,5,6,7-tetrahydro-3'-methylcyclopenta[d][1,3]thiazine-2-spirocyclohexane-4(2H)-thione (3e) and 1,5,6,7-tetrahydro-4'-methylcyclopenta[d][1,3]thiazine-2-spirocyclohexane-4(2H)-thione (3f), respectively.



SCHEME 4

(b) From the acid (1) and methylcyclohexanones.² To a solution of the acid (1) (1 g, 0.0063 mol) in methanol (40 ml) were added methylcyclohexanone (1 g, 0.009 mol) and sulphuric acid (0.7 g), and the mixture was refluxed for 1–1.5 h. After reduction of the volume of the mixture by 50% in a rotary evaporator, water was added to it. The

1,3-Thiazines (3e) and (3f) and 1,5,6,7-tetrahydro-2'-methylcyclopenta[d][1,3]thiazine-2-spirocyclohexane-4(2H)-thione (3g) were obtained from corresponding methylcyclohexanones.

Reaction of the Acid (1) with N-Cyclopentylideneanilines.—This reaction was carried out under the same conditions as those for the addition reaction described above. N-Cyclopentylideneaniline, N-cyclopentylidene-p-toluidine, N-cyclopentylidene-p-chloroaniline, and N-cyclopentylidene-p-anisidine were used as Schiff's bases. In every case 1,5,6,7-tetrahydrocyclopenta[d][1,3]thiazine-2-spirocyclopentane-4(2H)-thione (4) was obtained.

2-Phenyliminocyclopentanedithiocarboxylic Acid (5).—A mixture of the acid (1) (0.4 g, 0.0025 mol), N-2-methylcyclohexylideneaniline (or N-3-pentylideneaniline) (0.0085 mol), and ethanol (1 ml) was kept overnight at room temperature. The orange-yellow solid product was collected, washed with ethanol, and dried (yield *ca.* 20%), m.p. 69 °C; ν_{max} (KBr) 2450s (SH), 1604vs, 1590vs, and 1565vs cm^{-1} (conj. C=N, aromatic C=C); λ_{max} (EtOH) 251 (log ϵ 4.02), 317 (3.84), and 418 nm (4.33) (Found: C, 61.2; H, 5.5; N, 6.0; S, 27.0. C₁₂H₁₃NS₂ requires C, 61.3; H, 5.6; N, 6.0; S, 27.2%). The acid (5) produced a bluish green precipitate with Ni^{II} ions.

Methylation of the Acid (5).—The acid (5) (0.4 g, 0.0017 mol) was dissolved in a mixture of 1*N*-sodium hydroxide (20 ml) and ethanol (30 ml). To the mixture was added gradually a solution of methyl iodide (0.4 g, 0.0028 mol) in ethanol (20 ml) with stirring. After being stirred for an additional 30 min, the reaction mixture was kept for 1 h in a refrigerator. The yellow solid product was collected and dried. Recrystallisation from methanol-water gave *methyl 2-phenyliminocyclopentanedithiocarboxylate* (yield *ca.* 0.3 g, 71%), m.p. 69–70 °C; ν_{\max} (KBr) 2850m (CH₃), 1602vs, 1588s, and 1570vs (conj. C=N, aromatic C=C); λ_{\max} (EtOH) 252 (log ϵ 4.14), 325 (4.10), and 412 nm (4.43) (Found: C, 62.8; H, 6.1; N, 5.5; S, 26.0. C₁₃H₁₅NS₂ requires C, 62.6; H, 6.1; N, 5.6; S, 25.7%).

Oxidation of the Acid (5).—To a solution of the acid (5)

(0.1 g, 0.00043 mol) in ethanol (7 ml) was added gradually a solution of iodine (0.2 g) in *NN*-dimethylformamide (2 ml) with stirring. The dark red solid product was collected, washed with ethanol, and recrystallised from tetrahydrofuran-ethanol (yield *ca.* 0.05 g, 50%). The oxidative dimer,³ *bis-(2-phenyliminocyclopentylthiocarbonyl) disulphide* had m.p. 155 °C (slow heating) and 177 °C (rapid heating) (Found: C, 61.6; H, 5.2; N, 5.9; S, 27.7. C₂₄H₂₄N₂S₄ requires C, 61.5; H, 5.2; N, 6.0; S, 27.4%).

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³ T. Takeshima, N. Fukada, T. Ishii, and M. Muraoka, *J.C.S. Perkin I*, 1976, 1706.