

SYNTHESIS AND SPECTRAL STUDY OF 1-(1-HYDROXYCYCLOHEXANE-1-YL)-N-SUBSTITUTEDTHIOAMIDOFORMAMIDINO BENZYL

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ABSTRACT: A novel synthesis of series of 1-(1-hydroxycyclohexane-1-yl)-N-substitutedthioamidoformamidinobenzyl (3a-e) was synthesized by the reaction of 1-(1-hydroxycyclohexane-1-yl) benzylcyanide (1) with various thiocarbamides (2a-e) and hydrochloric acid in acetone-ethanol (1:1) medium. Firstly the formation of products was justified on the basis of gas chromatography technique. Their separation was carried out by column chromatography. On these two chromatographical technique, reaction conditions were set for the isolation of pure products. The structure of all the synthesized compounds were justified on the basis of usual chemical characteristics, IR, and NMR spectral analysis respectively.

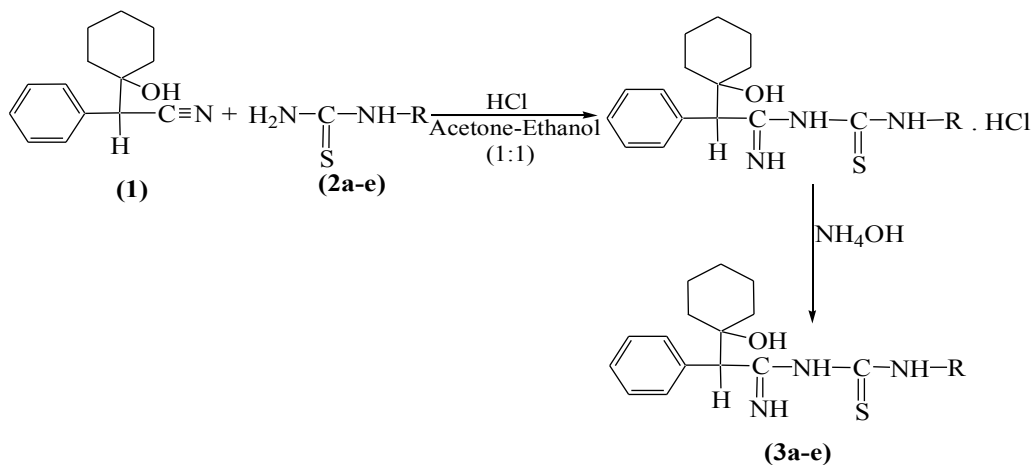
Key words: Synthesis, thioamidoformamidinobenzyl, cyclohexanol, benzylcyanide, thiocarbamides.

INTRODUCTION

Thiocarbamido, amidinothiocarbamido, and thioamido nucleus containing heterocycles and heterocycles possesses their own identity in pharmaceutical, industrial, agricultural and medicinal sciences.¹⁻¹⁰ These nucleus containing compounds enhance the potential and therapeutical value of that drug in drug chemistry. Hence, there is an evolution in drug, pharmaceutical and medicinal sciences and also focus on green chemistry for reducing and recycling the toxic/non-toxic chemicals by finding creative ways to minimize the human and environmental impact without stifling scientific process.

1-(1-Hydroxycyclohexane-1-yl)benzylcyanide¹¹⁻¹² found to possess anti-tumor and anti-cancer properties. These types of compounds have attracted much more attention due to their biological, agricultural and industrial importance due to anti-convalescent, anti-pyretic, anti-inflammatory, CNS depressant, fungicidal and insecticidal activities.¹³⁻¹⁵ Some are used in the treatment of liver diseases and their derivatives were also associated with the broad spectrum of biological activities including anti-tuberculosis, anti-tumor and analgesic properties.¹⁶⁻¹⁸ As evident from the structure of 1-(1-hydroxycyclohexane-1-yl)benzylcyanide, it is quite interesting that this compound contains cyano group. Hence, it can be easily reacted with various thiocarbamide in presence of hydrochloric acid in various organic solvents. This reaction is akin to the reaction of cyanoguanidine and various thiocarbamide in which related 1,3-diformamidothiocarbamide and 1-formamidinosubstituted-formamidinothiocarbamides were isolated.¹⁹⁻²⁰ The reaction of various isothiocyanates with cyano group had been investigated in sufficient details.²¹

These synthesized compounds are the best intermediate in the synthesis of novel series of thiadiazole, thiadiazines and triazines. With the above aim and objectives, the interaction of 1-(1-hydroxycyclohexane-1-yl)benzylcyanide with various thiocarbamides had been investigated.



Where: R a–hydrogen, b–henyl, c–methyl, d–ethyl, e–allyl.

Scheme 1

EXPERIMENTAL

All the chemicals used were of Analar grade (India make) alkyl/arylthiocarbamides were prepared according to literature method¹⁴, melting points of all synthesised compounds were determined in open capillary and uncorrected. IR-spectra were recorded on Perkin-Elmer spectrophotometer in the range 4000-400 cm^{-1} in KBr pellets. ¹H-NMR spectrums were recorded with TMS as internal standard using CDCl_3 and DMSO-d_6 . The purity of the compounds was checked on silica gel-G plates by TLC.

Synthesis of 1-(1-hydroxycyclohexane-1-yl)-thioamidoforamidinobenzyl (3a):

1-(1-Hydroxycyclohexane-1-yl)-thioamidoforamidinobenzyl (3a) was synthesized by refluxing a mixture of 1-(1-hydroxycyclohexane-1-yl)benzylcyanide (1) (0.01M), thiocarbamide (2a) (0.01M) and hydrochloric acid in acetone-ethanol (1:1) medium for 4 hours on water bath. During refluxing first clear solution was obtained which turned brownish in colour. It was filtered in hot condition and after distillation of solvent brownish crystals were isolated which on basification with dilute ammonium hydroxide afforded crystals, which were washed several times with ether, yield 64%, m.p. 112°C.

RESULTS AND DISCUSSION:

The synthesized compounds was separated using chromatographic techniques the data of Gas chromatogram of (3a) was given in Fig-I. After separation the physicochemical data of synthesized compounds are given in Table-I and Table-II.

Gas chromatography: The gas chromatography was carried out showed three peaks in chromatogram, clearly shows that the 64.43% of the product (3a) was found and the un-reacted thiocarbamide was found 34.94% which was clearly depicted in Figure-I.

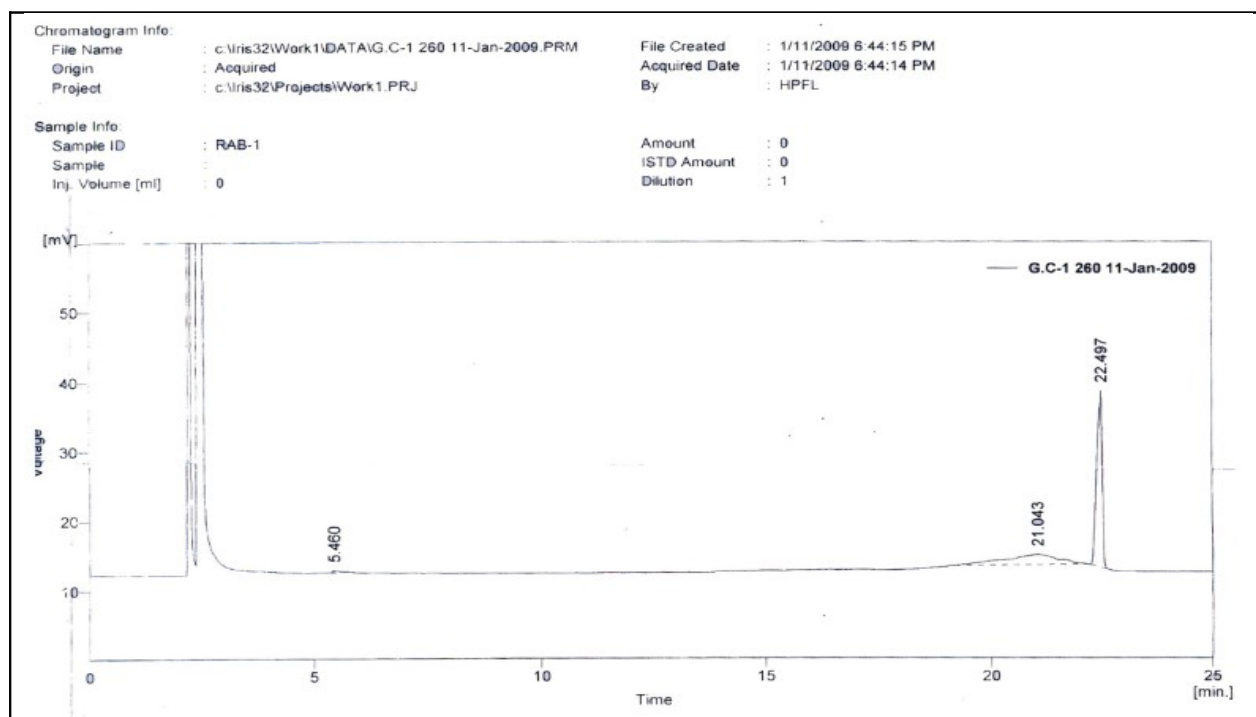


Figure - I

1-(1-hydroxycyclohexan-1-yl)-thioamidoforamidinobenzyl (3a):

It was needle shaped brown crystalline solid having m.p. 112°C., It gave positive test for nitrogen and sulphur. Desulphurized when boiled with alkaline plumbite solution. The benzene solution of compound when treated with pure and dry carbon disulphide a yellow colour was developed, which clearly indicated presence of basic imino (=NH) group²². Soluble in alcohol, acetone, dioxane, and DMSO, while insoluble in water.

IR (KBr): cm⁻¹ 3491.5 (B), 3491.5 (S), 1613.2, 1512.0, 1033.0, 790.1.

¹H NMR (CDCl₃+DMSO): δ 7.25-7.28 (-NH), 6.8-6.9 (Ar-H), 2.17 (Ar-CH), 1.7-1.1 (C-H).

1-(1-hydroxycyclohexan-1-yl)-phenylthioamidoforamidinobenzyl (3b):

It was needle shaped yellow crystalline solid having m.p. 145°C. It gave positive test for nitrogen and sulphur. Desulphurized when boiled with alkaline plumbite solution. The benzene solution of compound when treated with pure and dry carbon disulphide a yellow colour was developed, which clearly indicated presence of basic imino (=NH) group. Soluble in alcohol, acetone, dioxane, and DMSO, while insoluble in water.

IR (KBr): cm^{-1} 3453.2 (B), 3392.9 (S), 1632.1, 1571.2, 1062.4, 796.8.

$^1\text{H NMR}$ (CDCl₃+DMSO): δ 8.2-7.71 (-NH), 7.32-6.3 (Ar-H), 2.37 (Ar-CH), 1.9-1.5 (C-H).

Table-I: Physiochemical data (3a-e):

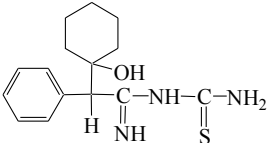
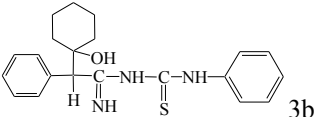
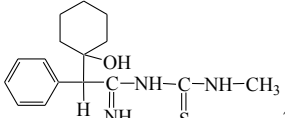
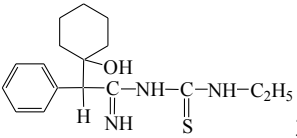
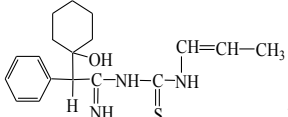
Compound	m.p. ($^{\circ}\text{C}$)	Mol. F. Mol. Wt.	Colour	Yield (%)	S.O.R. [$(\alpha)_D^{28}$]
 3a	112	C ₁₅ H ₂₁ N ₃ S ₁ 291	Brown	64	+34.88 ⁰ (C,0.05)
 3b	145	C ₂₁ H ₂₅ N ₃ S ₁ 367	Yellow	66	+63.49 ⁰ (C,0.05)
 3c	119	C ₁₆ H ₂₃ N ₃ S ₁ 307	Faint brown	81	+14.59 ⁰ (C,0.05)
 3d	162	C ₁₇ H ₂₅ N ₃ S ₁ 319	Brown	72	+71.21 ⁰ (C,0.05)
 3e	175	C ₁₈ H ₂₅ N ₃ S ₁ 331	Red	68	+39.30 ⁰ (C,0.05)

Table-II: CHNS analytical data of (3a-e) (Found/Calculated) :

Compound No.	C	H	N	S
3a	60.25/61.85	7.09/7.22	14.25/14.30	10.05/10.99
3b	68.29/68.66	6.20/6.81	11.08/11.44	8.33/8.72
3c	62.31/62.54	7.68/8.14	13.33/13.68	10.48/10.42
3d	62.03/63.95	7.19/7.84	12.34/13.17	9.05/10.03
3e	64.12/65.26	7.29/7.55	11.33/12.69	9.60/9.67

1-(1-hydroxycyclohexan-1-yl)-methylthioamidobenzylamine (3c):

It was needle shaped faint brown crystalline solid having m.p. 119⁰C. It gave positive test for nitrogen and sulphur. Desulphurized when boiled with alkaline plumbite solution. The benzene solution of compound when treated with pure and dry carbon disulphide a yellow colour was developed, which clearly indicated presence of basic imino (=NH) group. Soluble in alcohol, acetone, dioxane, and DMSO, while insoluble in water.

IR (KBr): cm^{-1} 3398.8 (B), 3331.2 (S), 1552.7, 1510.3, 1029.3, 771.1.

$^1\text{H NMR}$ (CDCl₃+DMSO): δ 7.17-7.08 (-NH), 6.21-6.07 (Ar-H), 2.08 (Ar-CH), 2.0-1.7 (C-H), 1.0 (CH₃).

1-(1-hydroxycyclohexan-1-yl)-ethylthioamidoforamidinobenzyl (3d):

It was needle shaped brown crystalline solid having m.p. 162°C. It gave positive test for nitrogen and sulphur. Desulphurized when boiled with alkaline plumbite solution. The benzene solution of compound when treated with pure and dry carbon disulphide a yellow colour was developed, which clearly indicated presence of basic imino (=NH) group. Soluble in alcohol, acetone, dioxane, and DMSO, while insoluble in water.

IR (KBr): cm^{-1} 3403.4 (B), 3326.7 (S), 1544.3, 1504.2, 1022.6, 782.3.

¹H NMR (CDCl₃+DMSO): δ 7.43-7.32 (-NH), 6.51-6.42 (Ar-H), 2.41 (Ar-CH), 2.1-1.9 (C-H), 1.3-1.1 (CH₂), 0.9 (CH₃).

1-(1-hydroxycyclohexan-1-yl)-allylthioamidoforamidinobenzyl (3e):

It was needle shaped red crystalline solid having m.p. 175°C. It gave positive test for nitrogen and sulphur. Desulphurized when boiled with alkaline plumbite solution. The benzene solution of compound when treated with pure and dry carbon disulphide a yellow colour was developed, which clearly indicated presence of basic imino (=NH) group. Soluble in alcohol, acetone, dioxane, and DMSO, while insoluble in water.

IR (KBr): cm^{-1} 3488.3 (B), 3451.6 (S), 1661.2, 1440.5, 1030.7, 730.6. **¹H NMR (CDCl₃+DMSO):** δ 7.95-7.82 (-NH), 7.3-6.4 (Ar-H), 2.81 (Ar-CH), 1.6-1.4 (C-H), 1.2-1.0 (=C-H), 0.8 (C-H₃).

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