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A clean procedure for the synthesis and characterization, spectral studies of some novel newly fluorine substituted thio-semicarbazides and substituted thio-semicarbazones

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ABSTRACT

A new class of highly efficient, convenient and rapid synthesis of fluorine substituted thio-semicarbazide derivatives containing different functional groups have been obtained by the condensation reactions of substituted phenyl-isothiocyanate with R-malon anilic acid hydrazides(1a-1l) and substituted thio-semicarbazones have also been synthesized by the condensation reactions between selected substituted aromatic aldehydes with newly synthesized substituted thio-semicarbazides(2a-2b) in the presence of glacial acetic acid. The structures of newly synthesized substituted thio-semicarbazides & substituted thio-semicarbazones have been characterized on the basis of their spectral studies viz: IR, Elemental analysis, Physical properties.

Key words: Synthesis, substituted thio-semicarbazides, substituted thio-semicarbazones, Glacial acetic acid, condensation, spectral analysis.

INTRODUCTION

Heterocyclic Thiosemicarbazide is a simple sulphur containing compound plays an important roll in pharmacology. It also represents a class of compounds having importance in the field of medi cine and agriculture. Thio-semicarbazide possessi ng the N-C-S group have been reported to show pronounced biological activities[1]. Substituted thiosemicarbazide have been reported as anti-bacterial[2], antifungal[3], anti-tubercular[4],Metabolic convulsants[5],hypotensive[6].Thio-semicarbazides have also been found to possess herbicidal and growth regul ating[7,8], hypoglyceamic[9] activity.

Thio-semicarbazone is a class of compound and have also been possess antitumor[10],antiviral[11], anti-tubercular[12], anti-bacterial[13] activity .

Thio-semicarbazones are studied due to it's biological activities, analytical,structural properties. By various workers several substituted thio-semi carbazides have been synthesized in our laboratory[14-21]. Keeping in view of the above observations, it is thought of interest to synthesize some new substituted thio-semicarbazides and new substituted thio-semicarbazones .

EXPERIMENTAL

Material and Methods

All melting points were determined in open capillary tubes and were uncorrected. All the used chemicals in the synthesis were procured from Sigma-Aldrich Company Germany . All the newly synthesized compounds were recrystallised by absolute ethanol 99%. The purity of newly synthesized compounds was ascertained by TLC on silica-gel-coated AI plates (E-Merck). The IR spectra (cm^{-1}) was taken in Kbr-disc method on a Perkin-Elmer spectrum RX-1 FT-IR spectrophotometer at Central Drug Research Institute (CDRI) Lucknow .

The analytical & Physical data, molecular for mula, molecular weight, m.p, colour, yield% are recorded in the Table 1 and spectral analysis are recorded in the Table 2.

General procedure of the Synthesis of N(R)-phenyl malon anilic acid hydrazide (1a-1i)

The substituted amine (0.025 mole) and diethyl malonate(0.05 mole) was added in the presence of DMF and refluxed for about 45 minutes, after that ethanol (20 ml) was added to it, and then concentrated over the boiling water-bath , add 20 ml of ethyl alcohol and hydrazine hydrate 99%, thus the solid product was obtained, recrystallized by ethanol, and was identified N(R)-phenyl malon anilic acid hydrazide (1a-1i).

General procedure of the Synthesis of Thio-semicarbazide (2a-2i)

To (1a-1i ; 0.001 mole) of substituted phenyl malonamic acid hydrazide and stirred solution of substituted phenyl-isothiocyanate (0.001 mole) in 15ml of absolute ethanol, was refluxed for 3-hours, cooling the product and then filtered, recr ystallized from ethanol 99% and was identified the corresponding 4-Fluoro phenyl thio-semicarbazides of N (R) phenyl malon anilic acid hydrazides (2a-2i).

General procedure of the Synthesis of Thio-semicarbazone (3a-3d, 4a-4d)

A mixture of substituted thio-semicarbazide (2a,2b ; 0.001 mole) and substituted aromatic alde hyde (0.001 mole) in absolute ethanol (15 ml) with 4-5 drops of glacial acetic acid, was refluxed for 3-hours, the solid obtained during refluxing, cooling the product, was recrystallized by absolute ethanol 99%, and identified to be 4-Fluoro thio-semicarb azone of substituted aldehydes (3a-3d, 4a-4d).

RESULTS AND DISCUSSION

The Infrared-spectra of the newly synthesized compounds of substituted thio-semicarbazides & substituted thio-semicarbazones have been recorded in the frequency region 400-450 cm^{-1}, these are recorded in the Table-2.

The IR Spectrum of 4-Fluoro phenyl thio-semicarbazide of N(2-Methoxy-5-Methyl) phenyl malonanilic acid hydrazide[2a], show -NH stretching vibrations at 3448.0 cm^{-1}, Aromatic (-C-H) stretching vibrations at 3021.8 cm^{-1}, $-CH_2$ stretching vibrations at 1429.7 cm^{-1} and absorption at 1517.1 cm^{-1} indicates the presence of -C=O, stretching vibrations at 1333.9 cm^{-1} shows -C=S, stretching vibrations at 1216.3 cm^{-1} show -N-N , stretching vibrations at 1673.4 cm^{-1} show -CONH, mono substitution at 670.9 cm^{-1}. These characters are lent support to the structures of the compounds 2a, 2b-2f and other compounds (2g-2i).

The IR Spectra of 4-Fluoro phenyl thio-semicarbazone of 2 - Nitro-benzaldehyde[3c],shows

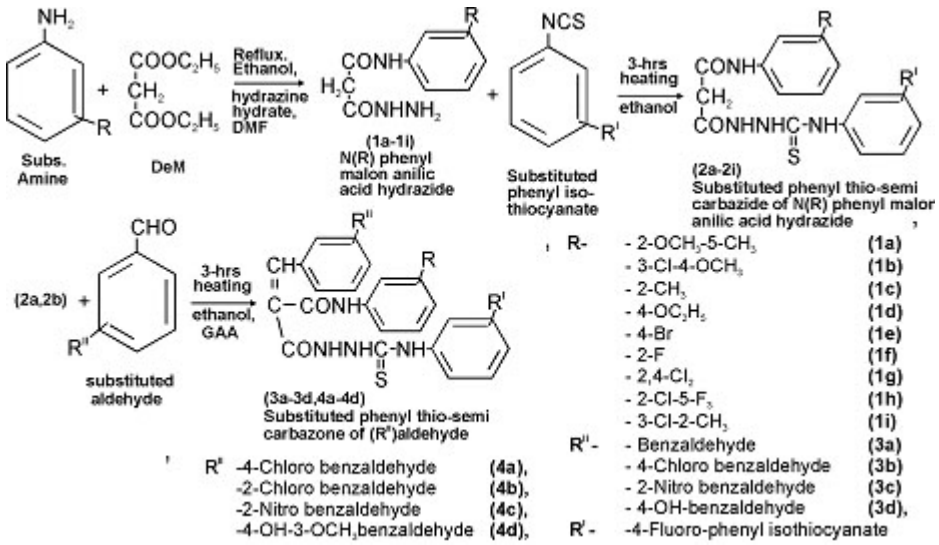

Table 1: Physical & Analytical data of Synthesized Compounds

Codes	Molecular formula	Molecular weight	% Analytical data C cal.	(found)	H cal.	(found)	N cal.	(found)	S cal.	(found)	M.P °C	Yield %	Colour
1a	$C_{11}H_{15}N_3O_3$	237.26	55.68	(55.72)	6.37	(6.38)	17.71	(17.75)	-	-	129°	44.23	white
1b	$C_{10}H_{12}N_3O_3Cl_1$	257.68	46.61	(46.65)	4.69	(4.70)	16.30	(16.33)	-	-	158°	56.30	white
1c	$C_{10}H_{13}N_3O_2$	207.23	57.96	(57.92)	6.32	(6.30)	20.28	(20.29)	-	-	094°	32.59	magnolia
1d	$C_{11}H_{15}N_3O_3$	237.26	55.68	(55.70)	6.37	(6.38)	17.71	(17.74)	-	-	134°	37.23	crystalline white
1e	$C_9H_{10}N_3O_2Br_1$	272.12	47.59	(47.62)	3.70	(3.71)	15.44	(15.47)	-	-	124	43.56	morning white
1f	$C_9H_{10}N_3O_2F_1$	211.20	51.18	(51.19)	4.77	(4.78)	19.89	(19.91)	-	-	089°	35.06	white pebble
1g	$C_9H_9N_3O_2Cl_2$	262.11	41.24	(41.26)	3.46	(3.47)	16.03	(16.05)	-	-	131°	50.40	crystalline white
1h	$C_{10}H_9N_3O_2Cl_1F_3$	295.66	40.62	(40.64)	3.07	(3.08)	14.21	(14.25)	-	-	135°	44.82	cream caress white
1i	$C_{10}H_{12}N_3O_2Cl_1$	241.68	49.69	(49.71)	5.00	(5.01)	17.38	(17.40)	-	-	108°	51.46	crystalline white
2a	$C_{18}H_{19}N_4O_3F_1S_1$	390.38	55.38	(55.41)	4.90	(4.92)	14.35	(14.39)	08.20	(08.24)	186°	45.68	creamish white
2b	$C_{17}H_{16}N_4O_3Cl_1F_1S_1$	410.80	49.70	(49.72)	3.92	(3.94)	13.64	(13.69)	07.79	(07.83)	196°	48.94	white
2c	$C_{17}H_{17}N_4O_2F_1S_1$	360.36	56.66	(56.64)	4.75	(4.72)	15.55	(15.59)	08.88	(08.91)	161°	34.13	light wheat sprig
2d	$C_{18}H_{19}N_4O_3F_1S_1$	390.38	55.38	(55.40)	4.90	(4.88)	14.35	(14.39)	08.20	(08.18)	190°	48.64	morning glory
2e	$C_{16}H_{14}N_4O_2F_1Br_1S_1$	425.23	45.19	(45.22)	3.32	(3.35)	13.17	(13.21)	07.52	(07.56)	187°	38.86	dirty sugared nut
2f	$C_{16}H_{14}N_4O_2F_1S_1$	364.32	52.75	(52.72)	3.87	(3.89)	15.38	(15.42)	08.78	(08.81)	178°	36.14	light row silk
2g	$C_{16}H_{13}N_4O_2F_1Cl_2S_1$	415.22	46.28	(46.31)	3.15	(3.17)	13.49	(13.54)	07.70	(07.73)	177°	42.09	white
2h	$C_{17}H_{13}N_4O_2F_4Cl_1S_1$	448.78	45.50	(45.52)	2.92	(2.94)	12.48	(12.52)	07.13	(07.18)	158°	40.82	cream caress
2i	$C_{17}H_{16}N_4O_2F_1Cl_1S_1$	394.80	51.72	(51.74)	4.08	(4.06)	14.19	(14.23)	08.10	(08.12)	166°	41.32	dirty white
3a	$C_{25}H_{24}N_4O_3F_1S_1$	479.50	62.62	(62.64)	5.04	(5.06)	11.68	(11.72)	06.67	(06.71)	184°	39.32	light cream
3b	$C_{25}H_{23}N_4O_3F_1Cl_1S_1$	513.95	58.42	(58.45)	4.51	(4.53)	10.90	(10.94)	06.22	(06.25)	188°	33.58	off white
3c	$C_{25}H_{23}N_5O_5F_1S_1$	524.50	57.24	(57.27)	4.42	(4.44)	13.35	(13.39)	06.10	(06.14)	203°	43.80	wild yellow
3d	$C_{25}H_{24}N_4O_4F_1S_1$	495.50	60.60	(60.62)	4.88	(4.90)	11.31	(11.35)	06.46	(06.49)	201°	32.81	dirty white
4a	$C_{24}H_{20}N_4O_3F_1Cl_2S_1$	534.37	53.94	(53.96)	3.77	(3.79)	10.48	(10.54)	05.98	(06.02)	196°	35.81	dirty cream caress
4b	$C_{24}H_{20}N_4O_3F_1Cl_2S_1$	534.37	53.94	(53.91)	3.77	(3.75)	10.48	(10.52)	05.98	(06.00)	204°	32.26	dirty white
4c	$C_{24}H_{20}N_5O_5F_1Cl_1S_1$	544.92	52.90	(52.88)	6.70	(6.67)	12.85	(12.89)	05.87	(05.84)	202°	42.96	sugarcane
4d	$C_{25}H_{23}N_4O_5F_1Cl_1S_1$	545.95	55.00	(55.02)	4.24	(4.26)	10.26	(10.30)	05.86	(05.90)	221°	33.62	cream caress

absorption at 3022.0 cm^{-1} represents Aromatic C-H), absorption at 3445.5 cm^{-1} show -NH, stretching vibrations at 1528.4 cm^{-1} indicates the -C=O,stretching vibrations at 1336.6 cm^{-1} reveals-C=S,stretching vibrations at 1216.6 cm^{-1} indicating -N-N, stretching vibrations at 1672.0 cm^{-1} indicates the -CONH, absorption at 2358.0 cm^{-1} indicates HC=C stretching vibrations, stretching vibrations at 671.9 cm^{-1} show the mono substitution ring.

These above absorption spectrum are lent support to the assigned structures of newly synthesized compounds 3c & 4d and other newly synthesized compounds 3a-3b, 3d, 4a-4c.

Thus the IR spectra of the newly synthesized compounds indicating the absorption spectrum was in agreement with the assigned structure . Substituted thio-semicarbazides and substituted thio-semicarbazones are stable solids,which are ratherspringly soluble in common solvents and with high melting points,they also have characteristic colour.

Table 2:Spectral data of the Newly Synthesized Compounds

Codes	-NH cm^{-1} stretching	Ar C -H cm^{-1} stretching	$-CH_2$ cm^{-1} stretching	-C=O cm^{-1} stretching	-C=S cm^{-1} stretching	N-N cm^{-1} stretching	mono subs.ring	-CONH cm^{-1} stretching	HC=C cm^{-1} stretching
2a	3448.0	3021.8	1429.7	1517.1	1333.9	1216.3	670.9	1673.4	-
2b	3441.9	3022.0	1429.3	1518.5	1334.5	1216.2	671.0	1671.8	-
2c	3424.0	3022.4	1429.0	1518.9	1335.3	1216.4	671.3	1657.3	-
2d	3465.6	3021.8	1429.3	1516.9	1334.9	1216.3	671.3	1673.1	-
2e	3462.0	3022.1	1431.4	1516.9	1333.4	1216.4	671.3	1669.4	-
2f	3446.9	3021.9	1429.9	1517.4	1334.0	1216.3	671.1	1668.8	-
3c	3445.5	3022.0	-	1518.4	1336.6	1216.6	671.9	1672.0	2358.0
4d	3426.2	3022.2	-	1520.9	1338.1	1216.5	671.9	1676.4	2358.9

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