



Preparation, Thermal and Spectroscopic Investigation of Fluorine Compounds Bearing 5,6-Diphenyl-1,2,4-triazine-3-hydrazone Moieties

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This study reports the preparation, thermal and spectroscopic evaluation of a series of new fluorine compounds containing nitrogen heterocyclic aromatic systems. In addition, the resulted products of fluorine labeled heterocyclic compounds were in good yield and purity. The characterization of these compounds was performed using ^1H NMR spectroscopy, FT-IR spectroscopy, thermal gravimetric analysis, UV-VIS spectroscopy and fluorescence spectroscopy. The results obtained using ^1H NMR and FT-IR measurements were in good agreement with chemical structure of synthesized fluorine labeled compounds. Thermal gravimetric analysis data suggested that fluorine labeled compounds have good thermal stability. The optical behavior of newly prepared fluorine labeled compounds provided that these compounds have significant absorption in the UV region. In addition, all fluorine compounds, except for chromone hydrazone derivatives (VI) are found to have very weak fluorescence background, which may lead to the advantages of using fluorine labeled compounds in optical studies of the other solutes.

Key Words: Fluorine substituted compounds, 5,6-Diphenyl-1,2,4-triazine-3-hydrazones, Thermal analysis, UV-VIS, Fluorescence.

INTRODUCTION

Environmental pollutions resulting from release of various trace toxic of organic compounds and/or trace toxic of heavy metal ions *via* anthropogenic activity by human, discharge of expired chemicals, quality control laboratories, hospitals and industries have recently seen an upsurge of interest.^{1,2} Over the past decade, much attention has been directed by both academic and industrial research communities towards the preparation, spectroscopic studies and complex formation of fluorine compounds, particularly those connected with hydrazono-1,2,4-triazine derivatives³⁻⁵.

Recently, fluorine compounds bearing nitrogen heterocyclic aromatic systems have been received considerable interest in different applications, including environmental, industrial and in pharmaceuticals⁶⁻¹¹. For example, fluorine bearing a 1,2,4-triazine moieties showed high activities as anti human immunodeficiency virus (HIV), anticancer agents and excellent chelating agents for heavy metal ions^{12,13}. They have also showed a broad spectrum of biological and pharmacological activities, such as chemotherapy, plant protection and extraction with subsequent determination of some toxic heavy metals. In fact, the need for aromatic heterocyclic compounds with tunable transmittance, refraction, polarization and color presents new challenges and opportunities. Thus, there is still

an increasing interest for preparation and investigation of new fluorine labeled heterocyclic compounds.

Considerable effort has also been directed toward the synthesis of fluorine compounds containing a 5,6-diphenyl-1,2,4-triazine-3-hydrazone moieties and their use as chelating agents for monitoring heavy metal ions in the environment. Recent literature revealed that only few reports are known on the chelating behavior of fluorine compounds, in particular those bearing 1,2,4-triazine-3-hydrazones^{3-5,12,13}. The present study focused on the preparation, thermal and spectroscopic evaluation of a series of new fluorine compounds containing 5,6-diphenyl-1,2,4-triazine-3-hydrazone derivatives. Physico-chemical and spectroscopic properties of fluorine labeled heterocyclic compounds were investigated by use of ^1H NMR spectroscopy, FT-IR spectroscopy, thermal gravimetric analysis, UV-VIS spectroscopy and fluorescence spectroscopy.

EXPERIMENTAL

5,6-Diphenyl-1,2,4-triazine-3-thione, hexafluoroacetic anhydride, hydrazine hydrate, trifluoroacetic acid, 2-amino-chromone-3-carboxylaldehyde, trifluoroacetyl chloride, 1,1,1,5,5,5-hexafluoro-2,4-pentadione, hydrogen cyanide and dimethyl formamide were obtained from Sigma-Aldrich (Milwaukee, WI). All reagents used were of the highest available purity and of at least analytical reagent grade.

TABLE-1
PHYSICOCHEMICAL AND ANALYTICAL DATA OF FLUORINE LABELED COMPOUNDS.
THE SYMBOL T_m REPRESENTS THE MELTING POINT

Compound No.	Yield (%)	T_m (°C)	m.f.	Calcd. (%)			Found (%)		
				C	H	N	C	H	N
II	90	179	C ₁₃ H ₁₃ N ₅	68.44	4.94	26.62	68.04	4.30	26.16
IIIa	88	285	C ₂₂ H ₁₆ N ₅ F	71.55	4.34	18.97	71.10	4.07	18.70
IIIb	79	269	C ₂₂ H ₁₅ N ₅ F ₂	68.22	3.88	18.09	67.96	3.60	17.94
IIIc	85	253	C ₂₂ H ₁₅ N ₅ FCI	65.43	3.72	17.35	65.28	3.49	17.13
IIIId	92	219	C ₂₅ H ₁₉ N ₆ OF ₃	63.03	3.99	17.65	62.69	3.17	17.18
IIIe	83	235	C ₃₀ H ₂₃ N ₆ F	74.07	4.73	17.28	73.89	4.25	17.08
IVa	77	262	C ₂₄ H ₁₅ N ₅ OF ₄	61.94	3.23	15.05	61.26	3.02	14.90
IVe	83	255	C ₃₂ H ₂₂ N ₆ OF ₄	65.98	3.78	14.43	65.59	3.27	14.13
Ve	81	223	C ₃₃ H ₂₃ N ₇ OF ₄	65.03	3.78	16.09	64.92	3.39	16.02
VI	86	335	C ₂₇ H ₁₆ N ₇ O ₃ F ₃	59.67	2.95	18.05	59.28	2.42	17.93
VII	77	231	C ₁₇ H ₁₂ N ₅ OF ₃	56.83	3.34	19.50	56.21	3.27	19.04
VIII	88	276	C ₂₀ H ₁₁ N ₅ F ₆	55.17	2.53	16.09	55.01	2.15	15.88

(0.015 mol) for 1 h. The reaction mixture was then cooled and the isolated solid product was filtered and recrystallized from THF (**Scheme-I** and Table-1).

5,6-Diphenyl-1,2,4-triazine cyano derivative (V): A solution of 0.01 mol from the appropriate hydrazone **IV** (R=CH₃) in ethanol (20 mL) was refluxed with hydrogen cyanide (2 mL) in presence of few drops of concentrated H₂SO₄ acid for 2 h. The reaction mixture was then cooled and poured in ice cold water. The separated solid product was filtered, washed with water and recrystallized from ethanol (**Scheme-I** and Table-1).

Chromone hydrazone derivatives (VI): A solution of the hydrazone derivative (**II**) (0.01 mol; 2.63 g) in trifluoroacetic acid (10 mL) was refluxed with 2-aminochromone-3-carboxyaldehyde (0.01 mol; 1.89 g) for 2 h. After cooling to room temperature, the reaction mixture was poured on crushed ice. The isolated solid product was filtered, thoroughly washed with water, dried and recrystallized from ethanol-benzene mixture (3:1), results are summarized in Table-1.

1-Trifluoroacetyl-2-(5,6-diphenyl-1,2,4-triazino-3-yl) hydrazone (VII): The hydrazone derivative (**II**) (0.01 mol; 2.63 g) was refluxed with trifluoroacetyl chloride (10 mL) for 2 h. After cooling to room temperature, the reaction mixture was poured on crushed ice and the separated solid product was filtered, washed with water and recrystallized from ethanol (**Scheme-I** and Table-1).

5,6-Diphenyl-3-[3',5'-di(trifluoromethyl) pyrazol-1-yl]-1,2,4-triazine (VIII): A solution of 5,6-diphenyl-3-hydrazino-1,2,4-triazine (**II**) (0.01 mol; 2.63 g) in THF (20 mL) was refluxed with 1,1,1,5,5,5-hexafluoro-2,4-pentadione (0.01 mol) for 2 h. The reaction mixture was then concentrated and the separated solid was collected and recrystallized from ethanol as needed (**Scheme-I** and Table-1).

Sample preparation: A stock solution of each compound was prepared individually in dimethyl formamide by dissolving an appropriate amount of the fluorine labeled compound. All stock solutions were stored in the dark at 4 °C. For both UV-VIS and fluorescence spectroscopic studies, standard solutions of 1 × 10⁻⁵ M fluorine compounds were individually prepared by adding appropriate amounts from stock solutions.

Detection method: One-dimensional ¹H NMR spectra were acquired in the single-pulse mode on a Perkin-Elmer

600 MHz spectrometer. All NMR measurements were recorded in CDCl₃ by use of tetramethyl silane (TMS) as an internal standard. ¹H NMR spectra were collected using a 7 μs pulse, 16 scans and 1 s delay between scans. The spectra were processed by zero filling the FID from 16-32 K and applying a linebroadening of 30 Hz. Fourier transform infrared (FT-IR) spectra were recorded on a Shimadzu FT-IR 470 spectrophotometer in the range 4000-600 cm⁻¹. The melting point (T_m) was determined by differential scanning calorimetry (DSC) using a thermal analysis instrument TA SDT2960 at a scanning rate of 5 °C min⁻¹. Thermal gravimetric analyses (TGA) were performed using a thermal analysis instrument TGA-7 HR V6.1A (module TGA 1400 °C). Determination of the thermal decomposition temperature (T_{dec}) for fluorine labeled compounds was obtained at a heating rate of 5 °C min⁻¹ under nitrogen from 20-600 °C. In addition, the UV/visible absorption measurements were collected by use of a Perkin-Elmer UV-VIS scanning spectrophotometer. Absorption spectra were collected using a 10 mm quartz cuvet. Fluorescence measurements were performed using a Perkin-Elmer luminescence spectrofluorometer equipped with a 20-KW for 8 μs duration xenon lamp and gated photomultiplier tube (PMT) and red-sensitive R928 PMT detectors. All fluorescence measurements were collected at room temperature. The emission spectrum of fluorine labeled compound **VI** was recorded in a 10 mm quartz fluorescence cuvette with slit widths set for entrance and exit bandwidths of 5 and 5 nm on both excitation and emission monochromators, respectively. Fluorescence emission spectrum of this compound was excited at 320 nm excitation wavelength and blank subtracted before proceeding in data analyses.

RESULTS AND DISCUSSION

Characterization of fluorine compounds: All synthesized fluorine labeled compounds are found to be pure as supported by data obtained from the elemental analysis, results are summarized in Table-1. Condensation of 5,6-diphenyl-1,2,4-triazine-3-thione (**I**) with hydrazine hydrate afforded the hydrazone derivative **II** in good yield. The FT-IR spectrum of **II** exhibited two bands in the region 3250 and 3372 cm⁻¹ for NH and NH₂ functions, respectively. Its ¹H NMR spectrum showed the aromatic protons as multiplet of δ 7.22-7.45 ppm as well as two exchangeable multiplet and doublet signals at δ 4.82 and

δ 2.45 ppm for the NH and NH₂, respectively (Table-2). Reaction of hydrazine derivative **II** with aromatic aldehydes and ketones afforded the corresponding hydrazones **III(a-e)**. The FT-IR spectra of these hydrazone showed broad bands in the region 3250-3150 cm⁻¹ for the NH groups. Their ¹H NMR spectra exhibited an exchangeable NH broad singlet in the region δ 4.13-6.85 ppm, a singlet one proton intensity at δ 7.98-8.52 ppm for CH=N function as well as the aromatic protons at δ 7.19-7.85 ppm, results are tabulated in Table-2.

Treatment of the appropriate hydrazine **III** with hexafluoroacetic anhydride in THF yielded the corresponding trifluoroacetyl derivatives **IV**. In addition, the reaction of **IV** (R=CH₃) with hydrocyanic acid is found to produce the triazine cyano derivative **V** in good yield. The FT-IR spectra of both **IV** and **V** showed a carbonyl band in the region 1715-1695 cm⁻¹. The cyano derivative **V** exhibited also two absorption bands at 2250 and 3210 cm⁻¹, indicative of the CN and NH groups, respectively. The ¹H NMR spectra of both **IV** and **V** are also in good agreement with their chemical structures, as illustrated in Table-2. The condensation reaction of the hydrazine derivative **II** with 2-aminochromane-3-carboxaldehyde in trifluoroacetic acid gave the corresponding hydrazone **VI** compound. The FT-IR spectrum of **VI** showed two carbonyl absorption bands at 1665 and 1710 cm⁻¹ as well as NH absorption band at 2185 cm⁻¹. The ¹H NMR spectrum of **VI** displayed two exchangeable NH broad singlet peaks in the region δ 4.15 and 8.10 ppm and the aromatic protons at δ 6.92-7.64 ppm.

However, the reaction of **II** with trifluoroacetyl chloride yielded the corresponding acyl derivative **VII**. Its FT-IR spectrum displayed a strong carbonyl absorption band at 1705 cm⁻¹ as well as two weak bands at 2165 and 2210 cm⁻¹ for the two NH groups. Moreover, condensation of the hydrazine derivative **II** with 1,1,1,5,5,5-hexafluoro-2,4-pentadione afforded the corresponding trizolo-triazine derivative **VIII**. The structures of prepared fluorine labeled compounds **VII** and **VIII** were further confirmed from their ¹H NMR spectra (Table-2).

Thermal stability of fluorine compounds: All prepared fluorine labeled compounds included in this study showed good thermal stability. The thermal decomposition temperature (T_{dec}) is found to range from moderate to high decomposition temperature (Fig. 1). A close examination of Fig. 1 demonstrates that the T_{dec} of fluorine compound **VI** is the highest (406 °C). This may be due to the difference in the structural

compositions of **VI** as compared to other fluorine labeled compounds. However, the T_{dec} (220 °C) of compound **II** is found to be the lowest in comparison to other fluorine compounds. The results of thermal stability indicate that these compounds can be used in high temperature reactions for different applications.

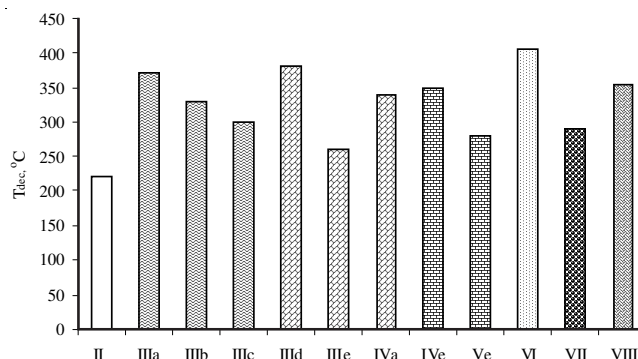


Fig. 1. Thermal gravimetric analysis data of fluorine labeled compounds, thermal decomposition temperature (T_{dec}) obtained at a heating rate of 5 °C min⁻¹ under nitrogen from 20-600 °C

Spectroscopic evaluation of fluorine compounds: As shown in Fig. 2, different characteristic bands appeared in the UV-VIS absorption spectra of fluorine labeled compounds. Fluorine compounds **II**, **III**, **IVa**, **Ve**, **VI**, **VII** and **VIII** showed only single characteristic band. However, two broad bands centered at 300 and 360 nm are observed in the UV-VIS absorption spectrum of compound **IVe**. This may be attributed to the distinctive structure composition of **IVe** as compared to those of other fluorine compound. These results further support the purity of synthesized fluorine labeled compounds and are in good agreement with the data obtained from the elemental analysis.

In general, weak background fluorescence was observed in the emission spectra of fluorine compounds, except for **VI** (Fig. 3). Weak fluorescence background of other fluorine compounds may lead to the advantages that these fluorine compounds may be used in optical studies of the other solutes. The fluorine compound **VI**, however, exhibits an interesting fluorescence behavior as compared to other fluorine labeled compounds. This may ascribed to the distinctive compositions of **VI** involving 4-chromone, which affords the fluorescence behavior of compound **VI**.

TABLE-2

Compound No.	R	¹ H NMR (δ ppm) DATA OF FLUORINE LABELED COMPOUNDS		
		Ar-H (m)	NH ₂ and/or NH	Others
II	–	7.22-7.45 (10H)	4.82 (m, 1H, NH); 2.45 (d, 2H, NH ₂)	–
IIIa	H	7.28-7.85 (14H)	4.13 (s, 1H, NH)	8.29 (s, 1H, CH=)
IIIb	H	7.19-7.51 (13H)	3.63 (s, 1H, NH)	8.42 (s, 1H, CH=)
IIIc	H	7.32-7.48 (13H)	3.34 (s, 1H, NH)	8.52 (s, 1H, CH=)
IIId	CH ₃	7.25-7.44 (14H)	6.97 (s, 1H, NH); 8.73 (s, 1H, NHCO)	2.32 (s, 3H, CH ₃)
IIIe	CH ₃	7.19-7.80 (18H)	6.85 (s, 1H, NH)	2.52 (s, 1H, CH ₃); 7.98 (s, 1H, CH=)
IVa	H	7.28-8.29 (14H)	–	8.29 (s, 1H, CH=)
IVe	CH ₃	7.36-7.54 (18H)	–	2.34 (s, 3H, CH ₃); 7.65 (s, 1H, CH=)
Ve	–	7.41-7.82 (18H)	2.29 (s, 1H, NH)	2.38 (s, 3H, CH ₃); 8.05 (s, 1H, CH=)
VI	–	6.92-7.64 (4H); 7.22-7.48 (10H)	4.15 (s, 1H, NH); 8.10 (s, 1H, NH)	–
VII	–	7.22-7.48 (10H)	4.10 (s, 1H, NH); 8.00 (s, 1H, NH)	–
VIII	–	7.38-7.50 (10H)	–	4.9 (s, 1H, CH=)

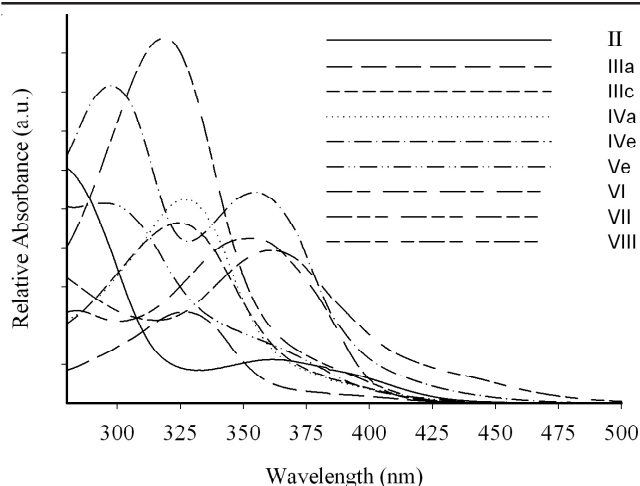


Fig. 2. UV-VIS absorption spectra of 10^{-5} M fluorine compounds in dimethyl formamide

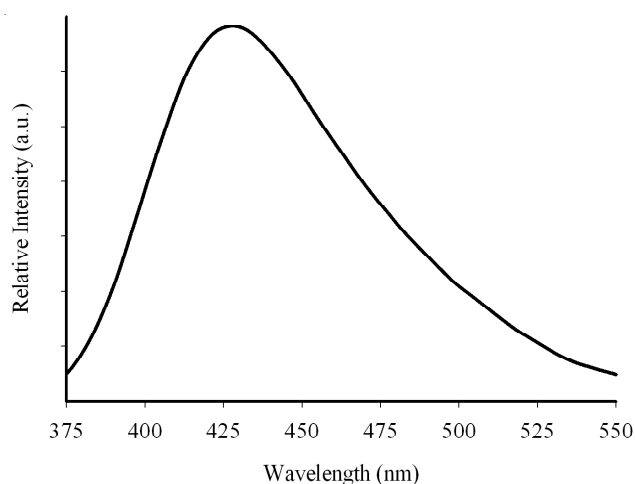


Fig. 3. Fluorescence emission spectrum of 10^{-5} M fluorine labeled compound **VI** in dimethyl formamide, excited at 320 nm

Conclusion

In this study, straightforward routes of fluorine compounds bearing 5,6-diphenyl-1,2,4-triazine-3-hydrazone moieties are

successfully achieved. Thermal gravimetric analysis results suggested that these fluorine compounds have good thermal stability. Thus, they can be used in gas chromatography or in high temperature reactions. The resulted fluorine compounds are found to have very weak fluorescence background, except for compound **VI**, which may offer the advantages of using fluorine labeled compounds in optical studies of the other solutes. Finally, the preparation, thermal and spectroscopic investigation of these novel fluorine labeled compounds may show considerable promise of using them in a range of applications, including environmental, industrial and pharmacological.

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