

Retraction Retracted: Facile and straightforward synthesis of Hydrazone derivatives

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This article has been retracted by Hindawi following an investigation undertaken by the publisher [1]. This investigation has uncovered evidence of one or more of the following indicators of systematic manipulation of the publication process:

- (1) Discrepancies in scope
- (2) Discrepancies in the description of the research reported
- (3) Discrepancies between the availability of data and the research described
- (4) Inappropriate citations
- (5) Incoherent, meaningless and/or irrelevant content included in the article
- (6) Peer-review manipulation

The presence of these indicators undermines our confidence in the integrity of the article's content and we cannot, therefore, vouch for its reliability. Please note that this notice is intended solely to alert readers that the content of this article is unreliable. We have not investigated whether authors were aware of or involved in the systematic manipulation of the publication process.

Wiley and Hindawi regrets that the usual quality checks did not identify these issues before publication and have since put additional measures in place to safeguard research integrity.

We wish to credit our own Research Integrity and Research Publishing teams and anonymous and named external researchers and research integrity experts for contributing to this investigation.

The corresponding author, as the representative of all authors, has been given the opportunity to register their agreement or disagreement to this retraction. We have kept a record of any response received.

References

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Research Article Facile and straightforward synthesis of Hydrazone derivatives

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This study was undertaken to report the swift, facile and convenient synthesis of novel hydrazones obtained by condensation reaction between 2-Amino-3-formylchromone and hydrazine derivatives. Various characterization techniques such as MALDI Mass, FTIR, ¹HNMR and ¹³CNMR spectrum analysis was done to determine the chemical structure of these novel six hydrazones. Furthermore, UV-Vis and fluorescence spectra was studied to calculate λ_{max} and ε_{max} . These hydrazones are quite useful for their facile synthesis and chemical structure. Such hydrazones require separate clinical research to find their applications in biomedical fields.

1. Introduction

Hydrazones are special organic compounds derived from the Schiff-base family and comprising of $>_C=_N-_N=_C<$ bonds with additional donor sites. The donor sites make hydrazones more flexible and versatile for their structural and functional properties [1]. For instance, hydrazones are very significant reactants in different reactions such as hydrazone iodination, Shapiro and Bamford-Stevens reaction. On the other hand, hydrazones act as intermediates in Wolff-Kishner reaction. The C and H atoms in hydrazones tend to react with organometallic nucleophiles. Due to its highly acidic nature, the alpha-hydrogen atom of hydrazones is comparatively more nucleophilic than that of ketones [2]. Different studies have reported the biological importance

of trigonal hybridized nitrogen atom in azomethine group of hydrazones which is remarkable for having one pair of electrons in its either π or sp² orbitals [3, 4]. Their hetero atomic nature and specific electronic properties make them very important structural compounds [5]. One of the most promising organic hole transporting materials are aromatic hydrazones. Recently, some researchers have reported the synthesis of polymeric hydrazones with remarkable properties such as high glass transition temperatures, good filmformation and moderate charge transport [6].

The ligation of hydrazones with surface immobilized hydrazines and aldehydes-modified antibodies can be used to anchor captured proteins on oxide coated biosensor substrates [7]. Hydrazones are also being used as inhibitors such as strong poly (ADP-ribose) glycohydrolase (PARG) [8].

Aroyl hydrazones have been reported to use in clinical theranostic applications due to their ferric ion scavenging activities [9]. The role of N, O and S in metal coordination at the active sites of numerous metallobiomolecules is also well known for various industrial, antimicrobial, anticancer and herbicidal applications [10, 11]. The chelating ligands get coordinated with metal ions by N, O or S as donor atoms. They have been found to show a wide variety of biological applications and are becoming a hotspot of research [12, 13]. The coordination of metal ions with the biologically active compounds can enhance their potential [14]. The polymeric hydrazones and their coordination in polymer drug conjugates is involved in hydrolysis. The rate of hydrolysis is significantly faster at acidic pH as compared to those of carbamates [15]. Hydrazone linkers are stable only in physiological conditions (pH7.4) but they are prone to get cleaved under acidic conditions such as the intracellular conditions of endosomes and lysosomes protects them by forming micelle around. The hydrophobic drugs are hence gets protected from the host defense system in the body [16]. For instance, the anticancer drug DOX is released at higher rate under acidic conditions due to the nature of linkage between the DOX and micelles [17]. Chromone derivatives have received great attention of researchers for their applications. These compounds show wide spectrum of biological activities such as antimicrobial, antitumor, anti-allergic, antiviral, anti-inflammatory and anticancer activities [18].

Due to the aforementioned applications of hydrazones, herein we have reported the quick, facile, and convenient synthesis of six novel hydrazones containing N, O, or S atoms derived from Chromone. Hopefully, the combination of the chromone moiety with hydrazides may provide more biologically active resulting compounds. The typical synthesis of hydrazones can be described as follows:

$$2 - \text{Amino-3-formylchromone} + \text{Hyadrazide} \xrightarrow{\text{Acetic Acid}} \text{Hydrazone}$$

(1)

2. Materials and Methods

2-Amino-3-formylchromone, 2-hydroxybenzhydrazide, 3hydroxy-2-napthoic acid hydrazide, isonicotinic acid hydrazide, 2-picolinyl hydrazide, thiophene-2-carboxylic hydrazide, and 2-furoic acid hydrazide were purchased from TCI (Japan) or J&K (China) with purity higher than 98% and used without further purification. UV-Vis spectra were recorded by using a UV-1000 spectrophotometer of Techcomp (China). Fluorescence spectra were recorded on F-7 Fluorescence spectrophotometer (Hitachi, Japan). MALDI mass spectra were obtained on time-of-flight Ultrflex II mass spectrometer (Bruker Daltonics). ¹H and ¹³CNMR spectra of hydrazones in DMSO-d6 solutions were recorded on a 300 MHz Bruker AV 300 spectrometer and chemical shifts are indicated in ppm.

The equimolar mixture of 2-amino-3-formylchromone and hydrazine derivative (i.e., 2-hydroxybenzhydrazide, 3hydroxy-2-napthoic acid hydrazide, isonicotinic acid hydrazide, 2-picolinyl hydrazide, thiophene-2-carboxylic hydra-

TABLE 1: Reaction conditions for the 6 hydrazones.

No.	Compd.	Solvent	Time(min)	Color	Yield (%)
1	CBH	Acetic acid	9	White	72
2	CNH	Acetic acid	1	Yellow	81
3	CISNH	Acetic acid	25	Yellow	69
4	CPH	Acetic acid	25	Yellow	73
5	CTPH	Acetic acid	25	Yellow	65
6	CFH	Acetic acid	25	Yellow	70

TABLE 2: MALDI mass data of the six synthesized hydrazones.

Serial no	Compd.	Calculated molecular mass	Observed molecular mass
1	CBH	323.302	323.592
2	CNH	373.360	373.531
3	CISNH	308.291	308.676
4	CPH	308.291	308.457
5	СТРН	313.331	313.487
6	CFH	297.265	297.280

TABLE 3: Fluorescence data of the 6 hydrazones.

No.	Compd.	Solvent	Conc. (µM)	Excitation (nm)	Emission (nm)
1	CBH	DMSO	100	374.0	458.0
2	CNH	DMSO	10	374.0	458.0
3	CISNH	DMSO	10	373.0	459.0
4	CPH	DMSO	10	390.0	458.2
5	CTPH	DMSO	10	374.0	456.4
6	CFH	DMSO	100	273.0	455.8

zide, or 2-furoic acid hydrazide) in acetic acid was refluxed for a certain time (Table 1). After reflux, the solution was cooled to room temperature, poured into ice-water and stirred. When the precipitates started to appear, the reaction mixtures were allowed to stand for an hour to afford maximum precipitates. Detail reflux times, colors of the precipitates, and yields of the hydrazones are shown in Table 1. MALDI mass, Fluorescence, FTIR, and ¹HNMR data of the 6 hydrazones are shown in Tables 2–5. UV-Vis and fluorescence spectra of the 6 hydrazones are shown in Figures 1 and 2, respectively.

3. Results

In this study, different hydrazides were used such as 2hydroxybezhydrazide (CBH), 3-hydroxy-2-napthoic acid hydrazide (CNH), isonicotinic acid hydrazide (CISH), 2picolinyl hydrazide (CPH), thiophene-2-carbhydrazide (CTPH), and 2-fouric acid hydrazide (CFH) for synthesis of hydrzones. The results of the study have revealed that it took only 9 min for CBH to obtain maximum white precipitates of the reaction mixture. On the other hand, the T

TABLE 4: FTIR data of the 6 hydrazones.

No.	Compd.	C=O	C=N-	-NH-	-OH	NH-C=O	-NH2
1	CBH	1641	1605	3080	3500	1550	3284
2	CNH	1646	1606	3083	3437	1554	3270
3	CISNH	1650	1605	3292		1550	3434
4	CPH	1675	1606	3293		1535	3439
5	CTPH	1652	1607	3272		1551	3404
6	CFH	1655	1606	3291		1551	3411

TABLE 5:	HNMK	data o	i the 6	nydrazones	(ppm).

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No.	Compd.	Deuterium Solvent	CH=N-	-NH-	-OH	-NH2
1	CBH	DMSO	8.96	12.15	11.98	9.70,9.36
2	CNH	DMSO	8.94	12.12	11.50	9.71,9.38
3	CISNH	DMSO	8.96	12.12		9.68,9.38
4	CPH	DMSO	9.08	12.34		9.88,9.28
5	CTPH	DMSO	8.91	11.94		9.65,9.31
6	CFH	DMSO	8.92	11.93		9.68,9.30



FIGURE 1: UV-Vis spectra of the 6 hydrazones in DMSO. The concentration of all hydrazones in μ M are shown in Table 3.

hydrazones through CNH was appeared with greenish precipitates in the reaction flask within one minute. The stirring of reaction mixture on heat was done to obtain maximum precipitates for few minutes. But it was not happened during the synthesis of hydrazones of CISNH, CPH, CTPH, and CFH. The precipitates were not appeared during reflux. In these reactions, a clear solution was observed for 25 min.

After reflux, the solutions were cooled at room temperature, poured into ice-water, and stirred. When the precipitates started to appear, the reaction mixtures were allowed to stand for an hour to afford maximum precipitates. The precipitates were then filtered, dried, and characterized. Structures of the precursors and synthesized hydrazones are listed in Table 6.



FIGURE 2: Fluorescence spectra of the 6 hydrazones in DMSO. The concentration of CBH and CFH is $100 \,\mu$ M, while the concentration of other 4 hydrazones is $10 \,\mu$ M.

The results obtained through MALDI mass are well consistent with the molecular weights of these six hydrazones, as shown in Table 2. The λ_{max} and ε_{max} values of these six hydrazones were calculated according to their UV-Vis spectra. Fluorescent properties of the hydrazones were also studied and their excitation and emission wavelengths are mentioned in Table 2. Furthermore, FTIR, ¹H and ¹³CNMR spectral data of the hydrazones confirmed the proposed structures of hydrazones.

4. Discussion

Detailed principle peaks on the FTIR and ¹HNMR spectra are listed in Tables 4 & 5, respectively. The signal at chemical shifts (δ , ppm) of 11.93-12.34 in ¹HNMR spectra are assigned to the -NH group, concomitant with the observation of rapid loss of these signals. Same is the case with -NH₂ groups whose peaks of both protons signals at chemical shifts of 9.28-9.88. The signals at δ of 11.98 ppm and 11.50 ppm are assigned to the aromatic -OH protons of CBH and CNH, respectively. The resonance peaks between 8.91 ppm to 9.08 ppm in the spectra are assigned to the azomethine (-CH=N-) of these hydrazones. Signals at δ 6.70-8.79 are assigned to the aromatic protons. In 13CNMR spectra of these hydrazones, four key resonance signals were observed. These are δ 153.0-153.4 for azomethine (-CH= N-), carbonyl carbon of chromone ring roughly at δ 162.9-165.0, carbon of chromone ring attached to carbon of azomethine at δ 92.6-92.8, and δ 173.3-173.7 for the carbon (– C-NH2) on the chromone ring in all hydrazones. The signals of carbonyl carbons from hydrazine motifs were observed roughly at δ 162.9, 160.7, 150.4, 160.1, 157.3, and 145.7 from CBH, CNH, CISNH, CPH, CTPH, and CFH, respectively. The detail of other carbons in all hydrazones is described as following: Six carbons on the benzene ring of chromone of CBH are shown at δ 145.6, 133.9, 128.1, 125.3, 121.8, and 117.6. Three carbons on chromone ring are δ 173.7, 165.0, and 92.6. Six carbons on the benzene ring having -



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OH were shown at δ 160.1, 133.9, 125.3, 119.0, 116.9 and 115.2. Six carbons on the benzene ring of chromone of CNH are shown at δ 150.4, 133.4, 129.0, 121.1, 121.1, and 117.1. Three carbons on chromone ring are at δ 173.5, 163.9, and 92.6. Ten carbons on the naphthyl ring are shown at δ 145.7, 129.0, 127.1, 125.9, 125.2, 125.2, 125.2, 125.2, 124.1, and 110.9. Six carbons on the benzene ring of chromone of CISNH are shown at δ 145.7, 128.7, 126.9, 125.0, and 116.8. Three carbons on the chromone ring are at δ 173.5, 163.0, and 92.6. Five carbons on the isonicotinic ring are shown at &133.6, 125.0, 125.0, 121.5, and 121.5. Six carbons on the benzene ring of chromone of CPH are shown at 150.0, 135.2, 127.1, 125.0, 122.2, and 117.1. Three carbons on chromone ring are at δ 173.4, 163.1, and 92.8. Five carbons on the pyridine ring are shown at δ 148.9, 146.1, 134.9, 125.0, and 122.2. Six carbons on the benzene ring of chromone of CTPH are shown at δ 144.2, 128.5, 125.3, 125.3, 121.8, and 117.1. Three carbons on the chromone ring are at 173.4, 162.9, and 92.8. Four carbons on the thiophene ring are shown at δ 138.1, 133.5, 131.6, and 128.5. Six carbons on the benzene ring of chromone of CFH are shown at & 133.4, 125.2, 125.2, 125.2, 121.7, and 116.8. Three carbons on the chromone ring are at δ 173.3, 163.0, and 92.8. Four carbons on the furan ring are shown at δ 145.7, 145.7, 114.5, and 112.2. These spectroscopic data confirmed the successful syntheses of the 6 hydrazones mentioned above. The λ_{\max} (nm) and ε max values of these six hydrazones were calculated according to their UV-Vis spectra, the λ_{max} , are in the range of 344 to 351 nm and $\varepsilon_{\rm max}$ was from 1.50 x 10⁴ to $3.26 \times 10^4 \text{ cm}^{-1} \text{ M}^{-1}$.

5. Conclusions

This study highlighted the synthesis and spectroscopic characterization of 6 novel hydrazones. The hydrazones were quickly synthesized through convenient and facile approach. This study reported the synthesis of CBH in 9 min. On the other hand, CNH was synthesized in 1 min only. After the reflux of 25 min, other 4 hydrazones were synthesized. The importance of these hydrazones can be realized in live cell imaging for detection of metal ions. These compounds are quite beneficial for their role as chemo sensors. As a future perspective of this study, these hydrazones containing oxygen, sulfur, and nitrogen atoms may lead biologists for its applications in biomedical fields.

Data Availability

No data were used to support this study.

Conflicts of Interest

There is no conflict of interest.

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