

Synthesis and Characterisation of New 2-(5-Fluoro-2-Methyl-1H-Inden-3-Yl) Acetohydrazide Derivatives

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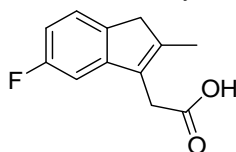
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ABSTRACT: Certain organic compounds such as formic acid, acetic acid, substituted piperazine-1-carbonylchloride and 2-bromomethylbenzoate are reacted with compound 2-(5-fluoro-2-methyl-1H-inden-3-yl)acetohydrazide to form new derivatives. These derivatives are found in good yield. These new compounds are characterised by various physicochemical techniques.

KEYWORDS: Acetohydrazide, carboxylic acid, acid chloride, TLC.

I. INTRODUCTION

It is evident that thiocarbohydrazide and 2-(5-fluoro-2-methyl-1H-inden-3-yl)acetohydrazide promptly forms immino derivatives with substituted carbonyl compounds¹⁻³. The precursor 2-(5-fluoro-2-methyl-1H-inden-3-yl) acetic acid of 2-(5-fluoro-2-methyl-1H-inden-3-yl)acetohydrazide holds the pharmaceutical as well as fungicide and herbicide activity⁴. The Fluorinated organic molecules are well known for a wide range of biological functions⁵⁻⁷. In the present paper the substituted derivatives of hydrazide of 5-fluoro-2-methyl indene-3-acetic acid are prepared and characterised.



Compound-1

II. MATERIALS AND METHODS

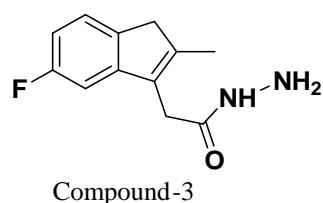
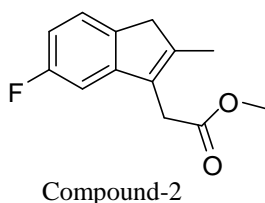
A. R. grade or purified L. R. grade chemicals were used for the synthesis of 2-(5-fluoro-2-methyl-1H-inden-3-yl)acetohydrazide.

Synthesis of Methyl-5-fluoro-2-methyl-1H-3-indenylacetate: The esterification of 2-(5-fluoro-2-methyl-1H-inden-3-yl) acetic acid (1) was carried out by refluxing compound-1 in excess of methanol in presence of the catalytic amount of sulphuric acid to form compound-2.

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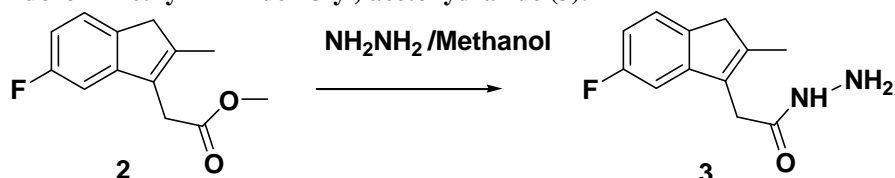
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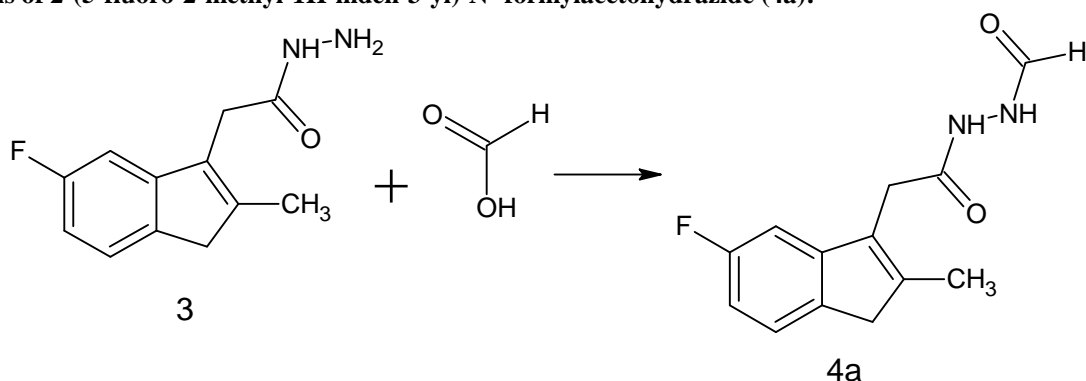
The hydrazinolysis of compound-2 was carried out in hydrazine hydrate in methanol to form compound-3 which is further used for the preparation of substituted acetohydrazide derivatives.

Synthesis of 2-(5-fluoro-2-methyl-1H-inden-3-yl) acetohydrazide (3):



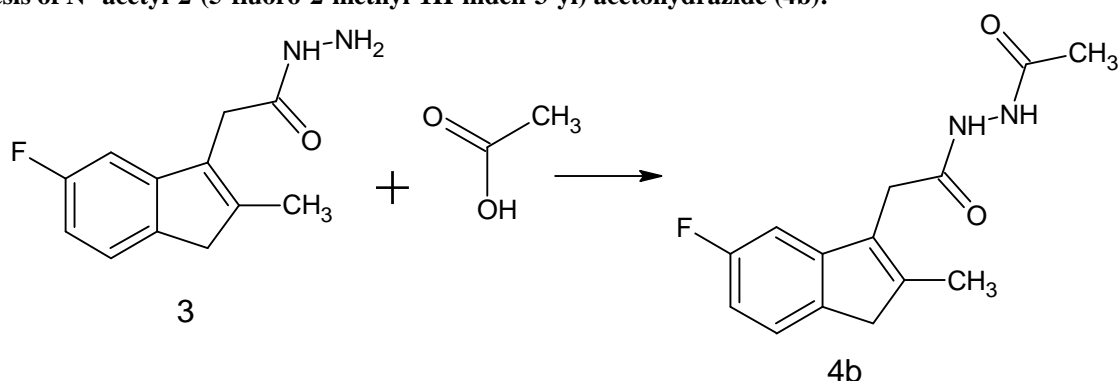
In one litre three neck flask was added Methyl-5-fluoro-2-methyl-1H-3-indenylacetate(2) (100 g, 0.45 mol) containing methanol (500 mL) at room temperature and stirred for 10 min. Hydrazine hydrate (10 g, 0.31mol) was then added drop wise and resulting mixture was refluxed for 10 hrs. Progress of the reaction was monitored by TLC (20 % Ethyl acetate in Hexane). After completion of the reaction, the content was cooled to 10°C for 2 hrs and filtered. Crude solid material was further recrystallized from ethanol to obtain 2-(5-fluoro-2-methyl-1H-inden-3-yl)acetohydrazide (3) as white solid (85g, 85 %). (Melting Point:175-178⁰C). The structure of the compound (3) was confirmed by spectroscopic techniques like IR, ¹H NMR and mass spectroscopy.

Synthesis of 2-(5-fluoro-2-methyl-1H-inden-3-yl)-N'-formylacetohydrazide (4a):



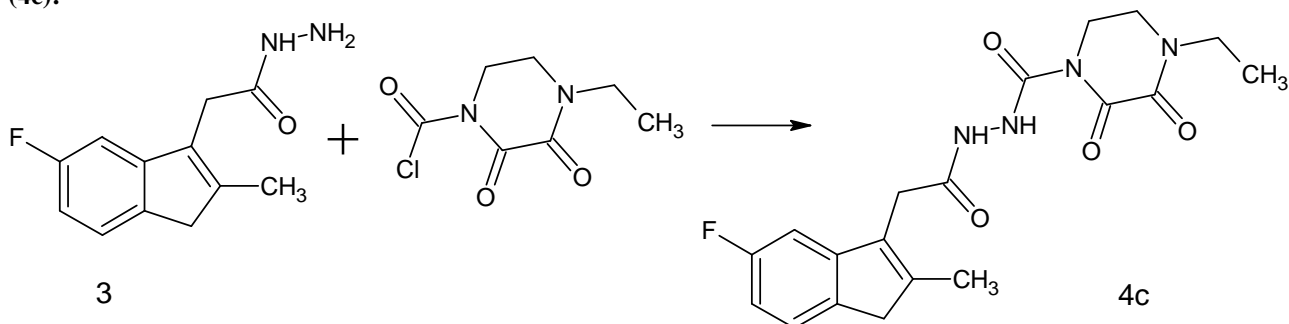
In 100 ml single neck flask containing formic acid (98% aq., 25mL)was added 6-fluoro-2-methyl-3H-inden-1-yl)-acetic acid hydrazide (3) (4.4g, 2.0 mmol) at room temperature and stirred for 16 hrs at room temperature. Starting material was consumed completely observed by TLC (20% Ethyl acetate in heptane). Reaction mixture was poured on ice-cold water to yield white solid, filtered, washed with water, dried and recrystallized with methanol to yield 2-(5-fluoro-2-methyl-1H-inden-3-yl)-N'-formylacetohydrazide (4a) as white solid (4.0 g,81%). (Melting point: 195-199°C). The structure of the novel compound (4a) was confirmed by Elemental analyses, IR, ¹H NMR and mass spectroscopy.

Synthesis of N'-acetyl-2-(5-fluoro-2-methyl-1H-inden-3-yl) acetohydrazide (4b):



In 100 ml single neck flask containing Acetic acid (25ml) was added 2-(5-fluoro-2-methyl-1H-inden-3-yl)acetohydrazide (3) (4.4g, 2.0 mmol) at room temperature and stirred for 12 hrs at room temperature. Starting material was consumed completely observed by TLC (20% Ethyl acetate in heptane). Reaction mixture was poured on ice cold water to yield white solid, filtered, washed with water, dried and recrystallized with methanol to yield N'-acetyl-2-(5-fluoro-2-methyl-1H-inden-3-yl)acetohydrazide (4b) as white solid (4.5 g, 86%). (Melting point: 204-206°C). The structure of the novel compound (4b) was confirmed by Elemental analyses, IR, ¹H NMR and mass spectroscopy.

Synthesis of 4-ethyl-N'-(2-(5-fluoro-2-methyl-1H-inden-3-yl) acetyl)-2,3-dioxopiperazine-1-carbohydrazide (4c):



To a well stirred solution of 2-(5-fluoro-2-methyl-1H-inden-3-yl)acetohydrazide (3) (4.4 g, 2.0 mmol) in methanol (40 ml) was added Triethyl amine (2.2g, 1.1 mmol) and cool it to 20°C. 4-Ethyl-2,3-dioxo-piperazine-1-carbonylchloride (4.1 g, 2 mmol) was then added lot wise during 30 min. The reaction mixture was then allowed to attain room temperature and stirred for 5-6 hrs. Starting material was consumed completely observed by TLC (20% Ethyl acetate in heptane). Solvent was removed under reduced pressure to yield white solid which was washed with water, dried and recrystallized in ethanol to yield 4-ethyl-N'-(2-(5-fluoro-2-methyl-1H-inden-3-yl) acetyl)-2, 3-dioxopiperazine-1-carbohydrazide (4c) as white crystals, Yield (6.7 g, 87%) (Melting point: 176-178°C).

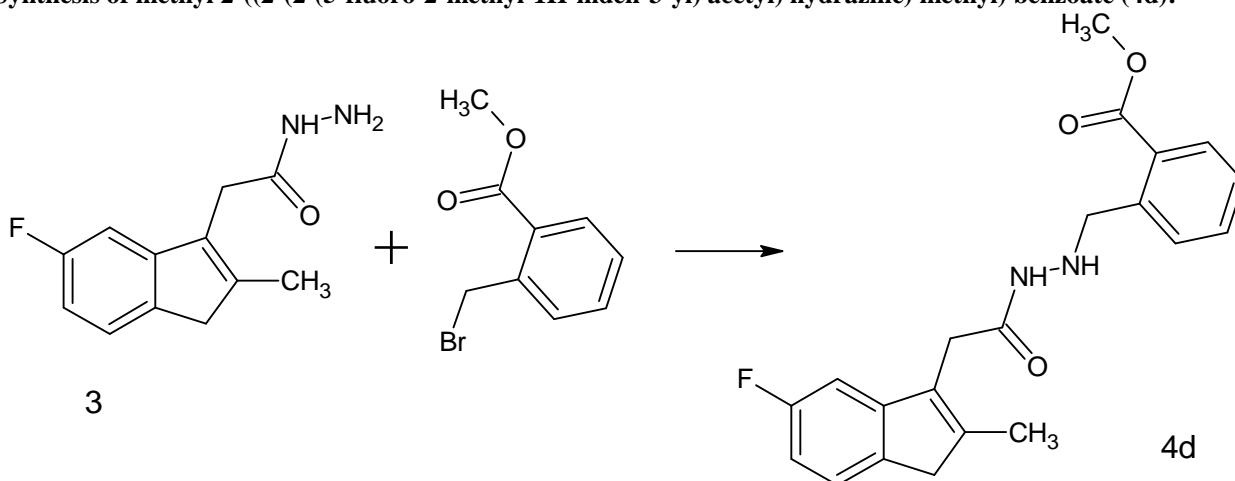
The structure of the novel compound (4c) was confirmed by Elemental analyses, IR, ¹H NMR and mass spectroscopy.

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Synthesis of methyl 2-((2-(2-(5-fluoro-2-methyl-1H-inden-3-yl) acetyl) hydrazine) methyl) benzoate (4d):-



To a well stirred solution of 2-(5-fluoro-2-methyl-1H-inden-3-yl)aceto-hydrazide (3) (4.4 g, 2.0 mmol) in methanol (40 ml) was added triethylamine (2.2g, 1.1 mmol) and cooled it to 20°C. 2-bromomethylbenzoate (4.58g, 2 mmol) was then added lot wise during 30 min. The reaction mixture was then allowed to attain room temperature and stirred for 8 hrs. Starting material was consumed completely observed by TLC(20% Ethyl acetate in heptane). Solvent was removed under reduced pressure to yield white solid which was washed with water, dried and recrystallized in ethanol to yield methyl 2-((2-(2-(5-fluoro-2-methyl-1H-inden-3-yl) acetyl) hydrazine) methyl) benzoate (4d) as white crystals, Yield (5.8 g, 79%) (Melting point: 188-190°C).

The structure of the novel compound (4d) was confirmed by Elemental analyses, IR, ¹H NMR and mass spectroscopy.

III. RESULTS AND DISCUSSIONS

The newly synthesised compounds are characterised by various analytical and spectroscopic methods as follows.

Table:1 Analytical Data

Compounds	Molecular formula	Molecular Weight	Colour	Observed/ (Calculated)				<i>m/z</i> [M+1] ⁺
				%C	%H	%F	%N	
3	C ₁₂ H ₁₃ FN ₂ O	220.24	Off White	64.95 (65.44)	5.85 (5.95)	8.55 (8.63)	12.80 (12.72)	221.10
4a	C ₁₃ H ₁₃ FN ₂ O ₂	248.25	White	62.71 (62.90)	5.21 (5.28)	7.59 (7.65)	11.16 (11.28)	249.01
4b	C ₁₄ H ₁₅ FN ₂ O ₂	262.28	White	63.89 (64.11)	5.62 (5.76)	7.11 (7.24)	10.51 (10.68)	263.04
4c	C ₁₉ H ₂₁ FN ₄ O ₄	388.39	White	58.34 (58.76)	5.31 (5.45)	4.76 (4.89)	14.22 (14.43)	389.30
4d	C ₂₁ H ₂₁ FN ₂ O ₃	368.40	White	68.14 (68.46)	5.61 (5.75)	5.03 (5.16)	7.46 (7.60)	369.21

Compound (3): ¹H NMR Spectrum (300 MHz, DMSO): δ 2.1(s, 3H, -CH₃), 3.2(s, 2H, CH₂), 3.3(s, 2H, CH₂), 4.2(s, 2H, NH₂), 6.8-7.3(m, 3H, Ar-H) and 9.2 (s, 1H, -NH).

¹³C NMR Spectrum (500 MHz, DMSO): 13.5, 31.3, 42.2, 106.6, 112.2, 125.6, 132.9, 138.7, 146.4, 150.0, 165.2 and 170.8 ppm.

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IR Spectrum (KBr):- 786, 933, 1010, 1172, 1273, 1365, 1465, 1535(C=C), 1627(C=O), 2901(C-H), 3039 (-NH) and 3189(-NH₂)cm⁻¹.

Compound (4a) : ¹H NMR Spectrum (300 MHz, DMSO) δ 2.09(s, 3H, -CH₃), 3.2(s, 2H, CH₂), 3.4(s, 2H, -CH₂), 6.8-7.3(m, 3H, Ar-H), 8.0(s, 1H, C=CH), 9.9(s, 1H, NH, D₂O Exchangeable) and 10.2(s, 1H, NH, D₂O Exchangeable).
IR (KBr, cm⁻¹) : 825, 920, 991, 1090, 1209, 1214, 1287, 1344, 1391, 1414, 1531, 1577, 1622(CONH), 2905, 2979(-CH), 3012(-NH), and 3162 (-NH)cm⁻¹.

Compound(4b): ¹H NMR Spectrum of 5b(300 MHz, DMSO) δ 1.8(s, 3H, COCH₃), 2.09(s, 3H, -CH₃), 3.2(s, 2H, CH₂), 3.4(s, 2H, -CH₂), 6.8-7.6(m, 3H, Ar-H), 9.8(s, 1H, NH, D₂O Exchangeable) and 9.9(s, 1H, NH, D₂O Exchangeable).
IR (KBr, cm⁻¹): 856, 920, 999, 1163, 1247, 1276, 1365, 1433, 1479, 1620(CONH), 2912, 2983(-CH), 3039(-NH), and 3200 (-NH)cm⁻¹

Compound(4c): ¹H NMR Spectrum of 6a (300 MHz, DMSO): δ 1.1(t, 3H, -NCH₂CH₃), 2.1(s, 3H, -CH₃), 3.2(s, 2H, CH₂), 3.4(q, 2H, -NCH₂CH₃), 3.5 and 3.9(m, 4H, 2x N-CH₂-), 3.5(s, 2H, CH₂), 6.8-7.5(m, 3H, Ar-H), 10.4 and 10.6(s, 2H, 2X NH, D₂O Exchangeable).
IR (KBr, cm⁻¹): 858, 916, 1087, 1161, 1224, 1338, 1384, 1471, 1573, 1602(CONH), 1689(CONH), 2912, 2960(-CH), 3022(-NH), 3109 and 3171 (-NH)cm⁻¹.

Compound (4d): ¹H NMR Spectrum of 6b(300 MHz, DMSO): δ 2.0(s, 3H, -CH₃), 3.1(s, 2H, CH₂), 3.3(s, 2H, -NCH₂), 3.2 (s, 2H, CH₂), 3.8(s, 3H, OCH₃), 6.8-7.8(m, 7H, Ar-H), 9.9 and 11.1(s, 2H, 2X NH, D₂O Exchangeable).
IR (KBr, cm⁻¹): 800, 916, 1012, 1166, 1267, 1473, 1531, 1593(-C=C), 1639(-CONH), 1735(-COOMe), 2912, 3039(-CH), 3203(-NH), 3286(-NH) cm⁻¹.

IV. ACKNOWLEDGEMENT

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