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Synthesis of New seleno[2,3-*b*]quinoline-2-carboxylates

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ABSTRACT

A new method for the synthesis of substituted condensed seleno[2,3-*b*]quinoline-2-carboxylates derivatives has been achieved. Very first, 2-chloro-3-formylquinolines **2a-d** are synthesized from substituted acetanilides **1a-d**. Thus obtained 3-formyl-2-chloro-quinolines **2a-d** were converted into substituted 2-seleno-3-formylquinolines **3a-d**. Seleno quinolines thus obtained on refluxing with chloroacetic acid gave 3-formylquinolin-2-yl)seleno acetic acids **4a-d**. Thus obtained on refluxing with methanol, ethanol and isopropanol in presence of $POCl_3$ gave uncyclised substituted [(3-formylquinolin-2-yl)seleno]acetates **5a-d** in quantitative yield. The cyclisation was achieved on refluxing with methanol in DMF at room temperature forms **6a-b**. The structures of all the newly synthesized compounds were elucidated on the basis of elemental analysis, IR, ^{1}H NMR and mass spectral data.

Keywords: 3-Formyl-2-mercaptoquinolines; 3-Formyl-2-chloroquinolines; Seleno[2,3-b] quinolines; 3-Formylquinolin-2-yl)seleno acetic acids; Methyl seleno[2,3-b]quinoline-2-carboxylates.

INTRODUCTION

During the past few decades, interest has been rapidly growing in gaining insight into the properties and transformations of these heterocycles. It is evident from literature that, substituted quinolines are important and widely used heterocyclic compounds in heterocyclic chemistry. Quinoline ring system is an essential structural fragment of a large number of natural and unnatural compounds displaying interesting biological activities such as antimalarial, antibacterial, anti-asthmatic, antihypertensive, and anti-inflammatory[1-4].

Quinolines and their derivatives have been found applications as pharmaceuticals and agrochemicals, as well as being general synthetic building blocks[5-8]. Quinolines and their derivatives are receiving increasing importance due to their wide range of biological activities.

Selenium is an element, which resembles the sulfur in terms of its chemical properties. It has been successfully introduced into organic compounds either as an electrophile or as a nucleophile. Humans and animals need selenium for various biological functions, which involve some organoselenium compounds[9]. It is also known that many selenium containing organic molecules are antibacterial and antifungal agents1[10]. Sulfur and selenium are considered to be isosteric as defined by Langmuir[11] and Erlenmeyer[12]. Even though sulfur and selenium are considered to be isosteric, reports about selenium containing heterocycles are relatively scares[13-15]. However Klayman and Gunther1[16] have reviewed the medicinal applications of isosterism.

In continuation of our research program directed towards the studies on selenium compounds and other heterocycles.[17-30] Their wide range of biological properties led promoted us to investigate the synthesis and antimicrobial activities of selenopyrano [2,3-*b*]quinolines.

RESULTS AND DISCUSSION

In continuation of thienoquinolies[25] instead of sulfur in five membered fused heterocycle. Effort has been made to synthesize seleno quinolines in the current communication.

At first the key intermediates 3-formyl-2-chloroquinolines **(2a-d)**[31] and 3-formyl-2-selenoquinolines **(3a-d)**[32] have been prepared from available reported methods. When 3-formyl-2-selenoquinolines on refluxing with chloroacetic acid in the presence of aqueous potassium hydroxide and ethanol affords 3-formylquinolin-2-yl-selenoacetic acids **(4a-d)**.

When 3-formylquinolin-2-yl-selenoacetic acids **4a-d** on refluxing with $POCl_3$ in methanol afforded methyl(3-formylquinolin-2-yl)selenoacetate **5a-d** intermediates. This intermediate on stirring with DMF underwent smooth cyclisation at room temperature produced methyl thieno[2,3-*b*]quinoline-2-carboxylates **6a-d** at room temperature.

The ^{1}H NMR spectrum of **5a** exhibits singlet at δ 10.30 ppm corresponding to –CHO proton, which was found absent in **6a**. In addition to these, the singlet at δ 4.20 ppm corresponding to -S-CH_2- of **5a** was found to be absent. In IR spectrum, absence of band at 1640-1644 cm^{-1} corresponds -CHO group and reappearance of band at 1735 cm^{-1} confirms the ring cyclisation. Further, the structure assigned was confirmed by its mass spectrum. It gave molecular ion peak at 290.

EXPERIMENTAL

IR spectra were taken on a Perkin Elmer 157 Infrared spectrophotometer. The ^{1}H NMR spectra (300 MHz) were recorded on a Bruker supercon FT NMR instrument using TMS as internal standard and mass spectra on a Jeol JMS-D 300 Mass spectrometer operating at 70 eV. Melting points were determined in open capillary and are uncorrected. Purity of the compounds was checked by TLC on silica gel and were purified by column chromatography.

Preparation of [(3-formylquinolin-2-yl)thio]acetic acid 4a

A mixture of **3a** (1890 mg, 10 mmole), Chloroaceticacid (1461 mg 15 mmole) and K_2CO_3 (2760 mg 40 mmol) in dry acetone (50ml) was refluxed on water bath for 4-5 h. The progress of the reaction was monitored by TLC. After the completion of the reaction, the reaction mixture was filtered solvent was evaporated and dried. Finally solid obtained was purified by column chromatography. Resulting solid obtained was recrystallized (1778 mg, 72%) from alcohol. In a similar way, the same procedure was followed for the synthesis of **4b-e** (65-72%).

[(3-Formylquinolin-2-yl)seleno]acetic acid 4a

^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm): 4.23 (2H, s, -SeCH_2-), 7.58-9.54 (5H, m, Ar-H), 10.30(1H, s, CHO); IR (KBr) ν (cm^{-1}): 1683. [M+], 294. Calcd. (%) for $C_{10}H_{11}NO_3Se$: C; 49.00, H; 3.08, N; 4.76, Se, 26.84. Found: C; 49.04, H; 3.06, N; 4.82, Se, 26.87.

[(3-formyl-6-methylquinolin-2-yl)seleno]acetic acid 4b

^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm): 2.56 (3H, s, CH_3), 4.24 (2H, s, -SeCH_2-), 7.57-9.54 (5H, m, Ar-H), 10.31(1H, s, CHO); IR (KBr) ν (cm^{-1}): 1680. [M+], 308. Calcd. (%) for $C_{13}H_{11}NO_3Se$: C; 50.66, H; (3.60, N; 4.54, Se, 25.62. Found: C; 50.69, H; (3.64, N; 4.59, Se, 25.59.

[(7-Chloro-6-fluoro-3-formylquinolin-2-yl)seleno]acetic acid 4c

^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm): 4.26 (2H, s, -SeCH_2-), 7.58-9.55 (4H, m, Ar-H), 10.32 (1H, s, CHO); IR (KBr) ν (cm^{-1}): 1682. [M+], 346. Calcd. (%) for $C_{12}H_7ClFNO_3$ Se: C; 41.58%, H; 2.04, N; 4.04, Se; 22.78. Found: C; 41.61%, H; 2.09, N; 4.08, Se; 22.78.

[(6-Chloro-3-formylquinolin-2-yl)seleno]acetic acid 4d

^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm): 4.25 (2H, s, -SeCH_2-), 7.55-9.56 (4H, m, Ar-H), 10.30(1H, s, CHO); IR (KBr) ν (cm^{-1}): 1680. [M+], 328. Calcd. (%) for $C_{12}H_8ClNO_3Se$: C; 43.86, H; 2.45, N; 4.26, Se; 24.03. Found: C; 43.89, H; 2.47, N; 4.28, Se; 24.08.

Preparation of [(3-formylquinolin-2-yl)seleno]acetate (5a-d)

A mixture of **4a** (2472 mg, 10 mmol), methanol (50 ml) in presence of $POCl_3$ (15 ml) was refluxed on water bath for 2h. The completion of the reaction was monitored by TLC. After the completion of the reaction, the excess of $POCl_3$ was distilled off under reduced pressure. Then the residue obtained was poured into ice water, the solid obtained was filtered, dried. The crude product was recrystallized from DMF to provide 1992 mg (82%) of pure **5a**. In a similar way, **5b-d** were prepared in 73-82% yield and purified by column chromatography.

[(3-Formylquinolin-2-yl)seleno]acetate 5a

^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm): 3.84 (3H, s, OCH_3), 4.20 (2H, s, -SeCH_2-), 7.60-9.64 (4H, m, Ar-H), 10.30 (1H, s, CHO); IR (KBr) ν (cm^{-1}): 1680. [M+], 308. Calcd. (%) for $C_{13}H_{11}NO_3Se$: C; 50.66, H; 3.60, N; 4.54, Se, 25.62. Found: C; 50.69, H; 3.64, N; 4.59, Se, 25.65.

[(3-Formyl-6-methylquinolin-2-yl)seleno]acetate 5b

^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm): 2.56 (s, CH_3), 3.82 (3H, s, OCH_3), 4.20 (2H, s, -$SeCH_2$-), 7.65-9.62 (5H, m, Ar-H), 10.30 (1H, s, CHO); IR (KBr) ν (cm^{-1}): 1682. [M+], 322. Calcd. (%) for $C_{14}H_{13}NO_3Se$: C; 52.19, H; 4.07, N; 4.35, Se, 24.51. Found: C; 52.22, H; 4.10, N; 4.38, Se, 24.54.

[(7-Chloro-6-fluoro-3-formylquinolin-2-yl)seleno]acetate 5c

^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm): 3.82 (3H, s, OCH_3), 4.26 (2H, s, -$SeCH_2$-), 7.62-9.64 (3H, m, Ar-H), 10.31 (1H, s, CHO); IR (KBr) ν (cm^{-1}): 1680. [M+], 360. Calcd. (%) for $C_{12}H_7ClFNO_3Se$: C; 43.30, H; 2.52, N; 3.88, Se; 21.90. Found: C; 43.34, H; 2.56, N; 3.82, Se; 21.88.

[(6-Chloro-3-formylquinolin-2-yl)seleno]acetate 5d

NMR (300 MHz, DMSO-d_6) δ (ppm): 3.85 (3H, s, OCH_3), 4.22 (2H, s, -$SeCH_2$-), 7.65-9.66 (4H, m, Ar-H), 10.32 (1H, s, CHO); IR (KBr) ν (cm^{-1}): 1682. [M+], 326. Calcd. (%) for $C_{13}H_{10}ClNO_3Se$: C; 47.87, H; 3.09, N; 4.29, Se; 24.21. Found: C; 47.82, H; 3.13, N; 4.26, Se; 24.25.

Preparation of methyl seleno[2,3-*b*]quinoline-2-carboxylate (6a-e)

A mixture of **5a** (2612 mg, 10 mmol), DMF (30 ml) was stirred by means of magnetic stirrer. The completion of the reaction was monitored by TLC. After the completion of the reaction, the excess of DMF was distilled off under reduced pressure. Then the reaction mixture was poured into crushed ice, the solid obtained was filtered, dried. The crude product was and purified by column chromatography ethyl acetate-carbon tetrachloride (9:1) to provide 2055 mg (85%) of pure **6a**. In a similar way, **6b-d,** were prepared in 70-85% yield.

Methyl seleno[2,3-*b*]quinoline-2-carboxylate 6a

^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm): 3.80 (3H, s, OCH_3), 7.60-9.69 (5H, m, Ar-H), IR (KBr) ν (cm^{-1}): 1735. [M+], 290. Calcd. (%) for $C_{13}H_9NO_2Se$: C; 53.81, H; 3.13, N; 4.83, Se, 27.21. Found: C; 53.84, H; 3.16, N; 4.88, Se, 27.25.

Methyl 6-methylseleno [2,3-b]quinoline-2-carboxylate 6b

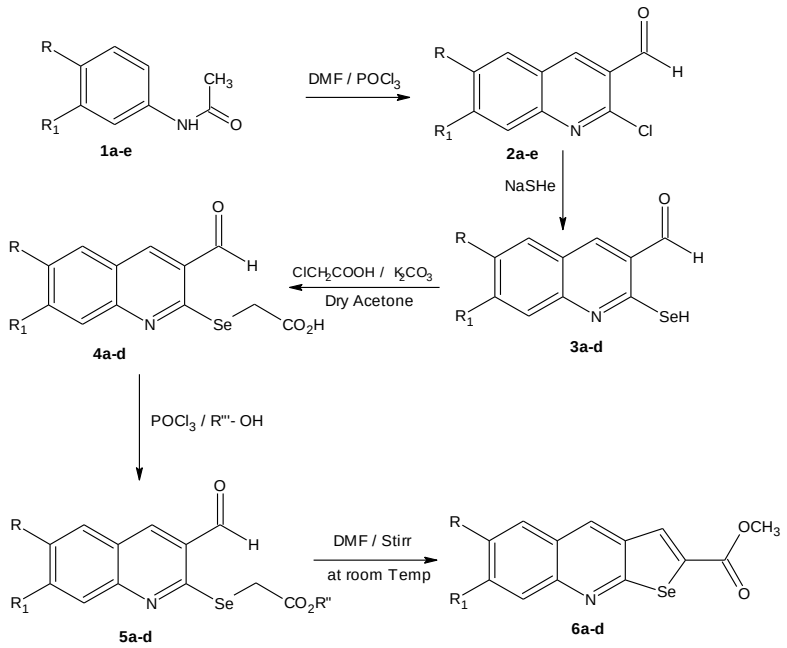
^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm): 2.53 (s, CH_3), 3.85 (3H, s, OCH_3), 7.60-9.66 (5H, m, Ar-H), IR (KBr) ν (cm^{-1}): 1737. [M+], 304. Calcd. (%) for $C_{14}H_{11}NO_2Se$: C; 55.28, H; 3.64, N; 4.60, Se, 25.96. Found: C; 55.32, H; 3.66, N; 4.64, Se, 25.98.

Methyl 7-chloro-6-fluorotseleno[2,3-*b*]quinoline-2-carboxylate 6c

^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm): 3.80 (3H, s, OCH_3), 7.62-9.65 (4H, m, Ar-H), IR (KBr) ν (cm^{-1}): 1732. [M+], 342. Calcd. (%) for $C_{13}H_7ClFNO_2Se$: C; 45.57, H; 2.06, N; 4.09, Se, 23.05. Found: C; 45.61, H; 2.02, N; 4.12, Se, 23.09.

Methyl 6-chloroseleno[2,3-*b*]quinoline-2-carboxylate 6d

^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm): 3.82 (3H, s, OCH_3), 7.62-9.65 (5H, m, Ar-H), IR (KBr) ν (cm^{-1}): 1733. [M+], 324. Calcd. (%) for $C_{13}H_8ClNO_2Se$: C; 48.10, H; 2.48, N; 4.31, Se, 24.32. Found: C; 48.13, H; 2.52, N; 4.35, Se, 24.28.



Scheme -Seleno[2,3-b]quinoline-2-carboxylates derivatives

R	**R_1**	
a	**H**	**H**
b	**CH_3**	**H**
c	**F**	**Cl**
d	Cl	H

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