

Synthesis of New Seleno-Nitrone Compounds

Haddad Batool S., Majeed Nisreen N. and Al-Rubaie Ali Z.

Department of chemistry, college of Science, University of Basrah, Basrah, IRAQ

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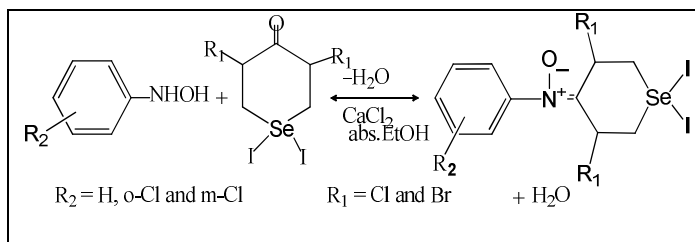
Abstract

The 1,1-Diiodo-1-seleno-4-cyclohexanone were synthesized from the reaction of 1,1-Dibromo-3-penta-none with selenium and then converted to nitrones by the condensation of carbonyl group with substituted N-phenylhydroxylamine. The resulting products were identified by physical properties such as melting poin (m.p.), retardation factor (Rf) and color. Also compounds showed the expected data in identification techniques such as FTIR, ¹HNMR, mass spectroscopy and Elemental analysis (CHN). The results proved the validity of the expected chemical structures of synthesized compounds.

Keywords: Nitrone, seleninium, seleno-nitrone.

Introduction

Nitrone has been extensively investigated, because of their utility as versatile synthetic intermediates¹ and their relative stability². Nitrone has been considered as a promising group of anti-cancer agents³ by intercalating DNA with higher affinity⁴ and found it was easily metabolized with low toxicity⁵. Nitrones were synthesized by the condensation of carbonyl group in 1,1-diiodo-1-seleno-4-cyclohexanone with N-phenylhydroxylamine⁶, as shown in scheme-1.



Scheme-1

CaCl₂ was used as a drying agent⁷ in the synthesis of nitrones to remove the water that obtained during the reversible reaction and because of that the reaction can be shifted to the right direction to obtain the nitrones in a good yield. 3 drops of benzene sulfonic acid⁸ was added to protonated the ketocarbonyl groups, this will increase the reaction rate.

Material and Methods

A series of substituted (1, 1-diiodo-1-seleno-4-cyclohex anone) were synthesized to condensation with synthesized N-phenylhydroxylamine in order to synthesize the corresponding nitrone compounds. The general structures of 1, 1-diiodo-1-seleno- 4-cyclohexanone), N-phen- yl h-ydroxylamine and nitrones are illustrated below in figure-1.

General method of Preparation 1, 1-Di iodo-1-seleno-4-cyclohexaneone: 1,5-dibromo-3-pentanone (5.78 gm ,0.04gm)

was used in a mixing with Selenium powder (5.1 g 0.04 mol) and Sodium Iodide (23 g, 0.16mol) in 2-butoxy ethanol (100 ml) (was refluxed for 1 hr, after that cooled and added water the precipitated was filtered off and washed with water and recrystallization from DMF. The m.p (153-155) °C, (160-162)°C and (159-161) °C , and the yield 80%, 71% and 69%, for compounds (R=H,Br and Cl) respectively⁹. The six member ring, selenapyran, can be obtained by the reaction shown in scheme-2.

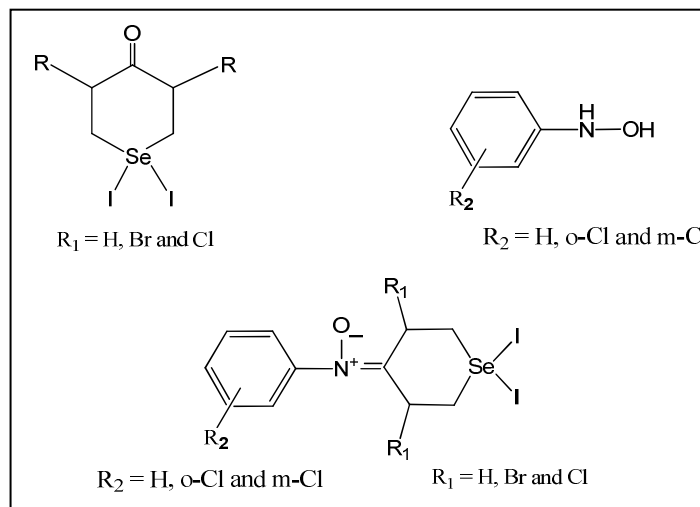
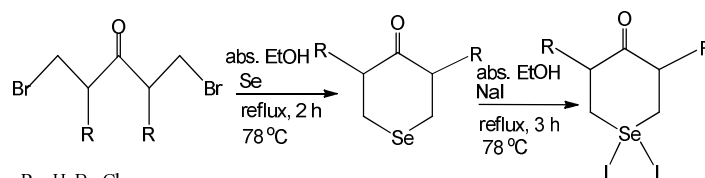


Figure-1

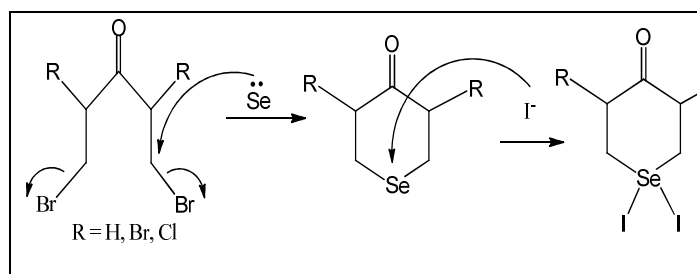
The general structures of Preparation 1, 1-Di iodo-1-seleno-4-cyclohexaneone, N- phenylhydroxylamine and nitrones



Scheme-2

The substituted (1-seleno-4-cyclohexanone) was easily decomposed¹⁰, because of that it used as an intermediate to synthesize the corresponding substituted (1,1-diiodo-1-seleno-4-cyclohexanone).

Three derivatives of 5-Dibromo-3-pentanone were prepared and studied in this research. These compounds were formed by the nucleophilic attack of selenium metal at the carbon atom of carbon-halide. The mechanism of the reaction, as illustrated in scheme-3



Scheme-3
The mechanism of the formation of (1,1-Diiodo-1-seleno-4-cyclohexanone)

Synthesis of nitrone: In a 250ml one-necked round bottomed flask 15gm of CaCl_2 and 0.02mol of (1,1-diiodo-1-seleno-4-cyclohexanone) was placed with addition 30ml of absolute ethanol. This solution was stirred and a solution of N-benzyl hydroxyl amine (0.02mol) in 30ml of absolute ethanol was added, 3 drops of benzene sulfuric acid was added to the mixture. After the addition was completed, the reaction mixture

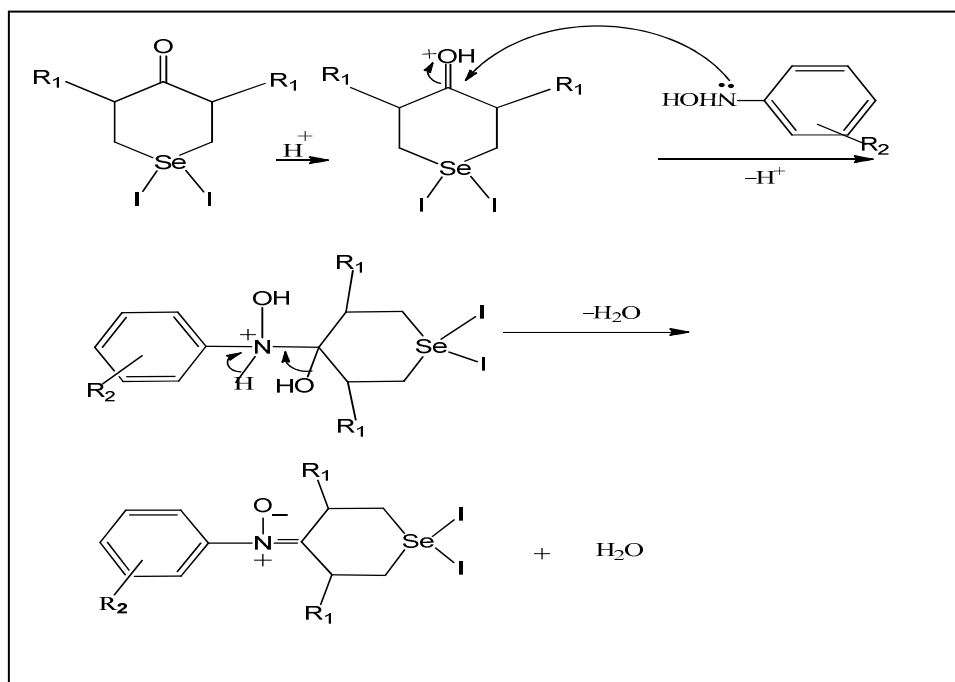
was refluxed with stirring in dark place for several hours according to the type of substituents. The reaction mixture was filtered by suction filtration and the product was recrystallized by abs. ethanol¹¹. Nitron structures are represented in table-1.

Table-1
The Structures of nitrones

compound	Structures
Ba ₁	
Ba ₂	
Ba ₃	
Ba ₄	
Ba ₅	

A series of nitron compounds have been synthesized and studied in our research. These reactions were monitored by thin layer chromatography TLC.

The mechanism of the reaction, as illustrated in scheme-4.



Scheme-4
The mechanism of the formation of nitrone

The synthesized nitron compounds were first purified by recrystallization in abs. ethanol and tested by thin layer chromatography TLC using different eluents. The best separation was obtained in mixture of (n-Hexane: DCM) having a ratio (6:4), respectively as eluent. The compounds were second purified column chromatography using the above eluent.

Results and Discussion

The resulting data were obtained for the synthesised compounds from analysis data as following:

N-1,1-Diiodo-1-seleno-4-cyclohexylidene ph- enyl N-oxide (N1) melting point (m.p.) 169-170 °C, orange Needles yield 76%, TLC, n-hex- ane: ethylacetate 6:4, retardation factor $R_f = 0.52$, FTIR $\bar{\nu}$ /cm⁻¹ : 1600 (C=N), 1198 (N-O), 1343(C-N) and 579 (C-Se). ¹HNMR(500 MHz, dimethyl sulfoxide(DMSO); δ : 8.00 (AA`BB` Harom), 6.65-7.70 (m, Harom) and 1.29, 1.68(t, t selenopyran). Mass (m/z): 522 [M]⁺, 508, 399, 147, 91, 53. For C₁₁H₁₃NOSeI₂ (found): 25.79 % C, 2.85 % H, and 2.90 %

N -1,1-Diiodo-1-seleno-4-cyclohexylidene (2-chloro) benzyl-N-oxide, (N2), melting point (m.p.) 47.87-49.21°C, orange, yield 55%, TLC, n-hexane: ethylacetate 8:2, retardation factor $R_f = 0.50$, FTIR $\bar{\nu}$ /cm⁻¹: 1604 (C=N), 1187 (N-O), 1345(C-N) and 581 (C-Se). ¹HNMR (500) MHz, dimethylsulfoxide (DMSO); δ : 8.06 (AA`BB` Harom), 6.9-7.81 (m, Harom) and 1.27, 1.98 (t, t selenopyran). Mass (m/z): [M]⁺, 542, 399, 147, 125, 53. For C₁₁H₁₂NOSeCl₂ (found): 24.16 % C, 2.28 % H, and 2.67% N.

N-1, 1-Diiodo-1-seleno-4-cyclohexylidene (3-chloro) phenyl-N-oxide, (N3), melting point (m.p.) 64.8-63.9°C, orange, yield 61%, TLC, Diethylether:chloroform 6.5:3.5, retardation factor $R_f = 0.58$, FTIR $\bar{\nu}$ /cm-1: 1635 (C=N), 1190 (N-O), 1348 (C-N) and 588 (C-Se). ¹HNMR(500)MHz, dimethylsulfoxide(DMSO); δ : 7.9 8.08 (AA`BB` Harom), 7.0-7.81 (m, Harom) and 1.31, 1.52 (d, t selenopyran). Mass (m/z): [M]⁺, 542, 399, 147, 125, 53. For C₁₁H₁₂NOSeCl₂ (found): 24.80 % C, 2.38 % H, and 2.61% N.

N-1, 1-Diiodo-1-seleno-3,5-dibromo-4-cyclohexylidene-phenyl-N-oxide, (N4), melting point (m.p.) 243-244°C, Pale yellow crystals, yield 75%, TLC, n-hexane: chloroform 5:5, retardation factor $R_f = 0.5$, FTIR $\bar{\nu}$ /cm-1: 1587 (C=N), 1200 (N-O), 1340(C-N) and 571 (C- Se ¹HNMR (500) MHz, dimethylsulfoxide (DMSO); δ : 8.08 (AA`BB` Harom), 7.2-7.91 (m, Harom) and 2.05, 2.30 (d, t selenopyran). Mass (m/z): [M]⁺, 566, 557, 305, 91, 211. For C₁₁H₁₁NOSeBr₂I₂ (found): 19.82 % C, 1.71 % H, and 1.98% N.

N-1, 1-Diiodo-1-seleno-3,5-dichloro-4-cyclohexylidene benzyl-N-oxide, (N5), melting point (m.p.) 67-65°C, orange, yield 64%, TLC, n-hexane:ethylacetate 5.7:4.3, retardation factor $R_f = 0.6$, FTIR $\bar{\nu}$ /cm-1: 1599 (C=N),

1220 (N-O), 1329 (C-N) and 579 (C-Se). ¹HNMR(500)MHz, dimethylsulfoxide (DMSO); δ : 7.7(s, CH= N→O), 8.00

(AA`BB` Harom), 7.5-7.9 (m, Harom) and 2.21, 2.50 (d, t selenopyran). Mass (m/z): [M]⁺, 576, 467, 305, 91, 121. For C₁₁H₁₃NOSeCl₂I₂ (found): 22.83% C, 1.83 % H, and 2.51% N.

The relevant IR spectra of nitron compounds showed the disappearance of (C=O) band and the appearance of (C=N), (N-O) and (C-N) bands in the region (1599-1635) cm⁻¹, (1195-1198) cm⁻¹ and (1334-1379) cm⁻¹ respectively.

In ¹HNMR the spectra of nitrones which they have (R= H) showed two triplet signals ¹² at (1.31-2.21) ppm and (1.28-2.50) ppm which belonged to the protons of (C3 and C5) and (C2 and C6) position respectively in the selenopyrans ring, while which have (R= Br or Cl) at 3-position and 5-position, showed two signals with (doublet and triplet) ¹³ in the region (1.37-1.41) ppm and (1.50-1.53) ppm, due to the interaction between one proton at 3-position with the two protons at 2-position, and the same case for 5 and 6 position, respectively.

Mass spectrscopy give the molecular ion and other fragments which indicated the structure of prepared nitrones. The elemental analysis found resemble to theoretical values.

Conclusion

New nitron were obtained from the condensation between carbonyl group in selenopyran ring and N-phenylhydroxylamine. This method was easier than other methods to produce nitron. The chemical structures of new sulfaselenonitron compounds were characterized by identification methods.

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