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Synthesis and Characterization of Novel Selenium N,S-Heterocyclic Carbene Compounds

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Yeni Selenyum N,S-heterosiklik Karben Bileşiklerinin Sentezi ve Karakterizasyonu

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Öz

Benzotiyazol ve ilgili benzil halojenürler kullanılarak iki yeni benzotiyazolyum tuzu N-(4-metoksibenzil)benzotiyazolyum klorür (1a) ve N-(4-tert-bütilbenzil)benzotiyazolyum bromür (1b) hazırlandı. Selenoüre N,S-heterosiklik bazlı türevler (2a ve 2b), tuzların KOBu^t bazı varlığında selenyum ile reaksiyonu sonucu elde edildi. Sentezlenen bileşiklerin karakterizasyonu için ^{1}H NMR, ^{13}C NMR, FT-IR ve elementel analiz kullanıldı. Ayrıca, selenyum katılma ürünlerinin molekül ağırlıkları LC-MS/MS analizi ile doğrulandı.

***Anahtar Kelimeler**: Benzotiyazolyum; N,S-Heterosiklik Karben; Selenyum; Selenoüre*

Abstract

Two novel benzothiazolium salts, N-(4-methoxybenzyl)-benzothiazolium chloride (1a) and N-(4-tert-butylbenzyl)-benzothiazolium bromide (1b), were prepared by using benzothiazole and related benzyl halides. Selenourea N,S-heterocyclic-based derivatives (2a and 2b) were obtained by the reaction of the salts with selenium in the presence of KOBu^t base. ^{1}H NMR, ^{13}C NMR, FT-IR and elemental analysis were used for characterization of the synthesized compounds. Also, molecular weights of the selenium adducts were validated by LC-MS/MS analysis.

***Keywords:** Benzothiazolium; N,S-Heterocyclic Carbene; Selenium; Selenourea*

1. Introduction

Strongly σ-basic N-heterocyclic carbenes (NHCs) and their stable organometallic compounds are of great importance in organometallic chemistry. NHCs have numerous applications, especially in homogeneous catalysis. While studies of NHCs mainly concern N,N-heterocyclic carbenes (Zhao et al. 2021, Huang et al. 2021, Demir Atlı 2021), studies of N,S-heterocyclic carbenes (NSHCs) are less common. In an earlier study on NSHCs, vitamin B1 was used as a catalyst for the condensation reactions of benzoin (Breslow 1958). The first NSHC, a thiazol-2-ylidene compound, was isolated in 1997 (Arduengo et al. 1997). The use of electron-rich olefins can be mentioned as the first applied method when listing the synthesis methods of NSHC complexes. The first nucleophilic compounds were synthesized by this method (Cardin et al. 1973). Another one is transmetallation of lithiated thiazoles (Fraser et al. 1974). Nowadays, direct or indirect metallation methods have been used to prepare many transition metal complexes (Huynh et al. 2006, Han et al. 2009, Yen et al. 2009, Purohit et al. 2016). NSHC ligands have become an alternative in catalysis due to the presence of more electropositive and softer sulphur compared to nitrogen. For this reason, the use of metal complexes as effective catalysts has been the subject of much research. The reactions catalysed by NSHC complexes are as follows: Multicomponent Click reaction catalyzed by copper(I) complexes (Purohit et al. 2014), Ullmann coupling catalyzed by nickel(II) complexes (Ding et al. 2009), hydroalkoxylation of allenes catalyzed by gold(I) complexes (Dince et al. 2017), transfer hydrogenation of carbonyls catalyzed by ruthenium(II) complexes (Ding and Hor 2010, Oruc et al. 2016, Karakaş et al. 2022), Heck and Suzuki coupling catalyzed by palladium(II) complexes (Calo et al. 2000, Yen et al. 2006, Yen et al. 2007, Yen at al. 2008). In addition, gold(I) NSHC compounds derived from peptides with excellent cytotoxicity have been prepared (Gutiérrez et al. 2014).

Selenium is one of the most important trace elements in human biology and health. The main source of supply is food. Selenium, which is toxic in high amounts, is essential for the body. It is essential for the cellular metabolism of seleno-proteins such as thioredoxin reductase, glutathione peroxidase, etc., which are involved in maintaining antioxidant functions (Sun et al.

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2017, Spengler et al. 2019, Papp et al. 2007). Selenium adducts are potent anti-carcinogens (Banerjee and Koketsu 2017, Rafique et al. 2015, Liang et al. 2016, Cierpiał et al. 2016).

In this work, two new benzothiazolium salts and their selenium adducts were synthesized and characterized.

2.Experimental

2.1. General Remarks

Benzothiazole was used as freshly distilled. THF was distilled over sodium/benzophenone. Other solvents and chemicals were purchased commercially and used without any pre-treatment. Elemental analysis was carried out on a CHNS-932 (LECO) elemental analyser. A BRUKER ULTRASHIELD PLUS BIOSPIN GmbH Nuclear Magnetic Resonance Spectrometer, Agilent LC-MS/MS device and Perkin Elmer Spectrophotometer were used for NMR, LC-MS/MS and FT-IR measurements. The measurements of the melting point (mp) were carried out with an Electrothermal 9100 instrument.

2.2. Synthesis of N-(4-methoxybenzyl)benzothiazolium chloride (1a)

The mixture of benzothiazole (0.48 g, 3.58 mmol) and 4-methoxybenzyl chloride (0.5 mL, 3.58 mmol) was stirred at 80 °C for 24h. The solidified mixture was dissolved in a small amount of methanol and the solids were precipitated with the addition of Et_2O. After filtration, the product was abundantly washed with Et_2O. Yield: 1.03 g, 98%. mp: 134-135 °C. FT-IR (KBr) ν_{CN}: 1423 cm^{-1}. ^1H NMR (400 MHz, dmso-d_6): δ = 3.68 (s, 3H, OCH_3), 6.09 (s, 2H, NCH_2), 6.92 (d, *J* = 8.8 Hz, 2H, Ar-H), 7.52 (d, *J* = 8.8 Hz, 2H, Ar-H), 7.80 (dt, *J* = 27.5, 7.1 Hz, 2H, Ar-H), 8.37 (d, *J* = 8.4 Hz, 1H, Ar-H), 8.53 (d, *J* = 8.0 Hz, 1H, Ar-H), 10.99 (s, 1H, NCHS) ppm. ^{13}C NMR (100 MHz, dmso-d_6): δ = 55.19, 55.64 (NCH_2, OCH_3), 114.85, 117.96, 125.06, 125.94, 128.82, 129.94, 130.36, 132.35, 140.41, 160.13 (Ar-C), 165.45 (NCS) ppm. Anal. Calcd. for $C_{15}H_{14}NSOCl$ (%): C, 65,33; H, 5.13; N, 5.08; S, 11.61. Found: C, 65.21; H, 5.10; N, 5.01; S, 11.53.

2.3. Synthesis of N-(4-tert-butylbenzyl)benzothiazolium bromide (1b)

Benzothiazole (0.32 g, 2.39 mmol) ve 4-tert-butylbenzyl bromide (0.46 mL, 2.39 mmol) in DMF (2 mL) were stirred at 80 °C for 24h. After cooling to room temperature, Et_2O was added to the orange solution for precipitation. Filtration and washing with Et_2O processes were performed. Yield: 0.75 g, 87%. mp: 192-193 °C. FT-IR (KBr) ν_{CN}: 1430 cm^{-1}. ^1H NMR (400 MHz, dmso-d_6): δ = 1.21 (s, 9H, Bu^t), 6.09 (s, 2H, NCH_2), 7.38 – 7.48 (m, 4H, Ar-H), 7.78 – 7.90 (m, 2H, Ar-H), 8.35 (d, *J* = 9.1 Hz, 1H, Ar-H), 8.53 (d, *J* = 8.0 Hz, 1H, Ar-H), 10.79 (s, 1H, NCHS) ppm. ^{13}C NMR (100 MHz, dmso-d_6): δ = 31.40, 34.84 (Bu^t), 55.30 (NCH_2), 117.90, 125.93, 126.35, 128.67, 128.93, 130.10, 130.35, 132.34, 140.50, 152.83 (Ar-C), 165.91 (NCS) ppm. Anal. Calcd. for $C_{18}H_{20}NSBr$ (%): C, 59.67; H, 5.58; N, 3.87; S, 8.83. Found: C, 58.89; H, 5.83; N, 3.75; S, 8.84.

2.4. General procedure for the synthesis of NSHC-based selenoureas

The mixture of benzothiazolium salt (1 mmol), KOBu^t (2 mmol) and Se (2.5 mmol) was stirred in dry THF (10 mL) for 24h at room temperature under argon atmosphere. The post-reaction processes were carried out in air. THF was removed. CH_2Cl_2 (20 mL) was added and the suspension was filtrated through celite. After removing of CH_2Cl_2, the residue was purified by column chromatography on silica gel.

2.4.1. N-(4-methoxybenzyl)benzothiazole-2-selenone (2a)

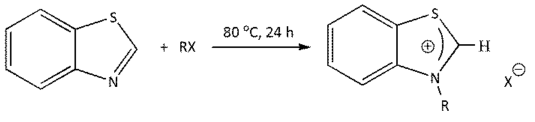
For the column chromatography, CH_2Cl_2 was used as eluent. Then, the obtained product was recrystallized CH_2Cl_2 / n-hexane (1/4) at room temperature. Yield: 40%. mp: 157-158 °C. FT-IR (KBr) ν_{CN}: 1366 cm^{-1}, $\nu_{C=Se}$: 963 cm^{-1}. ^1H NMR (400 MHz, dmso-d_6): δ = 3.71 (s, 3H, OCH_3), 5.81 (s, 2H, NCH_2), 6.88 – 6.93 (m, 2H, Ar-H), 7.33 – 7.38 (m, 2H, Ar-H), 7.39 – 7.47 (m, 2H, Ar-H), 7.57 (dd, *J* = 7.5, 1.1 Hz, 1H, Ar-H), 7.86 (dd, *J* = 7.7, 1.2 Hz, 1H, Ar-H) ppm. ^{13}C NMR (100 MHz, dmso-d_6): δ = 50.21, 55.09 (NCH_2, OCH_3), 114.15, 114.35, 121.94, 125.38, 126.39, 127.43, 128.72, 129.55, 142.01, 158.87 (Ar-C), 184.80 (C=Se) ppm. Anal. Calcd. for $C_{15}H_{13}NOSSe$ (%): C, 53.86; H, 3.93; N, 4.19; S, 9.57. Found: C, 53.99; H, 3.78; N, 4.16; S, 9.57. LC-MS/MS (CH_2Cl_2): $[M + H + Na]^+$ at m/z 358.30, [4-methoxybenzyl]$^+$ at 121.24.

2.4.2. N-(4-tert-butylbenzyl)benzothiazole-2-selenone (2b)

For the column chromatography, CH_2Cl_2 /n-hexane (4/1) mixture was used as eluent. Yield: 36%. mp: 203-204 °C. FT-IR (KBr) ν_{CN}: 1368 cm^{-1}, $\nu_{C=Se}$: 950 cm^{-1}. ^1H NMR (400 MHz, dmso-d_6): δ = 1.23 (s, 9H, Bu^t), 5.84 (s, 2H, NCH_2), 7.28 (d, *J* = 8.5 Hz, 2H, Ar-H), 7.34 – 7.38 (m, 2H, Ar-H), 7.39 – 7.47 (m, 2H, Ar-H), 7.55 (d, *J* = 7.0 Hz, 1H, Ar-H), 7.88 (dd, *J* = 7.4, 1.7 Hz, 1H, Ar-H) ppm. ^{13}C NMR (100 MHz, dmso-d_6): δ = 31.02, 34.23 (Bu^t), 50.39 (NCH_2), 114.34, 121.97, 125.40, 125.51, 126.88, 127.52, 129.53, 131.47, 142.10, 150.24 (Ar-C), 184.96 (C=Se) ppm. Anal. Calcd. for $C_{18}H_{19}NSSe$ (%): C, 59.99; H, 5.32; N, 3.89; S, 8.88. Found: C, 59.70; H, 5.09; N, 3.88; S, 8.80. LC-MS/MS (CH_2Cl_2): [M + H + Na]$^+$ at m/z 384.30, [4-tert-butylbenzyl]$^+$ at 147.30.

3. Results and Discussion

The synthetic routes are presented in Scheme 1 and Scheme 2. Benzothiazolium salts **1a** and **1b** were prepared according to the literature (Oruc et al. 2016, Karakaş et al. 2022, Ding et al. 2009, Gutierrez et al. 2014, Yen et al. 2007). The reaction of benzothiazole with 4-tert-butylbenzyl bromide in DMF gave **1b** in 87% yield. When the same reaction was repeated with 4-methoxybenzyl chloride, the product **1a** was obtained in very low yield. Therefore, this reaction was carried out in solvent-free condition rather than in DMF and it was observed that the product was formed in very high yield. The salts formed in high yields are air stable. They are soluble in methanol, water, dimethylformamide and insoluble diethyl ether and n-hexane.



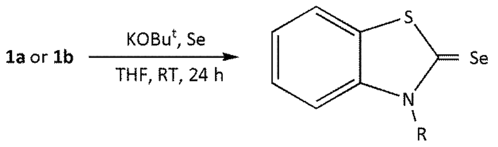
1a, 1b

1a: R = $CH_2C_6H_4(OMe)$-4 X = Cl
1b: R = $CH_2C_6H_4Bu^t$-4 X = Br

Scheme 1. Synthesis of **1a** and **1b**

The selenium adducts of the salts (**2a** and **2b**) were obtained by the reactions with excess selenium. KOBu^t was used as base for deprotonation in these reactions. After column chromatography, pure products were obtained, albeit with slightly lower yields. They are soluble in most of the organic solvents.

Since the experimental elemental analysis results of all the compounds synthesized are in agreement with the theoretical ones, this is an indication that the target compounds have been obtained.



2a, 2b

2a: R = $CH_2C_6H_4(OMe)$-4
2b: R = $CH_2C_6H_4Bu^t$-4

Scheme 2. Synthesis of **2a** and **2b**

NMR spectra are shown in Figures 1 to 4. Analysis of the ^{1}H NMR spectra of **1a** and **1b** reveals that the acidic C2 proton is present at 10.99 and 10.79 ppm, respectively. These downfield singlet signals are characteristic of such NSHC precursors (Karakaş et al. 2022). In the ^{1}H NMR spectrum of **1a**, the signals at 3.68 and 6.09 ppm were observed for the methoxy group and for the methylene protons bonded to the nitrogen atom. In the case of compound **1b**, the signals associated with the tert-butyl group and the NCH_2 protons are located at 1.21 ppm and 5.84 ppm, respectively. The downfield signals seen in the ^{1}H NMR spectra of the salts are absent in the ^{1}H NMR spectra of the selenoureas (Kamal et al. 2019). This is an indication that the salts are undergoing deprotonation and the formation of a carbene-selenium bond. In the ^{13}C NMR spectra of the salts and of the selenourea compounds, the carbon atoms number 2 resonate at about 166 ppm and at about 185 ppm, respectively. The formation of selenium compounds is indicated by this difference in values. These ^{13}C NMR chemical shift values are consistent with the literature (Demir Atlı 2020, Oruc at al. 2016, Časar et al. 2002, Yaqoob et al. 2020).

IR peaks concerning the stretching vibrations of -CN groups for the salts are present at 1423 and 1430 cm^{-1}. These frequency values decrease to 1366 and 1368 cm^{-1} for the selenoureas. Considering the literature data, the peaks at 963 cm^{-1} and 950 cm^{-1} in the spectra of **2a** and **2b** are thought to be the stretching vibration frequencies related to the C=Se bond (Devillanova et al. 1980). The proposed structures for the selenourea compounds **2a** and **2b** were also supported by LC-MS/MS spectra (Figures 5 and 6). In both spectra, signals were observed that were related to the [M+H+Na]$^+$ and to the R group attached to the benzothiazole ring.

4. Conclusions

In this study, N-(4-methoxybenzyl)benzothiazolium chloride **(1a)** and N-(4-tert-butylbenzyl)benzothiazolium bromide **(1b)** salts were prepared. These compounds were used for the synthesis of the selenium adducts, N-(4-methoxybenzyl)benzothiazole-2-selenone **(2a)** and N-4-tert-butylbenzyl)benzothiazole-2-selenone **(2b)**. The structures of the prepared compounds were corroborated by NMR spectroscopy and elemental analysis. Also, formation of the selenium adducts were supported by LC-MS/MS analysis. Synthesis of new complexes derived from these adducts and their catalytic and biological studies proceed.

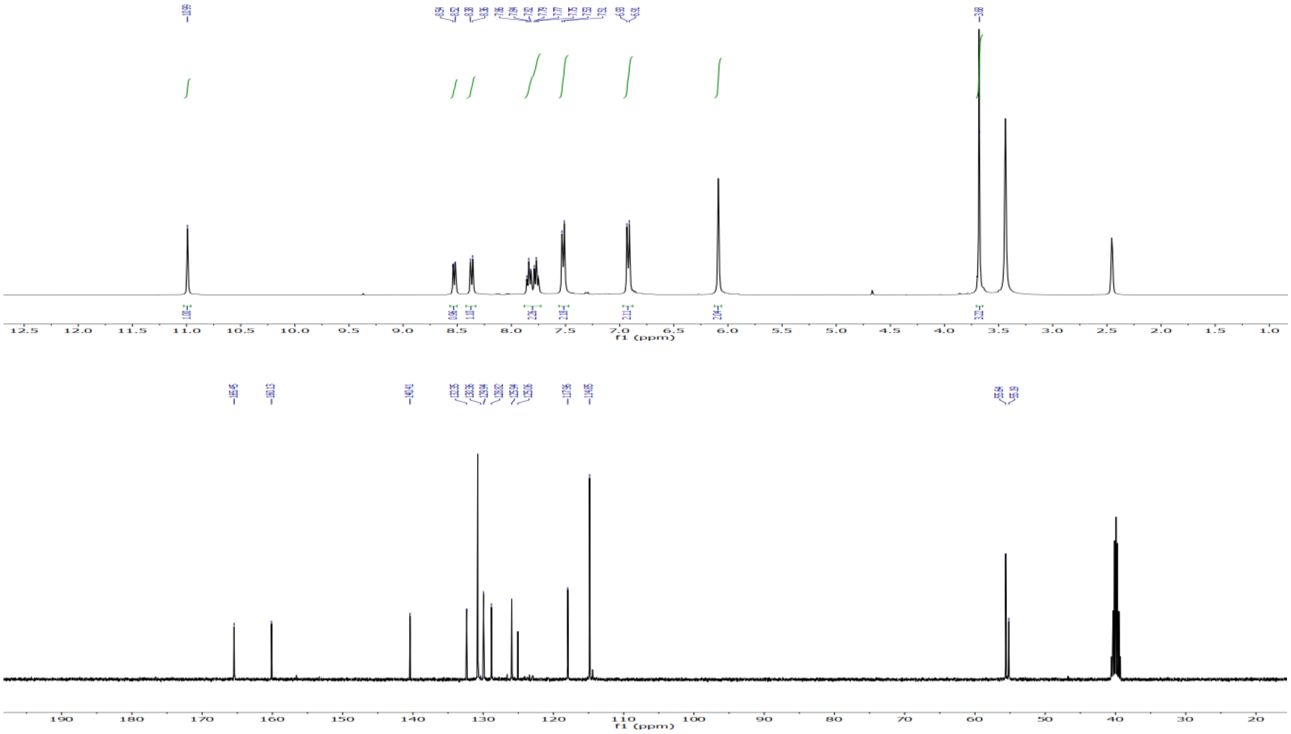


Figure 1. ^{1}H and ^{13}C NMR spectra of **1a**

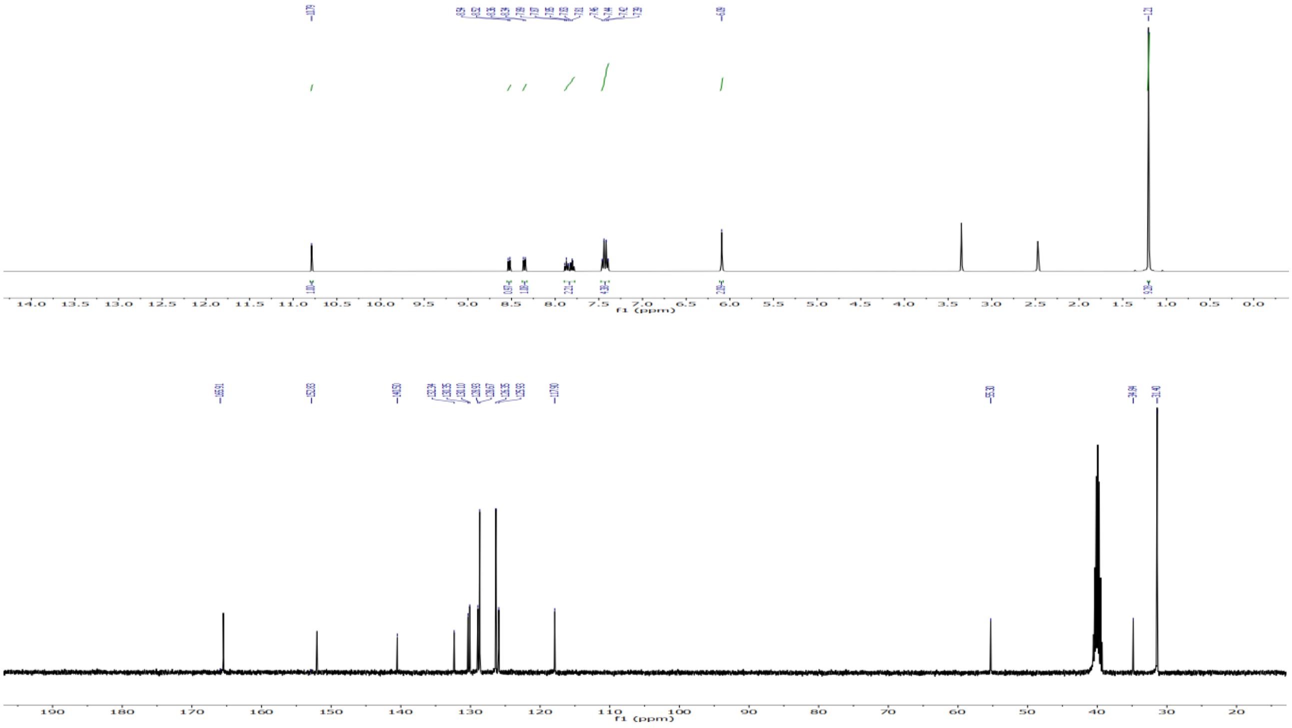


Figure 2. ^{1}H and ^{13}C NMR spectra of **1b**

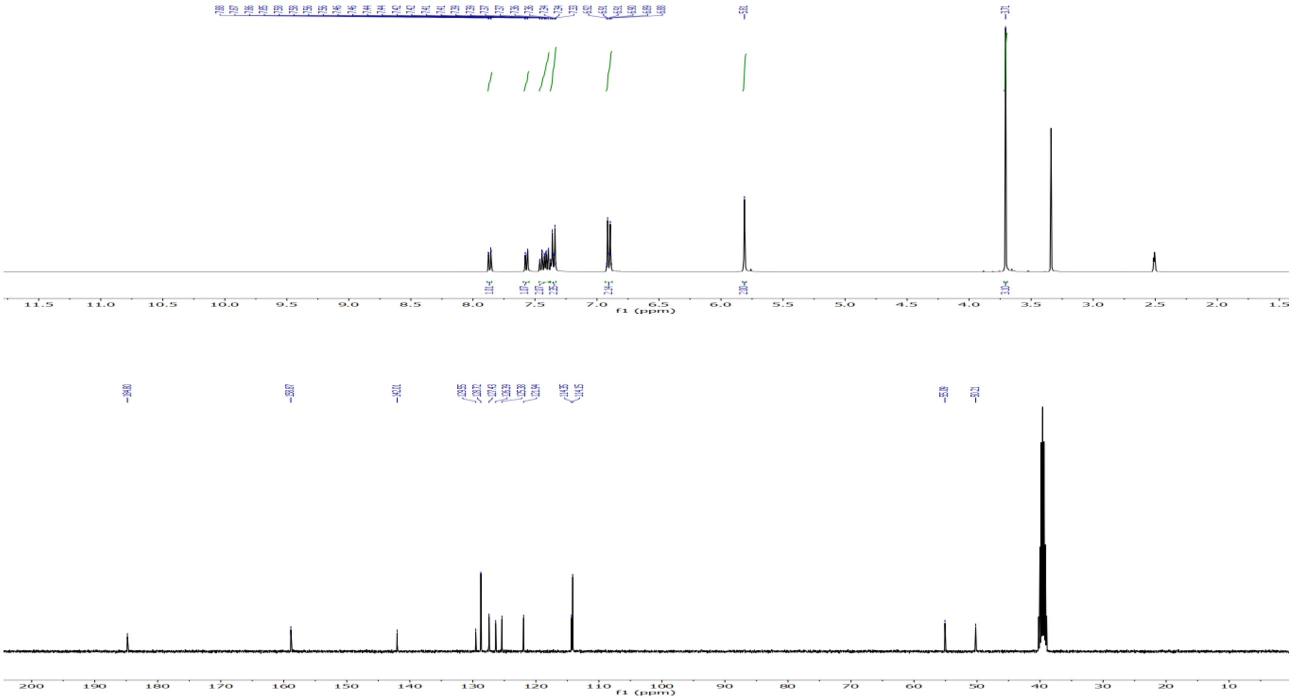


Figure 3. ^{1}H and ^{13}C NMR spectra of **2a**

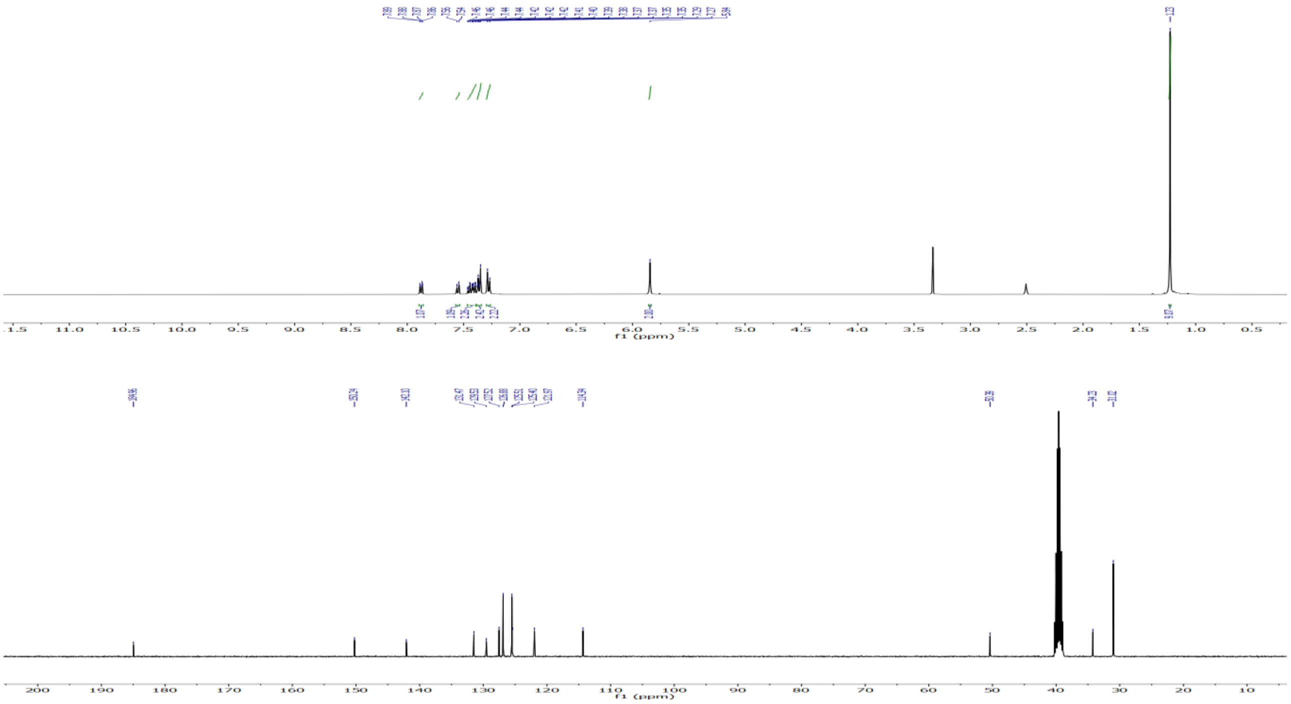


Figure 4. ^{1}H and ^{13}C NMR spectra of **2b**

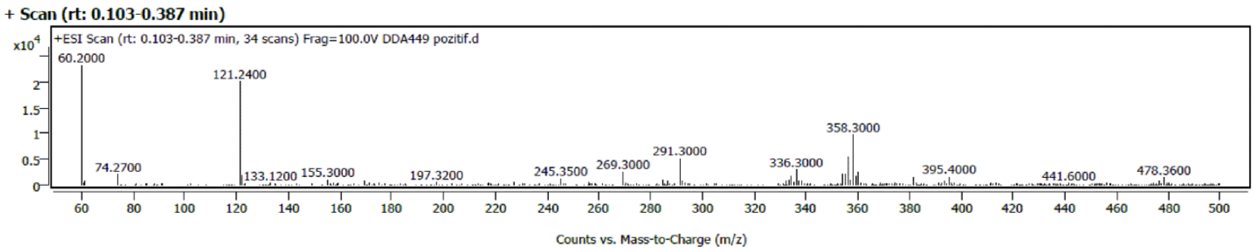


Figure 5. LC-MS/MS spectrum of **2a**

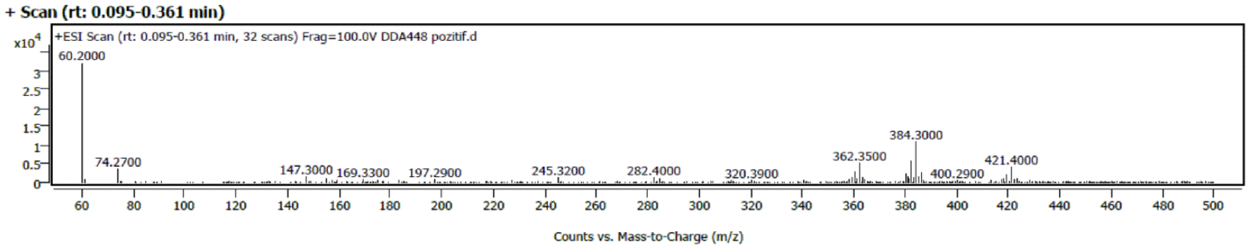


Figure 6. LC-MS/MS spectrum of **2b**

Declaration of Ethical Standards

All ethical rules regarding authorship, citation, reporting and publishing original research were followed.

Declaration of Competing Interest

The author has no conflicts of interest to declare regarding the content of this article.

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5. References

Arduengo III, A.J., Goerlich, J.R., Marshall, W.J., 1997. A stable thiazol-2-ylidene and its dimer. *Liebigs Annalen/ Recueil*, **1997**, 365–374. https:/doi.org/10.1002/jlac.199719970213

Banerjee, B., Koketsu, M., 2017. Recent developments in the synthesis of biologically relevant selenium-containing scaffolds. *Coordination Chemistry Reviews*, **339**, 104–127. https:/doi.org/10.1016/j.ccr.2017.03.008

Breslow, R., 1958. On the mechanism of thiamine action. IV. 1. Evidence from studies on model systems. *Journal of American Chemical Society*, **80**, 3719-3726. https://doi.org/10.1021/ja01547a064

Calo, V., Del Sole, R., Nacci, A., Schingaro, E., Scordari, F., 2000. Synthesis and crystal structure of bis(2,3-dihydro-3-methylbenzothiazole-2-ylidene)-palladium (II) diiodide: The first palladium complex with benzothiazole carbene ligands suitable for homogeneous catalysis. *European Journal of Organic Chemistry*, **2000**, 869–871. https:/doi.org/10.1002/(SICI)1099-0690(200003)2000:6%3C869::AID-EJOC869%3E3.0.CO;2-I

Cardin, D.J., Çetinkaya, B., Çetinkaya, E., Lappert, M.F., 1973. Carbene complexes. Part I.Electron-rich olefins as a source of carbene complexes of platinum(II) and palladium(II); and some experiments with (CF3)2CN2. *Journal Of Chemical Society, Dalton Transactions,* 514–522. https://doi.org/10.1039/DT9730000514

Časar, Z., Lorcy, D., Leban, I., Maréchal, A.M. 2002. A novel approach to N,N'-dimethyl and N,N'-ethylene bridged dibenzodithiadiazafulvalene. *Acta Chimica Solvenica*, **49**, 871-883.

Cierpiał, T., Łuczak, J., Kwiatkowska, M., Kiełbasiński, P., Mielczarek, L., Wiktorska, K., Chilmonczyk, Z., Milczarek, M., Karwowska, K., 2016. Organofluorine isoselenocyanate analogues of sulforaphane: synthesis and anticancer activity. *ChemMedChem*, **11**, 2398–2409. https:/doi.org/10.1002/cmdc.201600442

Demir Atlı, D., 2020. Synthesis and Characterization of Benzothiazolium Salts containing substituted benzyl groups. Science and Mathematics Sciences. Mehtap Düz (ed.), IVPE, 1-11.

Demir Atlı, D., 2021. Synthesis, characterization and catalytic properties of cationic N-heterocyclic carbene silver complexes. *Turkish Journal of Chemistry*, **45**, 577-584. https:/doi.org/10.3906/kim-2010-26

Devillanova, F.A., Verani, G., 1980. 'Selenation' as a diagnostic aid to reinvestigate the infrared spectra of benzimidazole-, benzoxazole- and benzothiazole-2-thiones. *Australian Journal of Chemistry*, **33**, 279-286. https://doi.org/10.1071/CH9800279

Dince, C.C., Meoded, R.A., Hilvert, D., 2017. Synthesis and characterization of catalytically active thiazolium gold(I)-carbenes. *Chemical Communications*, **53**, 7585–7587. https:/doi.org/10.1039/C7CC03791K

Ding, N., Zhang, J., Hor, A., 2009. Formation and crystallographic elucidation of stable [4+2]-coordinate nickel(II) N,S-heterocyclic carbene (NSHC) complexes. *Dalton Transactions*, **10**, 1853–1858. https:/doi.org/10.1039/B815876B

Ding, N., Hor, T.S.A., 2010. Ruthenium(II) N,S-heterocyclic carbene complexes and transfer hydrogenation of ketones. *Dalton Transactions*, **39**, 10179–10185. https:/doi.org/10.1039/C0DT00562B

Fraser, P.J., Roper, W.R., Stone F.G.A., 1974. Carbene complexes of iridium, rhodium, manganese, chromium, and iron containing thiazolidinylidene and pyridinyl- idene ligands. *Journal Of Chemical Society, Dalton Transactions*, **7**, 760-764. https://doi.org/10.1039/DT9740000760

Gutiérrez, A., Gimeno, M.C., Marzo, I., Metzler-Nolte, N., 2014. Synthesis, characterization, and cytotoxic activity of AuIN,S-heterocyclic carbenes derived from peptides containing L-thiazolylalanine. *European Journal of Inorganic Chemistry*, **2014**, 2512–2519. http:/dx.doi.org/10.1002/ejic.201402103

Han, X., Koh, L.L., Weng, Z., Hor, T.S.A., 2009. One-step formation of cyclometallated Au(III) N,S-heterocyclic carbene: crystallographic analysis. *Dalton Transactions*, 7248-7252. https://doi.org/10.1039/B909661B

Huang, M., Li, Y., Lan, X.B., Liu, J., Zhao, C., Liu, Y., Ke, Z., 2021. Ruthenium(II) complexes with N-heterocyclic carbene–phosphine ligands for the N-alkylation of amines with alcohols. *Organic & Biomolecular Chemistry*, **19**, 3451-3461. https:/doi.org/10.1039/D1OB00362C

Huynh, H.V., Meier, N., Pape, T., Hahn, F.E., 2006. Benzothiazolin-2-ylidene complexes of iridium(I). *Organometallics*, **25**, 3012-3018. https://doi.org/10.1021/om060006i

Kamal, A., Nazari V., M., Yaseen, M., Iqbal, M.A., Ahamed, M.B.K., Majid, A.S.A., Bhatti, H.N., 2019. Green synthesis of selenium-N-heterocyclic carbene compounds: Evaluation of antimicrobial and anticancer potential. *Bioorganic Chemistry*, **90**, 103042. https:/doi.org/10.1016/j.bioorg.2019.103042

Karakaş, H., Güzel, M., Ak, M., Kılınçarslan, R., Özdemir, N., 2022. N,S-heterocyclic carbene containing benzothiazol-2-ylidene-Ru(II) and Pd(II) new complexes functionalized with butyl linked carbazole moiety: Synthesis, characterization and their catalytic efficiency and electropolymerizations. *European Polymer Journal*, **181**, 111630. https:/doi.org/10.1016/j.eurpolymj.2022.111630

Liang, Y., Zhou, Y., Deng, S., Chen, T., 2016. Microwave-assisted syntheses of benzimidazole-containing selenadiazole derivatives that induce cell-cycle arrest and apoptosis in human breast cancer cells by activation of the ROS/AKT pathway. *ChemMedChem*, **11**, 2339–2346. https:/doi.org/10.1002/cmdc.201600261

Oruc, Z.I., Gok, L., Turkmen, H., Sahin, O., Buyukgungor, O., Cetinkaya, B., 2016. Pianostool benzothiazol-2-ylidene Ru(II) complexes for effective transfer hydrogenation of carbonyls. *Journal of Organometallic Chemistry*, **807**, 36–44. https:/doi.org/10.1016/j.jorganchem.2016.02.003

Papp, L.V., Lu, J., Holmgren, A., Khanna, K.K., 2007. From selenium to selenoproteins: synthesis, identity, and their role in human health. *Antioxidant Redox Signaling*, **9**, 775–806. https:/doi.org/10.1089/ars.2007.1528

Purohit, V.B., Karad, S.C., Patel, K.H., Raval, D.K., 2014. Cu(N-heterocyclic carbene) chloride: an efficient catalyst for multicomponent click reaction for the synthesis of 1,2,3-triazoles in water at room temperature. *RSC Advances*, **4**, 46002–46007. https:/doi.org/10.1039/C4RA08412H

Purohit, V.B., Karad, S.C., Patel, K.H., Raval, D.K., 2016. Palladium N-heterocyclic carbene catalyzed regioselective thiolation of 1-aryl-3-methyl-1H-pyrazol-5(4H)-ones using aryl thiols. *Tetrahedron*, **72**, 1114-1119. https://doi.org/10.1016/j.tet.2016.01.012

Rafique, J., Saba, S., Canto, R.F.S., Frizon, T.E.A., Hassan, W., Waczuk, E.P., Jan, M., Back, D.F., Da Rocha, J.B.T., Braga, A.L., 2015. Synthesis and biological evaluation of 2-picolylamide-based diselenides with non-bonded interactions. *Molecules*, **20**, 10095–10109. https:/doi.org/10.3390/molecules200610095

Spengler, G., Gajdács, M., Mar´c, M.A., Domínguez-Álvarez, E., Sanmartín, C., 2019. Organoselenium compounds as novel adjuvants of chemotherapy drugs—a promising approach to fight cancer drug resistance. *Molecules*, **24**, 336 . https:/doi.org/10.3390%2Fmolecules24020336

Sun, J., Zheng, X., Li, H., Fan, D., Song, Z., Ma, H., Hua, X., Hui, J., 2017. Monodisperse selenium-substituted hydroxyapatite: controllable synthesis and biocompatibility. *Materials Science and Engineering: C*, **73**, 596–602. https:/doi.org/10.1016/j.msec.2016.12.106

Yaqoob, M., Gul, S., Zubair, N.S., Iqbal, J., Iqbal, M.A., 2020. Theoretical calculation of selenium N-heterocyclic carbene compounds through DFT studies: Synthesis, characterization and biological potential. *Journal of Molecular Structure*, **1204**, 127462. https:/doi.org/10.1016/j.molstruc.2019.127462

Yen, S.K., Koh, L.L., Hahn, F.E., Huynh, H.V., Hor, T.S.A., 2006. Convenient entry to mono and dinuclear palladium(II) benzothiazolin-2-ylidene complexes and their activities toward heck coupling. *Organometallics*, **25**, 5105–5112. https:/doi.org/10.1021/om060510n

Yen, S.K., Koh, L.L., Huynh, H.V., Hor, T.S.A., 2007. Pd(II) complexes of N,S-heterocyclic carbenes with pendant and coordinated allyl function and their Suzuki coupling activities. *Dalton Transactions*, **35**, 3952–3958. https:/doi.org/10.1039/B706968E

Yen, S.K., Koh, L.L., Huynh, H.V., Hor, T.S.A., 2008. Pd(II) complexes with mixed benzothiazolin-2-ylidene and phosphine ligands and their catalytic activities toward C-C coupling reactions. *Dalton Transactions*, **5**, 699–706. https:/doi.org/10.1039/B713152F

Yen, S.K., Young, D.J., Huynh, H.V., Koh, L.L., Hor, T.S.A., 2009. Unexpected coordination difference in geometric-isomerism between N,S- and N,N-heterocyclic carbenes in cyclometallated platinum(II). *Chemical Communications*, 6831-6833. https://doi.org/10.1039/B914036K

Zhao, S., Yang, Z., Jiang, G., Huang, S., Bian, M., Lu, Y., Liu, W., 2021. An overview of anticancer platinum N-heterocyclic carbene complexes. *Coordination Chemistry Reviews*, **449**, 214217. https:/doi.org/10.1016/j.ccr.2021.214217