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Structural characterization and DFT studies of an oxazol-5-one derivative

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Abstract

In this study, the crystal and molecular structure of the compound (4-(3-thiophenylmethylene)-2-(4-tolyl)oxazol-5-one) was determined by the single-crystal X-ray diffraction method. In the crystal structure, molecules are linked by pairs of intermolecular C–H···O hydrogen bonds, forming centrosymmetric dimers with the $R_2^2(14)$ *graph-set motif. Crystal structure is also stabilized by the intramolecular weak interactions and C–O···π stacking interactions. Theoretical studies such as molecular geometry, frontier molecular orbitals and molecular electrostatic potential were performed using the Density Functional Theory (DFT) method B3LYP/6-311G(d,p) basis set. Geometric parameters were compared with the experimental data and it was observed that the theoretical results were in agreement with the experimental parameters.*

Keywords: *Oxazole-5-one, crystal structure, DFT, molecular orbitals, weak interactions.*

Yeni bir oksazol-5-on türevinin yapısal karakterizasyonu ve DFT çalışmaları

Özet

Bu çalışmada, (4-(3-tiyofenilmetilen)-2-(4-tolil)oksazol-5-on) bileşiğinin moleküler ve kristal yapısı tek-kristal X-ışını kırınımı yöntemiyle belirlendi. Kristal yapı içerisinde moleküller, moleküller-arası C–H···O hidrojen bağları ile bağlanarak $R_2^2(14)$ *motifi ile sentrosimetrik dimerler oluştururlar. Kristal yapı ayrıca zayıf molekül içi etkileşmeler ve C–O···π istiflenme etkileşmeleri sayesinde kararlıdır. Teorik çalışmalar (moleküler geometri, frontier moleküler orbitaller ve moleküler elektrostatik potansiyel) Yoğunluk*

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Fonsiyonu Teorisi (YFT) metodu ile ve B3LYP/6-311G(d,p) baz seti kullanılarak gerçekleştirildi. Geometrik parametreler deneysel verilerle karşılaştırıldı ve teorik sonuçların deneysel parametrelerle uyumlu olduğu gözlendi.

Anahtar kelimeler: *Oksazol-5-on, kristal yapı, YFT, moleküler orbitaller, zayıf etkileşmeler.*

1. Introduction

Oxazolone derivatives make a class of five-membered heterocycles, having two oxygen and one nitrogen atom. They have very important role in the medicinal chemistry, biology and physics. They are used as intermediates for the synthesis of several biologically active molecules. They exhibit a wide spectrum of pharmacological activities such as anticancer [1], antitumor [2], antimicrobial [3], analgesic [4], anti-inflammatory [5], antidepressant [6], anti-HIV [7,8], sedative [9,10], cardiotonic activity [11], antidiabetic and antiobesity [12,13]. Oxazolones are also involved in the synthesis of several organic molecules including amino acids, amino alcohols, thiamine, peptides and poly-functional compounds [14,15]. They are also used in semiconductor devices such as electro photographic photoreceptors and in nonlinear optical materials.

Thiophene and its derivatives are important heterocyclic compounds. They are used in technologies as a charge transporting molecules in transistors, super capacitors, organic solar cells, electrochromic materials, organic light-emitting diodes and nonlinear optic materials [16-21]. Thiophene based molecules are widely used in the syntheses of the charge transporting molecules used in organic field effect transistors, organic solar cells and organic light emitting diodes [22-24].

In this study, we characterized an oxazol-5-one derivative containing thiophene. The structural analysis of the compound was firstly performed by single-crystal X-ray diffraction method. Theoretical studies such as molecular geometry, frontier molecular orbitals and molecular electrostatic potential were carried out using the Density Functional Theory (DFT) method B3LYP/6-311G(d,p) basis set. The theoretical and experimental results were compared and discussed.

2. Material and method

2.1. X-ray crystallography

Single-crystal X-ray diffraction data was collected at 293(2) K on a Rigaku-Oxford Xcalibur diffractometer with an EOS-CCD detector using graphite-monochromated MoK$_\alpha$ radiation (λ= 0.71073 Å) with CrysAlis^{Pro} software [25]. Data reduction and analytical absorption correction was performed by CrysAlis^{Pro} program [26]. Utilizing OLEX2 [27], the structure was solved by *Intrinsic Phase* method with SHELXT [28] and refined by full-matrix least squares on F^2 in SHELXL [29]. Anisotropic thermal parameters were applied to all non-hydrogen atoms. Hydrogen atoms were placed using standard geometric models and with their thermal parameters riding on those of their parent atoms (C-H = 0.93-0.96 Å). The details of the crystal data and structure refinement of the title compound are given in Table 1.

2.2. Computational details

In this study, the computational studies were carried out on the basis of *Density Functional Theory* (DFT), with the Gaussian 09W and Gauss View molecular visualization program [30, 31]. The molecular structure of the compound was optimized at B3LYP/6-311G(d,p) level of the theory in the ground state [32, 33]. Highest occupied molecular orbital (HOMO), lowest unoccupied molecular orbital (LUMO) and MEP have also been calculated from optimized geometry of the molecules.

Table 1. Crystallographic data and structure refinement parameters for the title compound.

Empirical formula	$C_{15}H_{11}NO_2S$
Formula weight (g/mol)	269.31
Crystal system, space group	Monoclinic, P 1 2 1/n 1
a, b, c (Å)	15.791(2), 3.9311(5), 21.336(3)
β (^{0})	103.704(13)
V (Å^3)	1286.7(3)
Z	4
Density$_{calc}$ (g/cm^3)	1.390
Absorption coefficient (mm^{-1})	0.247
F(000)	560
Crystal size (mm)	0.266 × 0.126 × 0.088
Reflections collected / independent	3794 / 1221
Parameters	173
Goodness-of-fit on F^2	1.020
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.063$, $wR_2 = 0.113$
R indices (all data)	$R_1 = 0.147$, $wR_2 = 0.153$

3. Result and discussion

3.1. Crystal structure determination

The molecular structure and optimized geometry which has the most favourable conformation of the title compound is shown in Fig.1 and selected bond parameters together with corresponding values obtained by means of X-ray crystallographic analysis and DFT calculations are compared and listed in Table 2. The molecule consists of a thiophene moiety, which is connected to the oxazol-5-one ring bridged by the methine C5 atom and a p-tolyl group linked to the oxazol-5-one fragment. The whole molecule is almost coplanar with the dihedral angles between the oxazole and thiophene rings of 4.6(2)°, oxazole and p-tolyl rings of 1.7(2)°, and thiophene and p-tolyl rings of 5.91(2)°. Torsion angles also prove this planarity [C4–C5–C6–N1 = 1.1(7)°, C4–C5–C6–C7 = -177.5(4)°, N1–C8–C9–C14 = 1.7(6)° and O1–C8–C9–C10 = 1.7(5)°]. Bond lengths, bond angles and torsion angles are within normal ranges, and are close to those observed for a very similar structures in the literature [34,35].

Crystal structure of the compounds is stabilized by mainly intermolecular C–H···O type hydrogen bonds and intramolecular weak interactions in addition to C–O··π stacking interactions. Molecules display a dimeric arrangement around an inversion centre formed *via* a C1–H1···O2 intermolecular hydrogen bond, which is shown in Figure 2. This centrosymmetric hydrogen-bonded dimers are formed with an $R_2^2(14)$ ring motif [36, 37]. Molecules are also linked to each other through C–O··π interactions, are present between the oxazole ring (Cg2) and O2 atom of the adjacent molecule (Fig. 3) [Cg2: O1/C7/C6/N1/C8; O2···Cg2: 3.562(3) Å; symmetry code (ii): x, -1+y, z].

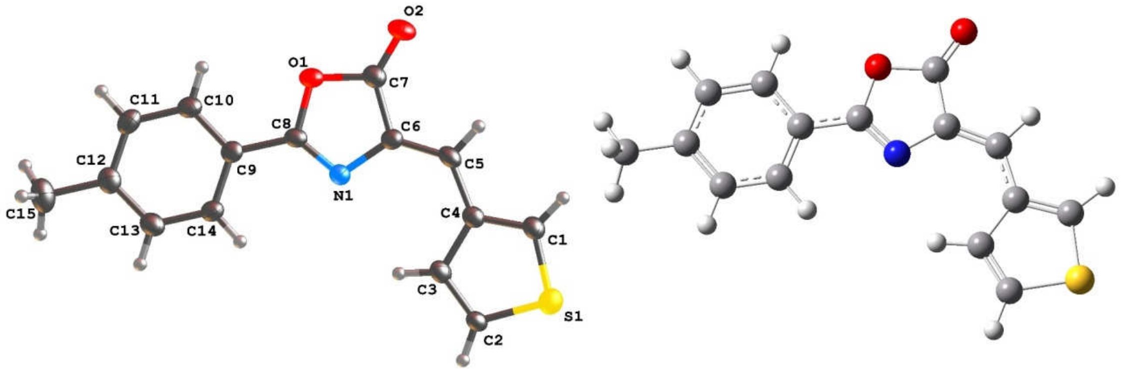

Figure 1. The molecular structure of the title compound, showing the atom labeling, and its optimized structure for DFT/B3LYP/6-311G(d,p). Displacement ellipsoids are drawn at the 30% probability level.

3.2. DFT optimized geometry

The optimized structure of the title compound shown in Figure 1 was obtained by DFT/B3LYP/6-311G(d,p) method. The optimized parameters, namely bond lengths, bond angles and torsion angles are given in Table 2. Comparing the theoretical values with the experimental ones shows that most of the optimized parameters are slightly different than the experimental values. This is because the theoretical calculations are performed for isolated a molecule in gaseous phase, whereas the experimental results are for a molecule in a solid state. The biggest bond length and bond angle differences are 0.037 Å at S1–C2 and 1.464° at O1–C7–O2.

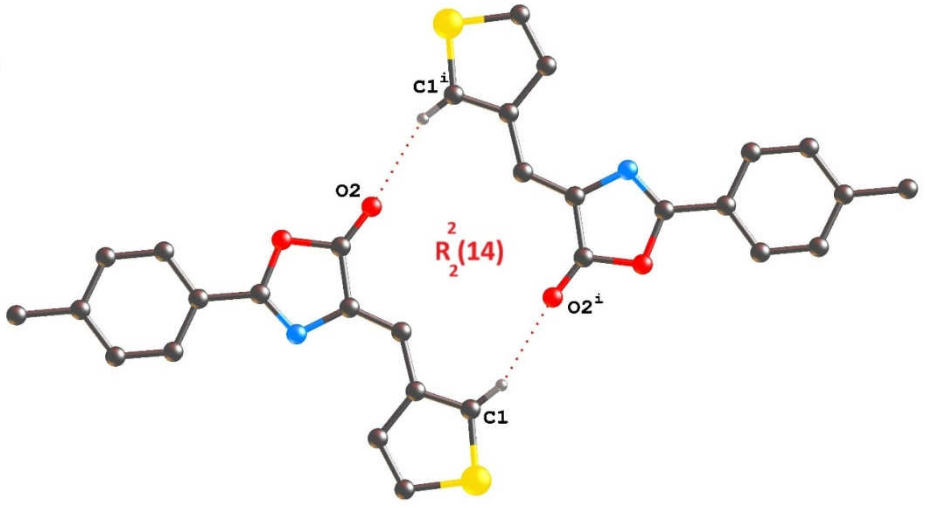

Figure 2. Pictorial view of the arrangement of centrosymmetric hydrogen-bonded dimer around an inversion centre. Dashed lines showed intermolecular hydrogen bonds C1–H1···O2^i [H1···O22.47Å, C1-O2 3.339(5) Å, C1–H1···O2 156°, symmetry code: (i) 1-x, -y, -z].

Table 2. Interatomic distances (Å), bond angles and torsion angles (°) for the title compound as observed experimentally and as calculated using DFT/B3LYP/6-311G(d,p) method.

Atoms	**Compound**	
Bond Lengths	**Experimental**	**Calculated**
S1 – C1	1.686(5)	1.7190
S1 – C2	1.704(4)	1.7411
N1 – C6	1.402(5)	1.3946
N1 – C8	1.288(6)	1.2922
O1 – C7	1.402(5)	1.4083
O1 – C8	1.384(5)	1.3756
O2 – C7	1.202(5)	1.1941
Bond Angles		
C1 – S1 – C2	92.7(2)	91.3206
C6 – N1 – C8	105.4(3)	105.7847
C7 – O1 – C8	105.5(3)	105.9829
O1 – C7 – O2	121.0(4)	122.4642
O1 – C8 – C9	116.7(4)	116.9499
O2 – C7 – C6	134.4(4)	133.7185
C4 – C5 – C6	128.5(4)	128.4686
N1 – C6 – C5	128.3(4)	129.0813
N1 – C8 – C9	127.5(4)	127.2098
Torsion Angles		
C1 – C4 – C5 – C6	178.6(4)	-179.9405
C3 – C4 – C5 – C6	2.2(7)	0.0266
C4 – C5 – C6 – N1	1.1(7)	-0.0155
C4 – C5 – C6 – C7	-177.5(4)	179.9759
C5 – C6 – C7 – O2	0.4(8)	0.0098
N1 – C8 – C9 – C10	-177.2(4)	-179.8369
N1 – C8 – C9 – C14	1.7(6)	-0.0005
O1 – C8 – C9 – C10	1.7(5)	0.2035
O1 – C8 – C9 – C14	-179.4(3)	-179.9601

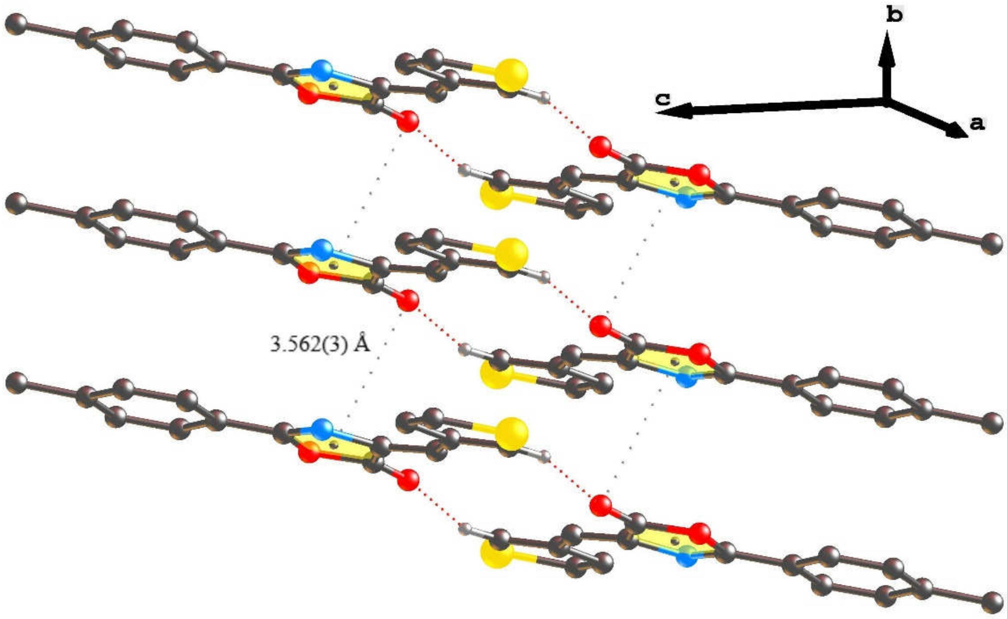

Figure 3. Part of packing view of the title compound, showing the C–O· · π stacking interaction.

3.3. Frontier molecular orbitals

The highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) are the basic orbitals and important in chemical stability. The HOMO shows the ability to donate an electron, whereas the LUMO as an electron acceptor shows the ability to obtain an electron. This also predicted that the nature of electrophiles and nucleophiles to the atom where the HOMO and LUMO are stronger [38, 39].

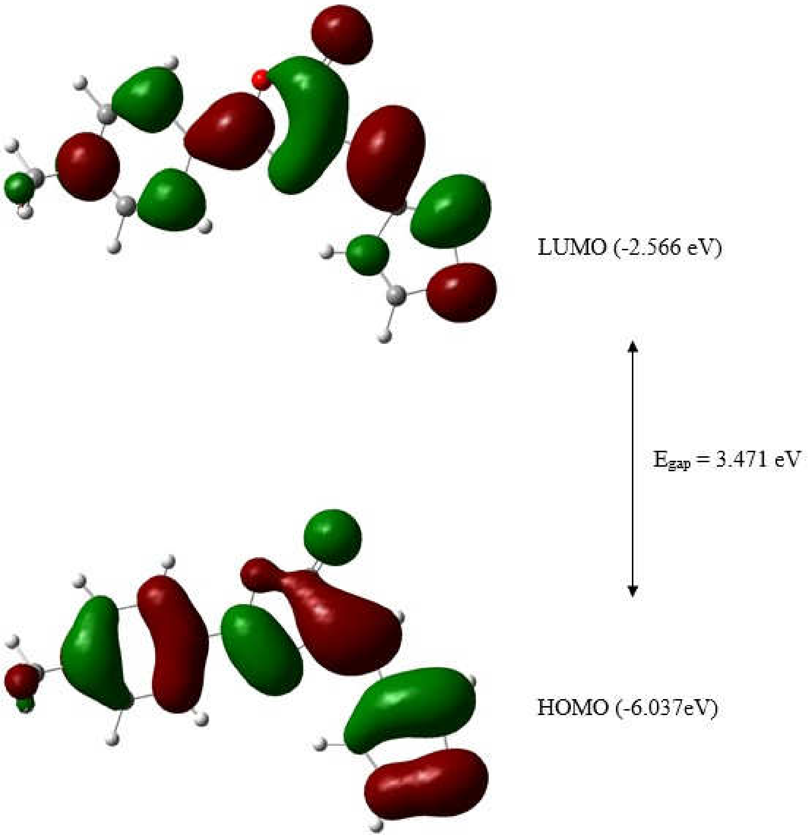

Figure 4. Molecular orbital surfaces and energy levels for the HOMO and LUMO of the studied molecule at B3LYP/6-311G(d,p).

The energy gap of the title compound was calculated using B3LYP/6-311G(d,p) level (Figure 4). In the HOMO, electrons are distributed over the whole molecule, and the HOMO energy level is calculated at -6.037 eV. On the other hand, the electrons are more distributed over the oxazol-5-one for the LUMO with the energy of -2.566 eV. The energy gaps of HOMO and LUMO could be determined about 3.471 eV which indicates the molecule becomes less stability and more reactivity.

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Supplementary

CCDC 1826448 contains the supplementary crystallographic data for the compound. Copies of the data can be obtained free of charge at http://www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Center, 12, Union Road, Cambridge CB2 1EZ, UK. Fax: (+44) 1223-336-033, email: deposit@ccdc.cam.ac.uk.

References

[1] Benedlt, D. and Daniel, V., Synthesis of 2-methyl-(Z)-4-(phenylimino)naphth[2,3-d]oxazol-9-one, a monoimine quinone with selective cytotoxicity toward cancer cells, **Journal of Medicinal Chemistry**, 37, 710–712, (1994).

[2] Gelmi, M.L., Clerici, F. and Melis, A., 5(4H)-oxazolones. Part X. Acid and base effects on the translactonization reaction of 4-(2-Oxa-alkylidene)-5(4H)-oxazolones: New synthesis of 5-alkylidene-3-benzoylamino-2(5H)-furanones, **Tetrahedron**, 53, 1843–1854, (1997).

[3] Martinez, A.P., Lee, W.W. and Goodman, L., Some 2-fluoroethylamines derived from hydrocinnamic acid, phenylpyruvic acid and DL-phenylalanine, **Tetrahedron**, 20, 2763–2771, (1964).

[4] Lesieur, S. and Aichaw, H., Eur PAT 1990, 390, 673, 03 OCT 1991; **Chemical Abstracts**, 114, 143, (1991).

[5] Ando, K. and Asai, N., EUR PAT, 385, 664, 05 SEPT 1990; **Chemical Abstracts**, 114, 143, (1991).

[6] Descas, P. and Jarry, C., EUR PAT, 392, 929, 17 OCT 1990; **Chemical Abstracts**, 114, 143, (1991).

[7] Abdel-Aty, A.S., Pesticidal effects of some imidazolidine and oxazolone derivatives, World **Journal of Agricultural Science**, 5, 105–113, (2009).

[8] Witvrouw, M., Pannecouque, C, Clercq, E.D., Fernandez-Alvarez, E. and Marco, J.L., Inhibition of human immunodeficiency virus type (HIV-1) replication by some diversely functionalized spirocyclopropyl derivatives, **Archiv der Pharmazie**, 332, 163–166, (1999).

[9] Khan, K.M., Mughal, U.R., Khan, M.T. H., Ullah, Z., Perveen, S. and Choudhary, M.I., Oxazolones: new tyrosinase inhibitors; synthesis and their structure–activity relationships, **Bioorganic & Medicinal Chemistry**, 14, 6027–6033, (2006).

[10] Pashas, M.A., Jayashankara, V.P., Venugopala, K.N. and Rao, G.K., Zinc Oxide (ZnO): an efficient catalyst for the synthesis of 4- arylmethylidene-2-phenyl-5-(4H)-oxazolones having antimicrobial activity, **Journal of Pharmacological and Toxicological Methods**, 2, 264–270, (2007).

[11] Schnettler, R.A., Jones Jr., W.D. and Claxton, G.P., **Cardiotonic heterocyclic oxazolones**, Merrell Dow Pharmaceuticals Inc., United States, Patent No.: US 4698353 (1987).

[12] Pereira, E.R., Sancelme, M., Voldoire, A. and Prudhomme, M., Synthesis and antimicrobial activities of 3-N-substituted-4,5-bis(3-indolyl)oxazol-2-ones, **Bioorganic & Medicinal Chemistry Letters**, 7, 190, 2503, (1997).

[13] Viti, G., Namnicine, R., Ricci, R., Pestelline, V., Abeli, L. and Funo, M., New antagonists of platelet-activating factor containing 2-oxazolidinone or 2-

morpholinone, **European Journal of Medicinal Chemistry**, 29, 401-406, (1994).

[14] Ismail, M.I., Physical characteristics and polarographic reduction mechanism of some oxazolones, **Canadian Journal of Chemistry**, 69, 1886–1892, (1991).

[15] Matsunaga, H., Ishizuka, T. and Kunieda, T., Synthetic utility of five membered heterocycles-chiral functionalization and applications, **Tetrahedron** Letters, 61, 8073–8094, (2005).

[16] Han, R., Lu, S., Wang, Y., Zhang, X., Wu, Q. and He, T., Influence of monomer concentration during polymerization on performance and catalytic mechanism of resultant poly(3,4-ethylenedioxythiophene) counter electrodes for dyesensitized solar cells, **Electrochimica Acta**, 173, 796–803, (2015).

[17] Hacioglu, S.O., Yiğit, D., Ermiş, E., Söylemez, S., Güllü, M. and Toppare, L., Syntheses and electrochemical characterization of low oxidation potential nitrogen analogs of pedot as electrochromic materials, **Journal of the Electrochemical Society**, 163, 10, E293-E299, (2016).

[18] Asatkar, A.K., Senanayak, S.P., Bedi, A., Panda, S., Narayan, K. S. and Zade, S. S., Zn(II) and Cu(II) complexes of a new thiophene based salphen-type ligand: solutionprocessable high-performance field-effect transistor materials, **Chemical Communications**, 50, 7036–7039, (2014).

[19] Ermiş, E., Yiğit, D. and Güllü, M., Synthesis of poly(N-alkyl-3,4-dihydrothieno[3,4-b] [1,4]oxazine) derivatives and investigation of their supercapacitive performances for charge storage applications, **Electrochimica Acta**, 90, 623–633, (2013).

[20] Pietrangelo, A., Sih, B.C., Boden, B.N., Wang, Z., Li, Q., Chou, K.C., MacLachlan, M.J. and Wolf, M.O., Nonlinear optical properties of Schiff-base-containing conductive polymer films electro-deposited in microgravity, **Advanced Materials**, 20, 2280–2284, (2008).

[21] Kingsborough, R.P. and Swager, T.M., Electroactivity enhancement by redox matching in Cobalt Salen-based conducting polymers, **Advanced Materials**, 10, 14, 1100–1104, (1998).

[22] Mas-Torrent, M. and Rovira, C., Novel small molecules for organic field-effect transistors: towards processability and high performance, **Chemical Society Reviews**, 37, 827–838, (2008).

[23] Shirota, Y. and Kageyama, H., Charge carrier transporting molecular materials and their applications in devices, **Chemical Reviews**, 107, 953–1010, (2007).

[24] Varis, S., Ak, M., Tanyeli, C., Akhmedov, I.M. and Toppare, L., Synthesis and characterization of a new soluble conducting polymer and its electrochromic device, **Solid State Sciences**, 8, 1477–1483, (2006).

[25] CrysAlisPro Software System, Version 1.171.38.43, Rigaku Corporation, Oxford, UK, (2015).

[26] Clark, R.C. and Reid, J.S., The analytical calculation of absorption in multifaceted crystals, **Acta Crystallographica**, A51, 887–897, (1995).

[27] Dolomanov, O.V., Bourhis, L.J., Gildea, R.J., Howard, J.A.K. and Puschmann, H., OLEX2: A complete structure solution, refinement and analysis program, **Journal of Applied Crystallography**, 42, 339–341, (2009).

[28] Sheldrick, G.M., SHELXT-Integrated space-group and crystal-structure determination, **Acta Crystallographica**, A71, 3–8, (2015).

[29] Sheldrick, G.M., Crystal structure refinement with SHELXL, **Acta Crystallographica**, C71, 3, 8, (2015).

[30] Frisch, M.J., Trucks, G.W., Schlegel, H.B., Scuseria, G.E., Robb, M.A., Cheeseman, J.R., Scalmani, G., Barone, V., Mennucci, B., Petersson, G.A., Nakatsuji, H., Caricato, M., Li, X., Hratchian, H.P., Izmaylov, A.F., Bloino, J., Zheng, G., Sonnenberg, J.L., Hada, M., Ehara, M., Toyota, K., Fukuda, R., Hasegawa, J., Ishida, M., Nakajima, T., Honda, Y., Kitao, O., Nakai, H., Vreven, T., Montgomery Jr. J.A., Peralta, J.E., Ogliaro, F., Bearpark, M., Heyd, J.J., Brothers, E., Kudin, K.N., Staroverov, V.N., Keith, T., Kobayashi, R., Normand, J., Raghavachari, K., Rendell, A., Burant, J. C., Iyengar, S. S., Tomasi, J., Cossi, M., Rega, N., Millam, J.M., Klene, M., Knox, J.E., Cross, J. B., Bakken, V., Adamo, C., Jaramillo, J., Gomperts, R., Stratmann, R.E., Yazyev, O., Austin, A.J., Cammi, R., Pomelli, C., Ochterski, J.W., Martin, R.L., Morokuma, K., Zakrzewski, V.G., Voth, G.A., Salvador, P., Dannenberg, J.J., Dapprich, S., Daniels, A.D., Farkas, O., Foresman, J.B., Ortiz, J.V., Cioslowski, J. and Fox, D.J., Gaussian 09, Revision B.01, Gaussian, Inc., Wallingford CT, (2010).

[31] Dennington, R., Keith, T. and Millam, J., GaussView, Version 5, Semichem Inc., Shawnee Mission, KS, (2009).

[32] Becke, A.D., Density Functional Thermochemistry III, The role of exact exchange, **The Journal of Chemical Physics**, 98, 5648, (1993).

[33] Ditchfield, R., Hehre, W.J. and Pople, J.A., Self Consistent Molecular Orbital Methods. IX. An Extended Gaussian Type Basis for Molecular Orbital Studies of Organic Molecules, **The Journal of Chemical Physics**, 54, 724–728, (1971).

[34] Sharma, P., Subbulakshmi, K.N., Narayana, B., Byrappa K. and Kant, R., Crystal structure of 2-methyl-4-[(thiophen-2-yl)methylidene]-1,3-oxazol5(4H)-one, **Acta Crystallographica**, E71, o123–o124, (2015).

[35] Gündoğdu, C., Alp, S., Ergün, Y., Tercan, B. and Hökelek, T., 2-(Naphthalen-1-yl)-4-(thiophen-2-ylmethylidene)-1,3-oxazol-5(4H)-one, **Acta Crystallographica**, E67, o1321–o1322, (2011).

[36] Bernstein, J., Davis, R.E., Shimoni, L. and Chang, N.L., Patterns in hydrogen bonding: Functionality and graph set analysis in crystals, **Angewandte Chemie International Edition in English**, 34, 1555–1573, (1995).

[37] Sen, I., Kara, H. and Azizoglu, A., Substituent effects on hydrogen bonding of aromatic amide-carboxylate, **Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy**, 167, 50-58, (2016).

[38] Govindarajan, M., Periandy, S. and Carthigayen, K., FT-IR and FT-Raman spectra, thermo dynamical behavior, HOMO and LUMO, UV, NLO properties, computed frequency estimation analysis and electronic structure calculations on α-bromotoluene, **Spectrochimica Acta**, A97, 411–422, (2012).

[39] Çiçek, B., Çakır, Ü. and Azizoglu A., The associations of macrocyclic ethers with cations in 1,4-dioxane/water mixtures; potentiometric Na+ and K+ binding measurements and computational study, **Journal of Inclusion Phenomena and Macrocyclic Chemistry**, 72, 121-125, (2012).