

Synthesis of novel C-2 substituted imidazoline derivatives having the norbornene/dibenzobarrelene skeletons

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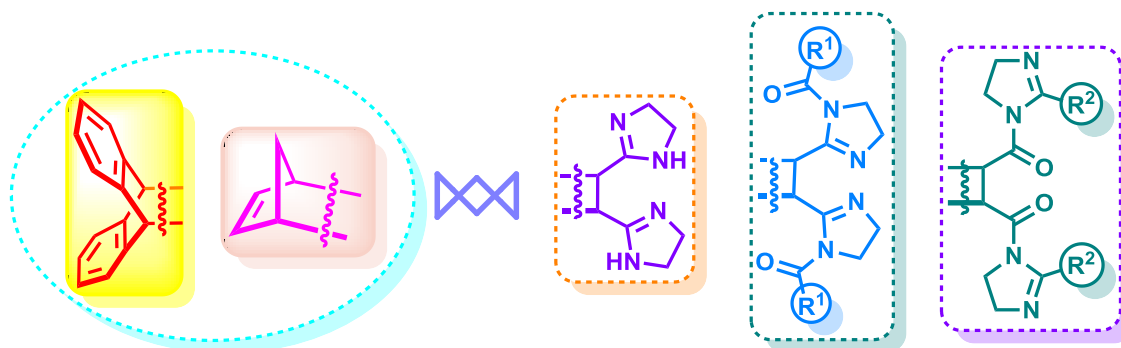
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Abstract

Novel imidazoline derivatives were synthesized from the norbornene and dibenzobarrelene skeletons which were obtained by the Diels-Alder reactions of anthracene and cyclopentadiene with the different dienophiles, such as fumaronitrile and fumaric acid. Synthesis of the C-2 substituted imidazolines was performed with high yields from various dinitriles and diacyl dichlorides.



Keywords: Cycloadditions, imidazoline, norbornene, dibenzobarrelene, guanidine, amide

Introduction

The chemistry of heterocyclic compounds is one of the most complex and important branches of organic chemistry. The imidazoline ring is an important member of the class of the diaza-heterocyclic compounds. Since natural or synthetic originated imidazolines are found in the molecular structure of many drugs as biologically active residues, imidazoline compounds are extensively used in medicinal and pharmaceutical chemistry. These compounds have widely attracted the focus of biologists because of their potent properties such as anti-inflammatory, antitumor, and antiviral activities.¹ Imidazoline derivatives, like topsentin B1, D, cylindrospermopsin, and spongatine A-C have been isolated from several sea sponges and numerous studies have been carried out on the artificial synthesis and biological activities of these marine compounds.²

The synthesis of C-2 substituted imidazolines such as nutlin compounds is of great importance in terms of both organic and medicinal chemistry because nutlin compounds are known to exhibit anti-tumor activity. Substitution at C-2 of the imidazoline ring system is a requirement for anti-tumor activity.³ Since the discovery of the imidazoline receptor, many biologically active 2-imidazoline derivatives have been synthesized.⁴ Clonidine, moxonidine, and phentolamine, which are the most well-known imidazoline receptors, are widely used in the treatment of the diseases such as heart diseases and high blood pressure.

There are quite a number of synthetic procedures developed using different starting materials for the synthesis of C-2 substituted imidazoline derivatives and some of them have been used for more than half a century.⁵ In the past two decades, imidazoline synthetic methods have been modified and optimized for better yields. In addition to classical methods,^{5,6} different procedures such as on a solid support,⁷ solvent-free,⁸ sonochemical⁹ and microwave-assisted methods are used in the synthesis of these compounds.^{10,11} Besides, effective and new enantioselective methods have been improved for the synthesis of chiral imidazoline compounds over the last years.^{12,13}

Imidazoline compounds are widely studied by organic chemists with regard to their different application areas as synthetic intermediates, protecting groups, chiral auxiliaries and catalysts for asymmetric synthesis. In recent years, they have gained importance as organocatalysts¹⁴⁻¹⁶ in very diverse stereoselective reactions due to their basicity and nucleophilicity¹⁷ as well as Brønsted acidity^{18,19} of their salts.

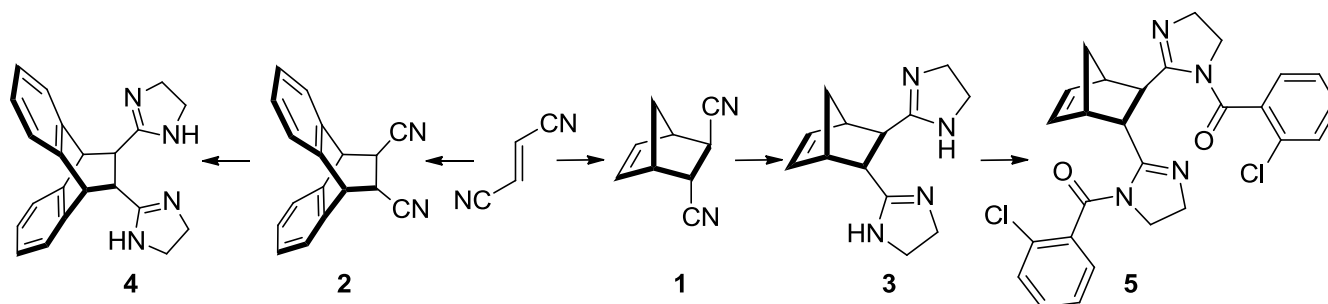
It has been determined that some compounds having the dibenzobarrelene skeleton show a high fluorescence property at room temperature.²⁰ Compounds which contain heterocyclic ring fused to the norbornene skeleton,²¹ anthracene-9-imidazoline hydrazone, and its copper (II) complex are known to have antitumor and cytotoxic effects.²²

There are no imidazoline derivatives associated with norbornene and dibenzobarrelene skeletons in the literature. In this respect, novel C-2 and N-acyl substituted imidazolines showing dibenzobarrelene or norbornene moieties were synthesized in this study for the first time.

Result and Discussion

In the first part of the work, Diels-Alder cycloaddition reaction was used to synthesize the starting reactants from the various dienophiles and dienes. In these reactions, while anthracene and cyclopentadiene were utilized as dienes, fumaronitrile and fumaric acid were employed as dienophiles. As the starting reactants, dinitriles **1** and **2** (Scheme 1), dicarboxylic acids **13**, **17** and **26**, and their acyl chlorides **14**, **18** and **27** (Schemes 3-5), which have norbornene and dibenzobarrelene skeletons, were synthesized on the basis of cited literature.²³⁻²⁶

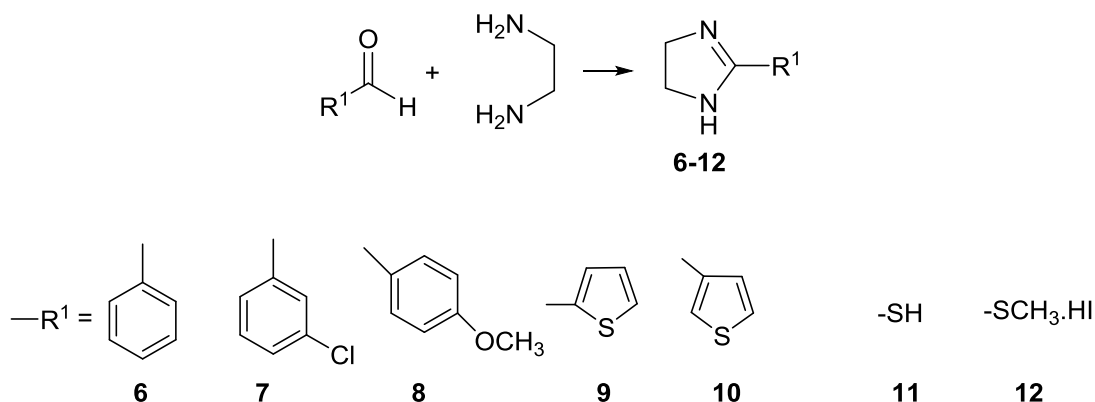
There are many various methods in the literature²⁷⁻³⁰ for the synthesis of 2-imidazoline derivatives from the compounds having a nitrile functional group. When these methods are analyzed, two different synthetic strategies come to the forefront. In the first one, the formation of the 2-imidazoline ring performs with two-step reaction from the imidic ester intermediate, which is also known as the Pinner method.^{27,28} In the second one, it proceeds with a one-step reaction using the catalyst.¹⁰



Scheme 1. Synthesis of imidazoline derivatives from the dinitriles having norbornene and dibenzobarrelene skeletons.

Unlike the literature, syntheses of compounds **3** and **4** were carried out through both conventional and microwave-assisted methods in the solvent-free conditions with high yields (Scheme 1). The reaction time, which is quite long in the conventional method, is rather short in the microwave-assisted procedure. Compound **3** was converted to the *N*-acyl derivative **5** by the reaction with 2-chlorobenzoyl chloride in basic medium. In the ¹H NMR spectrum of compounds **3** and **4**, while the imidazoline ring protons signals appeared at 3.0-4.0 ppm, the imidazoline methylene carbon signals were not observed in the APT ¹³C NMR spectrum. However, when the APT ¹³C NMR spectrum was taken over a very long time using CDCl₃, these signals were observed very weakly. To clarify this situation, *N*-acyl derivative of compound **3** was prepared from the reaction of 2-chlorobenzoyl chloride with compound **3**. In the APT ¹³C NMR spectrum of compound **5**, four different CH₂ carbon signals belonging to imidazoline ring were clearly observed at 48.3, 49.1 and 51.1 ppm.

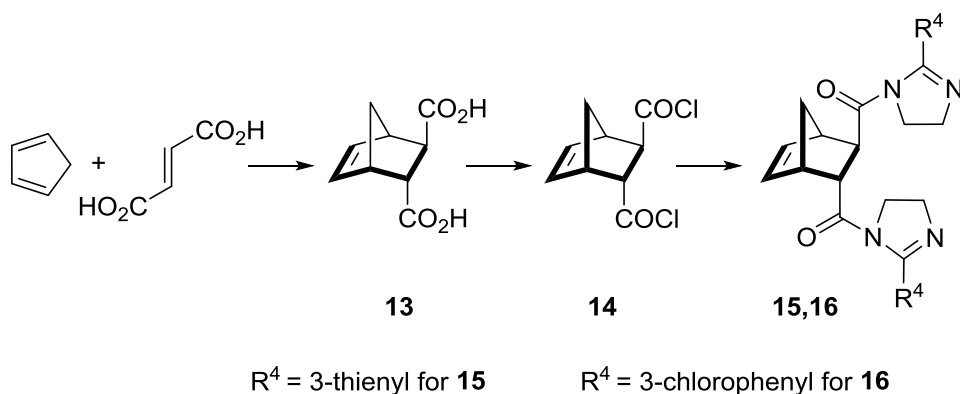
To use in subsequent reactions, aromatic and heteroaromatic substituted imidazolines **6-10** were synthesized from the reaction of the requisite aldehydes with ethylenediamine and *N*-bromosuccinimide (NBS) in basic medium (Scheme 2).^{31,32} Compounds **6-9** are reported in the literature;³³⁻³⁵ however, compound **10** was synthesized for the first time in this work. Compounds **11** and **12** are commercially available chemicals such as **6-9**.



Scheme 2. Synthesis of aromatic and heteroaromatic substituted imidazolines **6-10**.

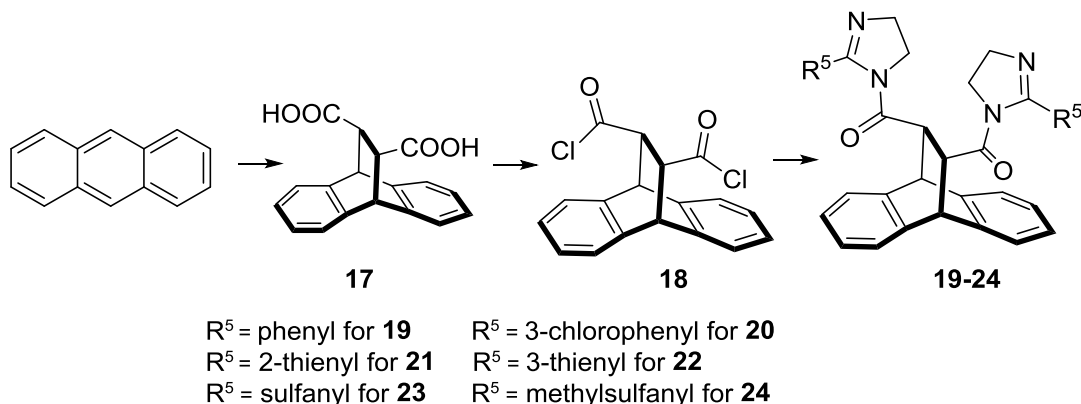
When the ^1H NMR spectra of compounds **6-10** were analyzed, the methylene protons belonging to the imidazoline ring were observed as a singlet.³¹⁻³⁴ In the APT ^{13}C NMR spectrum of compounds **9** and **10**, the methylene carbon signals were observed very poorly. The similar problem was observed in the ^1H and ^{13}C NMR spectra of compound **3**. The X-ray image of compound **10** was taken and the doubts about the structural analysis in NMR spectra were eliminated. (Details of the NMR analysis and experimental procedure of compounds **6-10** can be found in the Supporting Information section.)

Compounds **15** and **16** were synthesized through the reaction of acyl chloride **14** with required 2-imidazolines **10** and **7** (Scheme 3). The molecular structures of these compounds were characterized with HETCOR NMR spectra, as well as FT-IR, ^1H NMR, and APT ^{13}C NMR spectra. In the APT ^{13}C NMR spectra, two different methylene carbon signals belonging to imidazoline ring appeared without observing the situation mentioned above.



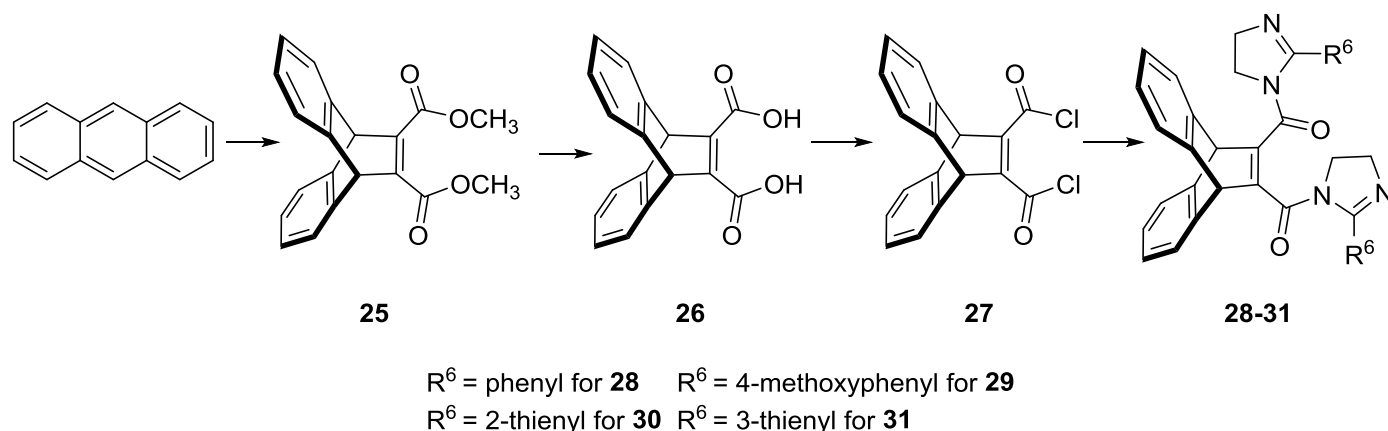
Scheme 3. Synthesis of compounds **15** and **16** from acyl chloride **14** having the norbornene skeleton.

Compound **18** was synthesized by reacting SOCl_2 with the diacid **17**, which was obtained from the cycloaddition reaction of anthracene and fumaric acid (Scheme 4). Similarly, the synthesis of compound **27** was performed by hydrolysis of the diester **25** obtained from the reaction of anthracene with dimethyl acetylenedicarboxylate (DMAD) followed by the reaction of the obtained diacid **26** with SOCl_2 (Scheme 5). Compounds **14**, **18** and **27** were synthesized in our previous work.²³ The various *N*-acyl C-2 substituted imidazoline derivatives **19-24** and **28-31** were prepared through an easy and simple nucleophilic substitution of the aromatic/heteroaromatic imidazolines with the two different acyl chlorides **18** and **27** having the dibenzobarrelene skeleton (Schemes 4 and 5).



Scheme 4. Synthesis of compounds **19-24** from acyl chloride **18** having the dibenzobarrelene skeleton.

In the FT-IR spectra, carbonyl stretching vibrations belonging to acyl chlorides **18** and **27** were observed at about 1789 and 1783 cm^{-1} , while in the spectra of compounds **19-24** and **28-31**, the signal belonging to amide carbonyl appeared at 1680 cm^{-1} . In the ^1H NMR spectra of the compounds **6-10**, the methylene protons of the imidazoline ring were observed as a singlet at 3.60 to 3.80 ppm, while the methylene protons belonging to the imidazoline ring of the compounds **19-24**, which has two protons equivalent to each other, appeared as four different triplets at 3.30-4.30 ppm. Unlike compounds **19-24**, in the ^1H NMR spectrum of compounds **28-31**, two of the four different methylene groups which has four protons equivalent to each other were observed at 3.30-3.60 ppm, while the other two methylene group protons appeared at lower fields (3.8 ppm, equivalent to four protons) as a singlet. In the APT ^{13}C NMR spectra of the compounds **19-24**, the methylene carbons belonging to the 2-imidazoline ring were seen at 48 and 54 ppm as two different methylene carbons, as expected. However, these methylene carbons of the compounds **28-31** appeared at about 45-47 ppm at higher fields than the other two methylene carbons. These findings were also supported by HETCOR NMR spectra.



Scheme 5. Synthesis of compounds **28-31** from acyl chloride **27** having the dibenzobarrelene skeleton.

Conclusions

In this work, C-2 substituted imidazoline derivatives **3** and **4** (Scheme 1) were synthesized from dinitrile compounds, having norbornene and dibenzobarrelene skeletons, in both conventional heating and microwave-assisted methods. These syntheses were carried out under neat reaction conditions unlike the methods in the literature. In addition, novel C-2 and N-substituted imidazolines **15**, **16**, **19-24**, **28-31** which contain aromatic, alicyclic, and heterocyclic structures (Schemes 3-5) were obtained in high yields starting from different diacyl dichlorides.

Experimental Section

General. Reagents were of commercial quality, and all solvents were used after purification. Infrared (IR) spectra were determined on a Perkin-Elmer Spectrum One Fourier transform-infrared (FT-IR) spectrometer. NMR spectra were recorded on Bruker 400 MHz spectrometer. Chemical shift δ is reported in parts per million relatives to CHCl_3 (^1H δ 7.27), CDCl_3 (^{13}C δ 77.0). X-ray analyses were carried out at Gebze Technical University.

The C, H, N and S elemental analyses were executed using Leco-932 CHNS/O Elemental Analyzer at the Faculty of Arts and Sciences, University of Bozok, Yozgat, Turkey. The microwave-assisted reactions were performed with single mode CEM Discover Labmate instrument (producing continuous irradiation at 2450 MHz), which has an in situ magnetic stirrer, irradiation monitored by PC computer, IR measurement, and continuous feedback temperature control. Thin layer chromatography was carried out on precoated 0.2 mm Merck Kieselgel 60 F254 plates. Melting points were determined with an Electrothermal IA 9100 apparatus.

The synthetic method and detailed spectral data of *trans*-bicyclo[2.2.1]hept-5-ene-2,3-dicarbonitrile (**1**), *trans*-9,10-dihydro-9,10-ethanoanthracene-11,12-dicarbonitrile (**2**), and *trans*-bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic acid (**13**) are given in the Supplementary Material section.

General synthesis of bis(4,5-dihydro-1H-imidazol-2-yl) derivatives **3** and **4**

Conventional synthesis (Method A). 6.94 mmol of compound **1** (or compound **2**) were dissolved in ethylenediamine (50 mL). The clear solution was heated with stirring in an argon atmosphere at 115 °C for 24 hours. The resulting yellow color solution was cooled to 25 °C and allowed to stand at this temperature for 24 hours. The occurred solid was filtered. The crude product was crystallized from benzene. Compound **3** was obtained as colorless powder (1.21 g, 5.25 mmol) in 76% yield. Compound **3** was washed with chloroform and recrystallized from ethanol. Compound **4** was obtained (1.69 g, 4.93 mmol) in 71% yield.

Microwave-assisted synthesis (Method B). 6.94 mmol of compound **1** (or compound **2**) were dissolved in ethylenediamine (40 mL). The solution was irradiated at atmospheric pressure using a mono-mode microwave device at 125 °C for 65 minutes with 250 W power. The resulting yellow color solution was cooled to room temperature and allowed to stand for 24 hours at this temperature. The occurred solid was filtered. The crude was crystallized from benzene. Compound **3** was obtained as colorless powder (1.41 g, 6.12 mmol) in 88% yield, and compound **4** was isolated as colorless powder (1.97 g, 5.76 mmol) in 83% yield.

***trans*-5,6-Bis(4,5-dihydro-1H-imidazol-2-yl)bicyclo[2.2.1]hept-2-ene (**3**).** Mp: 206-208 °C; IR (KBr) (ν_{\max} , cm^{-1}): 3162, 2973, 2928, 2862, 1653, 1604, 1498, 1470, 1288, 977; ^1H NMR (400 MHz, CDCl_3): δ_{H} = 6.37-6.35 (1H, dd, J 3.2, 1.7 Hz), 6.13-6.11 (1H, dd, J 3.0, 2.6 Hz), 4.14 (2H, br.), 3.64-3.62 (4H, dd, J 3.7, 1.7 Hz), 3.59 (4H, s), 3.19-3.16 (2H, dd, J 5.6, 3.3 Hz), 3.14 (1H, s), 2.58-2.56 (1H, d, J 4.6 Hz), 1.75 (1H, d, A part of AB system, J 8.6 Hz), 1.59 (1H, dd, B part of AB system, J 6.9, 1.7 Hz); ^{13}C NMR (100 MHz, CDCl_3): δ_{C} = 170.2, 169.4 (C=N), 138.3, 134.1 (C=C), 49.6, 49.4 ($\text{CH}_2\text{-N}$), 48.4 (CH_2), 46.3, 45.5 (CH-bridgehead), 44.2, 43.6 (CH); Anal. calc. for $\text{C}_{13}\text{H}_{18}\text{N}_4$ (230.31): C, 67.80; H, 7.88; N, 24.33; found C, 67.94; H, 8.06; N, 24.57%.

***trans*-11,12-Bis(4,5-dihydro-1H-imidazol-2-yl)-9,10-dihydro-9,10-ethanoanthracene (**4**).** Mp: 282-284 °C; IR (KBr) (ν_{\max} , cm^{-1}): 3137, 3074, 3022, 2936, 2865, 1612, 1596, 1496, 1472, 761; ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ_{H} = 7.30-7.27 (2H, m), 7.22-7.20 (2H, m), 7.08-7.04 (4H, m), 4.66 (2H, s), 3.32-3.22 (10H, m); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ_{C} = 168.4 (C=N), 143.9, 141.4 (Ar C $_{\text{ipso}}$), 126.0, 125.9, 125.2, 123.6 (CH $_{\text{Ar}}$), 46.94 (CH bridgehead), 42.70 (CH); Anal. calc. for $\text{C}_{22}\text{H}_{22}\text{N}_4$ (342.44): C, 77.16; H, 6.48; N, 16.36; found C, 77.33; H, 6.68; N, 16.53%.

***trans*-5,6-Bis[1-(2-chlorobenzoyl)-4,5-dihydro-1H-imidazol-2-yl]bicyclo[2.2.1]hept-2-ene (**5**).** To a solution of compound **3** (0.20 g, 0.87 mmol) in dry THF (50 mL), triethylamine (0.24 mL, 1.74 mmol) was added at 0 °C and the mixture was stirred for 10 minutes. 2-Chlorobenzoyl chloride (0.23 mL, 1.91 mmol) was added dropwise to the mixture and reflux maintained for 16 hours. The solvent was removed under reduced pressure. The residue was washed with 150 mL of water. After drying, the crude product was purified by column chromatography with a methanol / ethyl acetate 1:1 solvent mixture. The product **5** was obtained as colorless powder; yield: 0.38 g (0.75 mmol, 86%); mp: 201-203 °C; IR (KBr) (ν_{\max} , cm^{-1}): 3059, 3019, 2957, 2925, 2890, 2861, 1674, 1645, 1593, 1439, 1377, 1221, 767, 703; ^1H NMR (400 MHz, CDCl_3): δ_{H} 7.58-7.56 (2H, dd, J 6.2, 0.9 Hz), 7.41-7.31 (6H, m, Ar-H), 6.23-6.19 (2H, m), 3.67-3.39 (8H, m), 3.15 (1H, s), 3.06 (1H, s), 3.04-3.02 (1H, m),

2.37-2.35 (1H, dd, J 4.0, 1.5 Hz), 1.71 (1H, d, A part of AB system, J 8.6 Hz), 1.53 (1H, dd, B part of AB system, J 7.1, 1.6 Hz); ^{13}C NMR (100 MHz, CDCl_3): δ_{C} = 175.8, 174.6 (C=O), 168.1, 167.7 (C=N), 137.6, 135.2 (C=C), 134.8, 130.7 (Ar-C_{ipso}), 131.5, 131.3, 130.3, 130.2, 129.8, 129.6, 127.2, 127.09 (CH_{Ar}), 51.1, 49.1, 45.6, 44.4 (CH), 48.3 (CH₂), 40.7, 40.36, 40.24, 39.72 (N-CH₂). Anal. calc. for $\text{C}_{27}\text{H}_{24}\text{Cl}_2\text{N}_4\text{O}_2$ (507.41): C, 63.91; H, 4.77; N, 11.04; found C, 64.12; H, 4.94; N, 11.22%.

General synthesis of C-2 aromatic-heteroaromatic substituted imidazolines 6-10. Aromatic and heteroaromatic substituted imidazolines **6-10** were synthesized from the reaction of ethylenediamine and N-bromosuccinimide with the different aromatic and heteroaromatic aldehydes. The synthetic method and detailed spectra of compounds **6-10** are given in the Supplementary Material section.

4,5-Dihydro-2-(3-thienyl)-1H-imidazole (10). Colorless powder; yield: 94%; mp: 203-205 °C; IR (ATR) (ν_{max} , cm^{-1}): 3113, 3052, 2927, 2857, 1600, 1523, 1497, 1266, 1177, 981, 679; ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ_{H} = 7.92 (1H, s), 7.58-7.56 (1H, m), 7.45, 7.44 (1H, d, J 5.0 Hz), 6.86 (1H, br), 3.56 (4H, s); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ_{C} = 161.8 (C=N), 132.0 (Ar-C_{ipso}), 126.6, 126.3, 125.9 (CH_{Ar}), 48.8 (CH₂); Anal. calc. for $\text{C}_7\text{H}_8\text{N}_2\text{S}$ (152.22): C, 55.24; H, 5.30; N, 18.40; S, 21.07; found C, 55.46; H, 5.51; N, 18.63; S, 21.39%.

trans-Bicyclo[2.2.1]hept-5-ene-2,3-dicarbonyl dichloride (14). Compound **13** (5.49 mmol) was dissolved in dry benzene (25 mL) and DMF (0.1 mL) and then oxalyl chloride (1.02 mmol) rapidly added to the mixture. The mixture was refluxed for 4 hours until the HCl gas evolution had ceased. The gas evolved during the reaction was monitored by measuring the pH of the medium. After cooling the mixture to room temperature, the solvent was removed at reduced pressure. Anhydrous benzene (10 mL) was added to the crude product and stirred at room temperature for 10 minutes. The solvent was removed under reduced pressure. This process has been repeated three times. The light yellow liquid was isolated with 98% yield (1.18 g, 5.39 mmol). The product was used in the next step without purification.^{23,26}

General synthesis of trans-5,6-bis[[4,5-dihydro-1H-imidazol-1-yl]carbonyl]bicyclo[2.2.1]hept-2-enes 15 and 16. To a solution of compound **7** (3.28 mmol, or compound **10**), in dry THF (50 mL), triethylamine (3.66 mmol, 0.37 g, 0.51 mL) was added and stirred at room temperature for 30 minutes. Compound **14** (0.36 g, 1.64 mmol) was added dropwise to the mixture at 0 °C and stirred at room temperature for 24 hours. The white solid which occurred at the end of the process was filtered. The solvent was removed in vacuum from the filtrate. The oily product was dissolved in methanol (10 mL) and precipitated in ice water (200 mL). The crude product was filtered and dried in vacuo. The colorless solid was crystallized with ethyl acetate.

trans-5,6-Bis[[4,5-dihydro-2-(3-thienyl)-1H-imidazol-1-yl]carbonyl]bicyclo[2.2.1]hept-2-ene (15). Colorless powder; yield: 0.50 g (1.11 mmol, 68%); mp: 198-200 °C; IR (ATR) (ν_{max} , cm^{-1}): 3110, 3074, 2980, 2946, 2869, 1673, 1614, 1524, 1358, 1322, 1266, 1197, 1007, 710; ^1H NMR (400 MHz, CDCl_3): δ_{H} = 7.50-7.40 (3H, m), 7.35 (1H, d, J 2.8 Hz), 7.07 (2H, ddd, J 8.9, 5.0, 3.8 Hz), 6.36 (1H, s), 6.17 (1H, dd, J 5.5, 2.7 Hz), 4.26-4.09 (4H, m), 4.08-3.94 (4H, m), 3.81 (1H, t, J 3.9 Hz), 3.33 (1H, s), 3.20-3.07 (2H, m), 1.93 (1H, d, A part of AB system, J 8.7 Hz), 1.56 (1H, d, B part of AB system, J 7.7 Hz); ^{13}C NMR (100 MHz, CDCl_3): δ_{C} = 171.9, 171.2 (C=O), 155.1, 154.7 (C=N), 137.9, 134.2 (C=C), 133.2, 133.0 (thiophenyl-C_{ipso}), 130.7, 130.6 (thiophenyl-CH₅), 128.9 (thiophenyl-CH₄), 127.0 (thiophenyl-CH₃), 53.8, 53.5 (CH₂-imidazoline), 49.5, 48.67 (CH-bridgehead), 48.73, 48.6 (CH₂-N), 47.4 (bridge-CH₂), 48.5, 45.9 (O=C-CH); Anal. calc. for $\text{C}_{23}\text{H}_{22}\text{N}_4\text{O}_2\text{S}_2$ (450.58): C, 61.31; H, 4.92; N, 12.43; S, 14.23; found C, 61.59; H, 5.07; N, 12.65; S, 14.56%.

trans-5,6-Bis[[2-(3-chlorophenyl)-4,5-dihydro-1H-imidazol-1-yl]carbonyl]bicyclo[2.2.1]hept-2-ene (16). Colorless powder; yield: 0.37 g (1.70 mmol, 52%); mp: 110-112 °C; IR (ATR) (ν_{max} , cm^{-1}): 3069, 2975, 2938, 2872, 1672, 1595, 1569, 1358, 1277, 1261, 1145, 1000, 794, 753, 704; ^1H NMR (400 MHz, CDCl_3): δ_{H} = 7.49 (1H, s), 7.42 (3H, ddd, J 8.9, 6.1, 2.3 Hz), 7.40-7.29 (4H, m), 6.34 (1H, d, J 15.5 Hz), 6.12 (1H, s), 4.41-3.85 (8H, m),

3.68 (1H, t, J 3.8 Hz), 3.30 (1H, s), 3.06 (1H, s), 2.98 (1H, s), ' 1.83 (1H, d, A part of AB system, J 7.8 Hz), 1.54 (1H, d, B part of AB system, J 8.1 Hz). ^{13}C NMR (100 MHz, CDCl_3): δ_{C} = 171.6, 170.9 (C=O), 159.5 (C=N), 133.9, (C $_{\text{Ar-}}^{\text{ipso}}$), 133.9, 133.7 (C=C), 130.2, 130.1, 129.2, 128.2, 126.2, 126.0 (Ar $_{\text{CH}}$), 54.4, 54.0 (CH $_2$ -N), 49.0, 48.1 (CH $_{\text{bridgehead}}$), 48.5, 45.8 (O=C-CH), 48.0, 47.9 (CH $_2$ -N), 47.3, (CH $_2$ bridge); Anal. calc. for $\text{C}_{27}\text{H}_{24}\text{Cl}_2\text{N}_4\text{O}_2$ (507.41): C, 63.91; H, 4.77; N, 11.04; found C, 64.13; H, 4.83; N, 11.27%.

General synthesis of N-acyl substituted imidazolines with dibenzobarrelene skeleton 19-24. To a solution of the requisite imidazolines (3.72 mmol, compounds **6**, **7**, **9-12**) in dry THF (50 mL), triethylamine (0.37 g, 3.66 mmol, 0.51 mL) was added, and then stirred at room temperature for 30 minutes. Compound **18** (0.57 g, 1.72 mmol) was added to this mixture at 0 °C and stirred at room temperature for 24 hours. The formed colorless solid was filtered. The solvent was removed in vacuo. The oily product was dissolved in methanol (10 mL) and precipitated in ice-water (200 mL). The resulting colorless solid was filtered and dried at vacuum. The crude products were crystallized from THF, except for compound **23**, crystallized from methanol.

***trans*-11,12-Bis[(4,5-dihydro-2-phenyl-1H-imidazol-1-yl)carbonyl]-9,10-dihydro-9,10-ethanoanthracene (19).**

Colorless powder, yield: 0.85 g (1.54 mmol, 90%); mp: 250-251 °C; IR (ATR) (ν_{max} , cm^{-1}): 3059, 3026, 2948, 2866, 1685, 1625, 1364, 1273, 1139, 1023, 767, 691; ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ_{H} = 7.47 -7.40 (4H, m), 7.38 (2H, s), 7.36-7.31 (5H, m), 7.28-7.22 (4H, m), 7.19 -7.15 (3H, m), 4.85 (2H, s), 4.32 (2H, dd, J 19.3, 9.7 Hz), 4.11- 4.04 (2H, m), 4.03 -3.96 (2H, m), 3.93- 3.81 (2H, m), 3.49 (2H, s); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ_{C} = 170.2 (C=O), 160.1 (C=N), 143.2, 140.6 (dibenzobarrelene-C $_{\text{ipso}}$), 132.6 (C $_{\text{Ar-}}^{\text{ipso}}$), 128.5, 127.8 (dibenzobarrelene-CH), 129.9, 128.8, 126.6, 126.2, 125.5, 123.8 (CH $_{\text{phenyl}}$), 54.5, 48.1 (CH $_2$ -N), 48.5 (CH $_{\text{bridgehead}}$), 46.1 (CH); Anal. calc. for $\text{C}_{36}\text{H}_{30}\text{N}_4\text{O}_2$ (550.65): C, 78.52; H, 5.49; N, 10.17; found C, 78.73; H, 5.66; N, 10.39%.

***trans*-11,12-Bis[[2-(3-chlorophenyl)-4,5-dihydro-1H-imidazol-1-yl]carbonyl]-9,10-dihydro-9,10-ethanoanthracene (20).**

Colorless powder; yield: 0.86 g (1.40 mmol, 75%); mp: 241-243 °C; IR (ATR) (ν_{max} , cm^{-1}): 3073, 3026, 2964, 2867, 1730, 1680, 1629, 1459, 1355, 1261, 1143, 1000, 791, 762, 700, 560; ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ_{H} = 7.49 (2H, d, J 5.9 Hz), 7.45- 7.39 (4H, m), 7.31 (4H, d, J 9.5 Hz), 7.15 (6H, dd, J 12.5, 4.9 Hz), 4.89 (2H, s), 4.35 (2H, d, J 9.3 Hz), 4.14- 3.97 (4H, m), 3.97- 3.84 (2H, m), 3.55 (1H, s), 3.46 (1H, s); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ_{C} = 170.2 (C=O), 158.9 (C=N), 143.1, 140.5 (dibenzobarrelene-C $_{\text{ipso}}$), 134.8, 132.6 (C $_{\text{Ar-}}^{\text{ipso}}$), 130.0, 129.8, 128.2, 126.9, 126.7, 126.6, 125.4, 125.2, 124.0, 123.7 (Ar-CH), 54.7, 47.9 (CH $_2$ -N), 52.5, 48.3, 46.0, 45.9 (CH); Anal. calc. for $\text{C}_{36}\text{H}_{28}\text{Cl}_2\text{N}_4\text{O}_2$ (619.54): C, 69.79; H, 4.56; N, 9.04; found C, 69.81; H, 4.63; N, 9.17%.

***trans*-11,12-Bis[[4,5-dihydro-2-(2-thienyl)-1H-imidazol-1-yl]carbonyl]-9,10-dihydro-9,10-ethanoanthracene (21).**

Colorless powder; yield: 0.90 g (1.60 mmol, 86%); mp: 256-258 °C; IR (ATR) (ν_{max} , cm^{-1}): 3069, 3034, 2956, 2871, 1689, 1671, 1609, 1357, 1266, 1080, 681; ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ_{H} = 7.60 (2H, dd, J 4.5, 1.7 Hz), 7.47 (2H, d, J 6.7 Hz), 7.43 (1H, s), 7.33 (1H, s), 7.23- 7.12 (4H, m), 7.01-6.90 (4H, m), 4.85 (2H, s), 4.34 (2H, q, J 9.8 Hz), 4.15 (2H, td, J 9.5, 4.7 Hz), 3.98 (2H, ddd, J 14.7, 9.8, 4.7 Hz), 3.84 (2H, dt, J 15.5, 9.6 Hz), 3.64 (2H, s); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ_{C} = 170.6 (C=O), 154.6 (C=N), 143.1, 140.6 (dibenzobarrelene-C $_{\text{ipso}}$), 133.7 (C $_{\text{thiophene-}}^{\text{ipso}}$), 128.8, 127.2 (dibenzobarrelene-CH), 131.1, 129.4, 126.7, 126.3, 125.4, 123.9 (CH $_{\text{thiophene}}$), 54.0, 48.7 (CH $_2$ -N), 49.0 (CH $_{\text{bridgehead}}$), 46.3 (CH); Anal. calc. for: $\text{C}_{32}\text{H}_{26}\text{N}_4\text{O}_2\text{S}_2$ (562.70): C, 68.30; H, 4.66; N, 9.96; S, 11.40; found C, 68.53; H, 4.82; N, 10.11; S, 11.42%.

***trans*-11,12-Bis[[4,5-dihydro-2-(3-thienyl)-1H-imidazol-1-yl]carbonyl]-9,10-dihydro-9,10-ethanoanthracene (22).**

Colorless powder; yield: 0.96 g (1.71 mmol, 92%); mp: 243-245 °C; IR (ATR) (ν_{max} , cm^{-1}): 3105, 3026, 2949, 2862, 1688, 1679, 1620, 1457, 1365, 1259, 1208, 996, 767, 691, 564; ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ_{H} = 7.57 (2H, s), 7.47- 7.41 (2H, m), 7.38 (4H, dd, J 5.1, 2.8 Hz), 7.19- 7.12 (4H, m), 7.02 (2H, d, J 4.9 Hz), 4.80 (2H, s), 4.29 (2H, dd, J 19.2, 9.6 Hz), 4.06 (2H, ddd, J 15.1, 10.2, 5.3 Hz), 3.97 (2H, td, J 10.2, 5.0 Hz), 3.91-3.81 (2H, m), 3.55 (2H, s); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ_{C} = 170.2 (C=O), 155.5 (C=N), 143.1, 140.6 (dibenzobarrelene-

C_{ipso}), 133.3 (C_{thiophene-ipso}), 127.9, 126.6 (dibenzobarrelene-CH), 128.8, 128.4, 126.3, 125.3, 125.1, 123.9 (CH_{thiophene}), 53.9, 48.1 (CH₂-N), 48.7 (CH-bridgehead), 46.2 (CH); Anal. calc. for C₃₂H₂₆N₄O₂S₂ (562.70): C, 68.30; H, 4.66; N, 9.96; S, 11.40; found C, 68.52; H, 4.79; N, 10.12; S, 11.58%.

trans-11,12-Bis[(4,5-dihydro-2-sulfanyl-1H-imidazol-1-yl)carbonyl]-9,10-dihydro-9,10-ethanoanthracene (23). Colorless powder; yield: 0.52 g (1.13 mmol, 61%); mp: 249-250 °C; IR (ATR) (ν_{\max} , cm⁻¹): 3209, 3030, 2968, 2894, 1678, 1532, 1468, 1349, 1234, 1208, 1055, 1011, 765, 755, 608; ¹H NMR (400 MHz, DMSO-*d*₆): δ_{H} = 9.81 (2H, s), 7.32 (2H, d, *J* 7.1 Hz), 7.23 (2H, d, *J* 7.0 Hz), 7.14- 7.02 (4H, m), 5.72 (2H, s), 4.90 (2H, s), 3.94 (2H, td, *J* 10.9, 8.4 Hz), 3.80 (2H, td, *J* 10.5, 6.1 Hz), 3.58- 3.43 (4H, m); ¹³C NMR (100 MHz, DMSO-*d*₆): δ_{C} = 179.5 (C=O), 173.0 (C=N), 143.7, 140.6 (dibenzobarrelene-C_{ipso}), 126.2, 126.0, 124.9, 124.0 (dibenzobarrelene-CH_{Ar}), 48.2 (CH-bridgehead), 48.0 (CH₂-N), 46.8 (dibenzobarrelene-CH); Anal. calc. for C₂₄H₂₂N₄O₂S₂ (462.59): C, 62.31; H, 4.79; N, 12.11; S, 13.86; found C, 62.56; H, 4.91; N, 12.43; S, 14.06%.

trans-11,12-Bis[(4,5-dihydro-2-(methylsulfanyl)-1H-imidazol-1-yl)carbonyl]-9,10-dihydro-9,10-ethanoanthracene (24). Colorless powder; yield: 0.57 g (1.15 mmol, 62%); mp: 260-262 °C; IR (ATR) (ν_{\max} , cm⁻¹): 3072, 3037, 2958, 2925, 2885, 1666, 1588, 1458, 1411, 1371, 1190, 1004, 760, 746, 556; ¹H NMR (400 MHz, CDCl₃): δ_{H} = 7.34 (2H, d, *J* 6.8 Hz), 7.29- 7.24 (2H, m), 7.18 (4H, m, *J* 7.6, 1.5 Hz), 4.48 (2H, s), 4.30- 4.19 (2H, m), 4.12- 3.96 (6H, m), 3.56 (2H, s), 2.40 (6H, s); ¹³C NMR (100 MHz, CDCl₃): δ_{C} = 169.2 (C=O), 142.2, 138.6 (dibenzobarrelene-C_{ipso}), 126.8, 126.7, 125.3, 122.7 (dibenzobarrelene-CH), 54.2, 47.8 (CH₂-N), 48.4 (CH-bridgehead), 47.1 (CH), 15.3 (SCH₃); Anal. calc. for C₂₆H₂₆N₄O₂S₂ (490.64): C, 63.65; H, 5.34; N, 11.42; S, 13.07; found C, 63.71; H, 5.53; N, 11.64; S, 13.24%.

General synthesis of 11,12-bis[(4,5-dihydro-1H-imidazol-1-yl)carbonyl]-9,10-dihydro-9,10-ethenoanthracenes 28-31. To a solution of the requisite imidazoline (3.42 mmol, compounds **6**, **8-10**) in dry THF (50 mL), 3.76 mmol of triethylamine (0.38 g, 0.52 mL) was added and stirred at room temperature for 30 minutes. 1.71 mmol of compound **27** (0.56 g) was added to the mixture at 0 °C and then stirred at room temperature for 24 hours. The formed colorless solid was filtered. The solvent was removed in vacuum and the remaining solid was combined with the initially filtered solid and washed with water (100 mL). It was dried in vacuum. The crude products were crystallized with THF, and recrystallized from methanol / ethyl acetate 1:1 mixture.

11,12-Bis[(4,5-dihydro-2-phenyl-1H-imidazol-1-yl)carbonyl]-9,10-dihydro-9,10-ethenoanthracene (28). Colorless powder; yield: 0.84 g (1.54 mmol, 90%); mp: 238 °C (decomp.); IR (ATR) (ν_{\max} , cm⁻¹): 3090, 3061, 2955, 2869, 1680, 1621, 1594, 1559, 1381, 1354, 695; ¹H NMR (400 MHz, DMSO-*d*₆): δ_{H} = 8.01-7.98 (2H, m, *J* 8, 1.6, 0.8 Hz), 7.64-7.58 (3H, m, *J* 7.6, 7.2, 1.2 Hz), 7.54-7.50 (2H, m, *J* 7.2, 1.2 Hz), 7.42-7.36 (4H, m, *J* 4.8, 3.6 Hz), 7.32-7.30 (1H, d, *J* 7.6 Hz), 7.24-7.20 (2H, t, *J* 7.6 Hz), 7.00-6.97 (4H, m), 5.64 (1H, s), 5.38 (1H, s), 3.86 (4H, s), 3.69-3.65 (2H, t, *J* 8.8 Hz), 3.37-3.33 (2H, t, *J* 8.8 Hz); ¹³C NMR (100 MHz, DMSO-*d*₆): δ_{C} = 167.2, 167.0 (C=O), 164.9 (C=N), 159.3 (C=C), 146.1, 145.6 (dibenzobarrelene-C_{Ar-ipso}), 132.4 (C_{Ar-ipso}), 133.6, 129.9, 129.4, 128.8, 128.7, 127.6 (CH_{Ar}), 125.1, 125.0, 123.9, 123.7 (dibenzobarrelene-CH_{Ar}), 52.9, 52.0 (dibenzobarrelene-CH-bridgehead), 53.7, 48.3, 46.3 (CH₂-N); Anal. calc. for C₃₆H₂₈N₄O₂ (548.63): C, 78.81; H, 5.14; N, 10.21; found C, 78.06; H, 5.22; N, 10.44%.

11,12-Bis[(4,5-dihydro-2-(4-methoxyphenyl)-1H-imidazol-1-yl)carbonyl]-9,10-dihydro-9,10-ethenoanthracene (29). Colorless powder; yield: 0.81 g (1.33 mmol, 78%); mp: 238-240 °C; IR (ATR) (ν_{\max} , cm⁻¹): 3067, 2961, 2921, 2852, 1657, 1605, 1511, 1458, 1353, 1252, 1173, 1013, 837, 608; ¹H NMR (400 MHz, DMSO-*d*₆): δ_{H} = 7.50 (4H, d, *J* 8.8 Hz), 7.36 (4H, dd, *J* 5.3, 3.2 Hz), 7.06 (4H, dd, *J* 5.3, 3.2 Hz), 6.76 (4H, d, *J* 8.8 Hz), 5.34 (s, 2H), 3.89-3.83 (4H, t, *J* 8.3 Hz), 3.79 (s, 6H), 3.65 (4H, t, *J* 8.3 Hz); ¹³C NMR (100 MHz, DMSO-*d*₆): δ_{C} = 165.6 (C=O), 161.4 (CH₃O-C_{Ar-ipso}), 159.4 (C=N), 147.6 (C=C), 143.6 (dibenzobarrelene-C_{Ar-ipso}), 129.9, 125.6 (dibenzobarrelene-CH_{Ar}), 123.7 (CH_{Ar}), 123.0 (C_{Ar-ipso}), 113.4 (CH_{Ar}), 55.2 (dibenzobarrelene-CH-bridgehead), 54.0,

49.1 (CH₂-imidazoline); 53.2 (OCH₃), Anal. calc. for C₃₈H₃₂N₄O₄ (608.69): C, 74.98; H, 5.30; N, 9.20; found C, 75.12; H, 5.59; N, 9.46%.

11,12-Bis[[4,5-dihydro-2-(2-thienyl)-1H-imidazol-1-yl]carbonyl]-9,10-dihydro-9,10-ethenoanthracene (30). Colorless powder; yield: 0.82 g (1.47 mmol, 86%); mp: 234-236 °C; IR (ATR) (ν_{\max} , cm⁻¹): 3072, 3058, 2973, 2901, 2873, 1677, 1662, 1620, 1558, 1378, 1357, 1290, 1005, 715, 613; ¹H NMR (400 MHz, DMSO-*d*₆): δ_{H} = 7.83-7.81 (2H, d, *J* 10 Hz), 7.57- 7.47 (2H, m), 7.47- 7.35 (4H, m), 7.17 (1H, t, *J* 4.1 Hz), 7.07-6.96 (4H, m), 6.85 (1H, s), 5.64 (1H, s), 5.49 (1H, s), 3.73 (4H, s), 3.70- 3.63 (2H, t, *J* 8.0 Hz), 3.41 (2H, t, *J* 8.0 Hz); ¹³C NMR (100 MHz, DMSO-*d*₆): δ_{C} = 167.0, 166.2 (C=O), 159.4 (C=N), 153.6 (C=C), 145.7, 145.2 (dibenzobarrelene-C_{Ar}-ipso), 133.0 (C_{Ar}-ipso), 131.9, 129.5, 128.6 (CH_{Ar}), 127.3, 125.3, 125.2, 123.9 (dibenzobarrelene-CH_{Ar}), 53.3, 53.1 (dibenzobarrelene-CH_{bridgehead}), 51.4, 48.8, 47.7 (CH₂-N). Anal. calc. for C₃₂H₂₄N₄O₂S₂ (560.69): C, 68.55; H, 4.31; N, 9.99; S, 11.44; found C, 68.73; H, 4.53; N, 10.15; S, 11.67%.

11,12-Bis[[4,5-dihydro-2-(3-thienyl)-1H-imidazol-1-yl]carbonyl]-9,10-dihydro-9,10-ethenoanthracene (31). Colorless powder; yield: 0.88 g (1.57 mmol, 92%); mp: 138-139 °C; IR (ATR) (ν_{\max} , cm⁻¹): 3096, 2985, 2977, 2925, 2903, 2857, 1705, 1619, 1602, 1576, 1376, 1286, 669, 624; ¹H NMR (400 MHz, DMSO-*d*₆): δ_{H} = 8.71 (1H, d, *J* 1.5 Hz), 7.85 (1H, d, *J* 1.7 Hz), 7.80- 7.67 (2H, m), 7.45- 7.28 (6H, m), 6.99 (4H, dd, *J* 5.0, 3.3 Hz), 5.66 (1H, s), 5.39 (1H, s), 3.83 (4H, s), 3.63 (2H, t, *J* 8.4 Hz), 3.33 (2H, t, *J* 8.5 Hz); ¹³C NMR (100 MHz, DMSO-*d*₆): δ_{C} = 167.7, 167.5 (C=O), 159.9 (C=N), 154.9 (C=C), 146.3, 145.7 (dibenzobarrelene-C_{Ar}-ipso), 133.1 (C_{Ar}-ipso), 129.1, 128.8, 128.4, 127.1, (CH_{Ar}), 125.1, 124.9, 123.8, 123.7 (dibenzobarrelene-CH_{Ar}), 53.3, 52.9 (dibenzobarrelene-CH_{bridgehead}), 52.1, 48.2, 45.5, 45.4 (CH₂-N). Anal. calc. for C₃₂H₂₄N₄O₂S₂ (560.69): C, 68.55; H, 4.31; N, 9.99; S, 11.44; found C, 68.73; H, 4.43; N, 10.18; S, 11.62%.

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Supplementary Material

The synthesis of compounds **1**, **2**, **6-10**, **13** and the copies of IR, ¹H NMR, ¹³C NMR spectra of compounds **3-10**, **15**, **16**, **19-24**, **28-31** presented in the Supplementary Material.

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