



## 2-AMİNOBENZİMİDAZOLÜN METAL KOMPLEKSLERİ ve BİYOLOJİK ÖZELLİKLERİ

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### ÖZ

2-Aminobenzimidazol ve türevlerin, antibakteriyel, antikanser, antiviral, antiinflamatuvar, antiproliferatif, antifungal, antelmintik ve antihistaminik özelliklere sahip olduğu çalışmalar literatürde bulunmaktadır. 2-Aminobenzimidazol ve türevleri yapısında üç adet azot atomlarından dolayı metal iyonlarına bir ve iki dişli olarak bağlanmaktadır. 2-Aminobenzimidazol ve türevlerinin basit metal kompleksleri sentezlenmiştir. Ayrıca trimesik asit, tereftalik asit, isoftalik asit, glutarik asit, 2,6-piridindikarboksilik asit, 4-hidroksi-2,6-piridindikarboksilik asit, krotonik asit, okzalik asit, pirazin-2-karboksilik asit, p-simen, sakarin, disiyanamit, *N*-salisiliden-2-hidroksianilin, asetoasetanilit, o-asetoasetotoluidit, o-asetoasetanisidit, dehidroasetik asit, 4,4'-bipiridin, bis-(salisilaldehit)fenilendiimin, *N*-(dehidroasetik asit)-tiyosemikarbazit, *N*-(dehidroasetik asit)-4-metil-3-tiyosemikarbazit, 4,5-dimetil-*N,N*-bis(piridin-2-yil-metilen)benzen-1,2-diimin, *N*-(dehidroasetik asit)-4-fenilsemikarbazit ve *N*-(dehidroasetik asit)-4-fenil-3-tiyosemikarbazit ile karışık ligandlı geçiş metal kompleksleri sentezlenmiş ve bazılarının biyolojik aktiviteleri incelenmiştir. 2-Aminobenzimidazol ve türevlerinden elde edilen proton transfer tuzu ve metal komplekslerinin de benzer biyolojik özellik gösterebileceği aşıkardır.

**Anahtar kelimeler:** 2-Aminobenzimidazol, Metal kompleksi, Biyolojik aktivite.

### METAL COMPLEXES and BIOLOGICAL PROPERTIES of 2-AMİNOBENZİMİDAZOLE

#### ABSTRACT

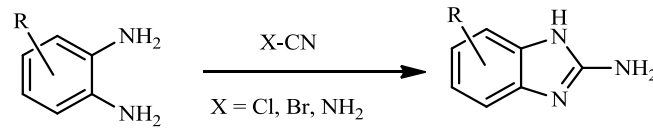
There are studies in the literature that 2-aminobenzimidazole and its derivatives have antibacterial, anticancer, antiviral, anti-inflammatory, antiproliferative, antifungal, anthelmintic and antihistamine properties. 2-Aminobenzimidazole and its derivatives are bonded to metal ions with one and two teeth due to three nitrogen atoms in their structure. Simple metal complexes of 2-aminobenzimidazole and its derivatives were synthesized. In addition, mixed ligand metal complexes of between 2-aminobenzimidazole and other ligands {trimesic acid, terephthalic acid, isophthalic acid, glutaric acid, 2,6-pyridinedicarboxylic acid, 4-hydroxy-2,6-pyridinedicarboxylic acid, crotonic acid, oxalic acid,

pyrazine-2-carboxylic acid, p-cymene, saccharin, dicyanamide, *N*-salicylidene-2-hydroxyaniline, acetoacetanilide, *o*-acetoacetoluidide, *o*-acetoacetanisidide, dehydroacetic acid, *N*-(dehydroacetic acid)-4-methyl-3-thiosemicarbazide, 4,4'-bipyridine, bis-(salicylaldehyde)phenylenimine, *N*-(dehydroacetic acid)-thiosemicarbazide, 4,5-dimethyl-*N,N*-bis(pyridine-2-yl-methylene)benzene-1,2-diimine, *N*-(dehydroacetic acid)-4-phenylsemicarbazide and *N*-(dehydroacetic acid)-4-phenyl-3-thiosemicarbazide} were synthesized and the biological activities of some of them were investigated. It is obvious that proton transfer salt and metal complexes obtained from 2-aminobenzimidazole and its derivatives can also exhibit similar biological properties.

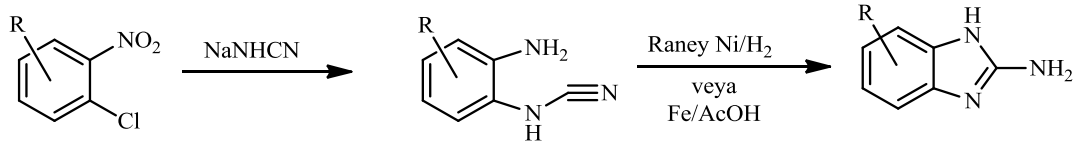
**Keywords:** 2-Aminobenzimidazole, Metal complex, Biological activity.

## 1. GİRİŞ

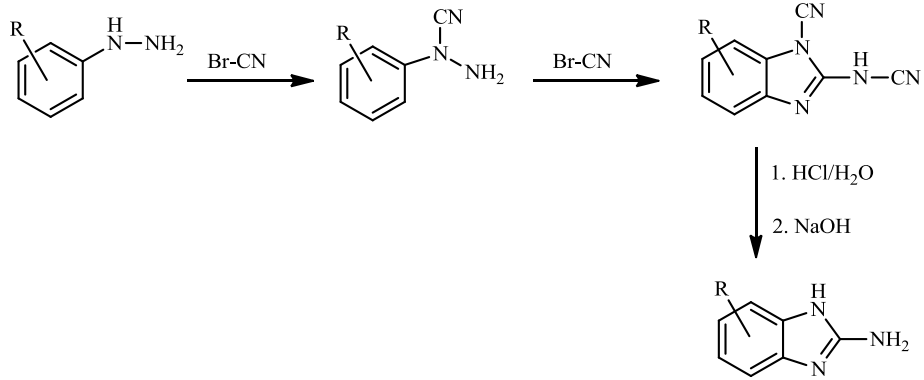
1*H*-Benzimidazol, imidazolün 4- ve 5-pozisyonlarında kaynaşmış bir benzen halkasına sahip düzlemsel ve bisiklik bileşiklerdir. 2-Aminobenzimidazol türevleri, 1*H*-benzimidazol halkasının 2 pozisyonuna bağlanmış -NH<sub>2</sub> türevleridir. 2-Aminobenzimidazol ve türevleri, antibakteriyel, antikanser, antiviral, antiinflamatuar, antiproliferatif, antifungal, antelmintik ve antihistaminik özelliklere sahip geniş bir ilaç yelpazesinden oluşmakta ve bu özellikleri inceleyen çalışmalar literatürde bulunmaktadır [1-6]. 2-aminobenzimidazol ve türevleri *o*-fenilendimin, *o*-nitroklorobenzen, fenilhidrazin ve tiyörelerin halkalandırılması sonucu sentezlenmektedir (Şekil 1-4) [7].



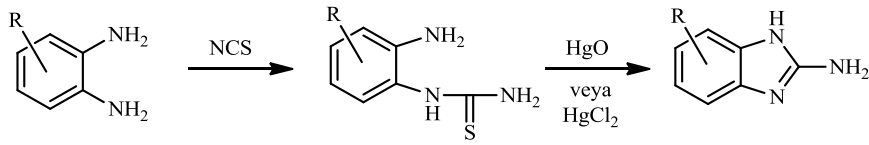
**Şekil 1.** *o*-Fenilendimin türevlerinden 2-aminobenzimidazol türevleri sentezi.



**Şekil 2.** *o*-Nitroklorobenzen türevlerinden 2-aminobenzimidazol türevleri sentezi.

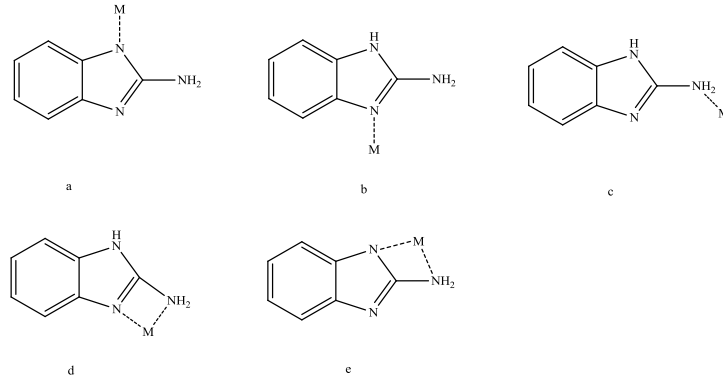


**Şekil 3.** Fenilhidrazin türevlerinden 2-aminobenzimidazol türevleri sentezi.



**Şekil 4.** Tiyüre türevlerinden 2-aminobenzimidazol türevleri sentezi.

2-Aminobenzimidazol ve türevleri yapısında üç adet azot atomlarından dolayı metal iyonlarına bir ve iki dişli olarak bağlanabilmektedir (Şekil 5). 2-Aminobenzimidazol ve türevlerinin gösterdiği biyolojik aktiviteleri metal komplekslerinde göstereceği aşikardır. Literatürde antimikrobiyal [8-13], anti-proliferatif ve antikanser [14] aktiviteleri incelenmiştir.



**Şekil 5.** 2-Aminobenzotiyazolün metal iyonlarına bağlanma yerleri.

## 2. 2-AMINO BENZİMİDAZOLÜN METAL KOMPLEKSLERİ

Literatürde yapılan 2-aminobenzimidazolün, Campbell ve ark. [15], Co(II) ve Ni(II) { [Et<sub>4</sub>N]<sup>+</sup>[M(abi)X<sub>3</sub>]<sup>-</sup>, M(abi)<sub>2</sub>X<sub>2</sub> (M = Co, Ni; X = Cl, Br, I), Co(abi)<sub>2</sub>I<sub>2</sub>.2Me<sub>2</sub>CO, Co(abi)<sub>2</sub>SO<sub>4</sub>.Me<sub>2</sub>CO,

Co(abi)<sub>2</sub>Cl<sub>2</sub>.2H<sub>2</sub>O, Ni(abi)<sub>2</sub>I<sub>2</sub>.3H<sub>2</sub>O ve Co(abi)<sub>2</sub>, Ihara ve Tsuchiya [16], Ni(II) {[Ni(abi)<sub>4</sub>]X<sub>2</sub>.nH<sub>2</sub>O, n = 0, X = I, ClO<sub>4</sub>, 0,5SO<sub>4</sub>; n = 1, X = NO<sub>3</sub>; n = 3, X = Cl, Br}, Shukla ve ark. [17], Ru(II) ve Ru(III) {[cis-RuCl<sub>2</sub>(SO)<sub>3</sub>(abi)], [trans-RuCl<sub>2</sub>(SO)<sub>3</sub>(abi)] ve [trans-RuCl<sub>4</sub>(SO)(abi)]<sup>-</sup>, SO = DMSO/tetrametilenesulfoksit}, Matyakubov ve ark. [18], Co, Sn ve Cd tuzlarını, Podunavac-Kuzmanovic ve ark. [9], Cu(II), Ni(II), Zn(II), Co(II) ve Ag(I) {M(abi)<sub>2</sub>(NO<sub>3</sub>)<sub>2</sub>.nH<sub>2</sub>O [M = Co (n = 6), Ni (n = 1), Zn (n = 2), Cu and Ag (n = 0)], Tamayo ve ark. [19], Sn(IV), Ti(IV) ve V(IV) {[MCl<sub>4</sub>(Habi)] (M = Sn or Ti), [TiCl<sub>4</sub>(Habi)<sub>2</sub>], [VCl<sub>3</sub>(abi)]}, Ardizzoia ve ark. [20], Cu(I), Ag(I) ve Au(I) {M(abi)}, Campbell ve ark. [21], Cu(II) {Cu(abi-H).H<sub>2</sub>O, Cu(abi)(CH<sub>3</sub>CO<sub>2</sub>)<sub>2</sub>, Cu(abi)<sub>2</sub>Cl<sub>2</sub>.HCl ve Cu(abi)<sub>3</sub>Cl<sub>2</sub>.3HCl}, Zhao ve ark. [22], Cd(II) {[Cd(abi)<sub>2</sub>(CH<sub>3</sub>COO)<sub>2</sub>].3H<sub>2</sub>O}, Garnovskii ve ark. [23], Cu(II) {Cu(Ac)<sub>2</sub>(abi)<sub>1 veya 2</sub>}, Esparza-Ruiz ve ark. [24], Co(II) {[Co(abi)<sub>2</sub>(CH<sub>3</sub>COO)<sub>2</sub>] ve Ni(II) {[Ni(abi)<sub>2</sub>(CH<sub>3</sub>COO)<sub>2</sub>]}, Kessentini ve ark. [25], Cd(II) {(abi)<sub>2</sub>CdI<sub>4</sub>}, Zhao ve ark. [26], Co(II) {[Co(abz)<sub>2</sub>(SCN)<sub>2</sub>]}, Hosny ve ark. [27], dimetilkalay(IV) {Sn(CH<sub>3</sub>)<sub>2</sub>(abi), Sn(CH<sub>3</sub>)<sub>2</sub>(abi)}, Mendiola ve ark. [28], Fe(II) {[Fe(abi)Cl<sub>2</sub>]}, Podunavac-Kuzmanovic ve ark. [10], Co(II) {[Co(abi)<sub>2</sub>Cl<sub>2</sub>]}, Lopez-Sandoval ve ark. [11], Co(II) {[Co(abi)<sub>2</sub>Cl<sub>2</sub>], [Co(abi)<sub>2</sub>Br<sub>2</sub>], [Co(abi)<sub>2</sub>(NO<sub>3</sub>)<sub>2</sub>].0,5H<sub>2</sub>O} ve Zn(II) {[Zn(abi)<sub>2</sub>Cl<sub>2</sub>].0,5H<sub>2</sub>O ve [Zn(abi)<sub>2</sub>Br<sub>2</sub>].0,5H<sub>2</sub>O}, Marcos ve ark. [29], Fe(III) {[Fe(abi)Cl<sub>3</sub>]}, Ramadan ve ark. [30], Pd(II) {[Pd(abi)Cl<sub>2</sub>]<sub>2</sub>.H<sub>2</sub>O} ve Maurya ve ark. [32], 2-aminobenzimidazol ve 2-amino-5,6-dimetilbenzimidazol'ün Cr(I) {[Cr(NO)(CN)<sub>2</sub>(abi)<sub>2</sub>(H<sub>2</sub>O)]}, Devi ve ark., 2-amino-5-benzoilbenzimidazol'ün (5bxabi) Ni(II), Zn(II) ve Cd(II) {[M(5bxabi)<sub>2</sub>X<sub>2</sub>] X = Cl, Br, I, NCS, NO<sub>3</sub>, CH<sub>3</sub>COO, ClO<sub>4</sub> or 1/2 SO<sub>4</sub><sup>2-</sup>} [32], Mn(II) ve Co(II) {[M(ABBI)<sub>2</sub>X<sub>2</sub>], X = Cl, Br, I, NO<sub>3</sub>, CH<sub>3</sub>COO, HCOO, ClO<sub>4</sub> and SO<sub>4</sub>} [14] metal komplekslerinin yapılarını çeşitli analiz yöntemleri (tek kristal X-ışını, elemental analiz, ICP-OES, AAS, NMR, IR, termal analiz, manyetik duyarlılık gibi) ile aydınlatılmış/önerilmiştir.

### 3. KARIŞIK LIGANDLI METAL KOMPLEKSLERİ

Ayrıca literatürde 2-aminobenzimidazol ile çeşitli organik asit veya bazlar ile yapılan çalışmalar vardır. Wang ve ark. [33], trimesik asit'in (H<sub>3</sub>tma), tereftalik asit'in (H<sub>2</sub>tp), isoftalik asit'in (H<sub>2</sub>iph), glutarik asit'in (H<sub>2</sub>ga) Cd(II) {[ (Habi)<sub>2</sub>[Cd<sub>2</sub>(tma)<sub>2</sub>(abi)<sub>4</sub>].5,5(H<sub>2</sub>O)]<sub>n</sub>, {[Cd(tp)(abi)<sub>2</sub>].(DMF)]<sub>n</sub>, {(Habi)<sub>2</sub>[Cd(iph)<sub>2</sub>]}<sub>n</sub>, {(Habi)<sub>2</sub>[Cd(ga)<sub>2</sub>]}<sub>n</sub>, Aliabadi ve ark. [34], 2,6-piridindikarboksilik asit'in ve 4-hidroksipiridin-2,6-dikarboksilik asit'in Ga(III), Al-Jibori ve ark. [35], sakarin'in Pd(II) {trans-[Pd(sac)<sub>2</sub>(abi)<sub>2</sub>]}, Das ve ark. [36], disiyanamit'in (dca) Co(II) {[Co(dca)<sub>2</sub>(abi)<sub>2</sub>]}<sub>n</sub>, Ni(II) {[Ni(dca)<sub>2</sub>(abi)<sub>2</sub>]}<sub>n</sub> ve Cd(II) {[Cd(dca)<sub>2</sub>(abi)<sub>2</sub>]}<sub>n</sub>, Ding ve ark. [37], Cd(II) {[Cd(μ<sub>1,5</sub>-dca)(μ<sub>1,3,5</sub>-dca)(abi)]<sub>n</sub>, Ali ve ark. [38], N-salisiliden-2-hidroksianilin'in (H<sub>2</sub>sha) Ru(II) {[Ru(CO)<sub>2</sub>(sha)(L)]}, Atria ve ark. [39], krotonik asit'in (Hcra) Ho(III) {(Habi)<sub>2</sub>[Ho<sub>2</sub>(cra)<sub>8</sub>]}, Mouchaham ve ark. [40], okzalik asit'in Zr(IV) {(Habi)<sub>4</sub>[Zr(C<sub>2</sub>O<sub>4</sub>)<sub>4</sub>]} ve Sun ve ark. [41], Fe(III) {(Habi)<sub>4</sub>[Fe(C<sub>2</sub>O<sub>4</sub>)<sub>1,5</sub>Cl<sub>2</sub>]}<sub>2</sub>, Malik ve Mir [42], asetoasetanilit'in, o-asetoasetotoluidit'in, o-asetoasetanisidit'in (HL) ve dehidroasetik asit'in (ahaH) VO<sub>2</sub>(IV) {[VO<sub>2</sub>(dhaH)(L)(abi)]} ve Mn(II) {[Mn(dhaH)(L)(abi)]}, Babaei ve Niad [43], polioksometalat'ın Co(II) {(abi)<sub>2</sub>Na<sub>12</sub>[Co<sub>4</sub>(PW<sub>9</sub>O<sub>34</sub>)<sub>2</sub>]}}, El-Medani ve ark. [44], pirazin-2-karboksilik asit'in (Hpc) Ni(II) {[Ni(pc)<sub>2</sub>(abi)<sub>2</sub>].2H<sub>2</sub>O}, Jiao ve ark. [45], 2,3,5,6-tetrabromotereftalik asit'in (H<sub>2</sub>tbta) Co(II) {(Habi)[Cd<sub>0,5</sub>(tbta)(H<sub>2</sub>O)]<sub>n</sub>.H<sub>2</sub>O}, Attia ve ark. [46], 4,4'-bipiridin'in Pt(II) {Pt(abi)(bpy)}, Ramadan ve ark. [12], bis-(salisilaldehit)fenilendiimin'in (H<sub>2</sub>salphen) Ru(II) {[Ru(CO)(salphen)(abi)]}, Mohamed ve ark. [47], 4,5-dimetil-N,N-bis(piridin-2-yil-metilen)benzen-1,2-diimin'in (dmpa) Cr(II) {Cr(dmpa)<sub>2</sub>(abi)<sub>2</sub>}, Malik ve ark. [13], N-(dehidroasetik asit)-tiyosemikarbazit'in, N-(dehidroasetik asit)-4-metil-3-tiyosemikarbazit'in, N-(dehidroasetik asit)-4-fenil-3-tiyosemikarbazit'in, N-(dehidroasetik asit)-4-fenilsemikarbazit'in (H<sub>2</sub>L)

Co(II) {[Co(L)(abi)].4H<sub>2</sub>O}, de Jongh ve ark. [48], Trifenilfosfin'in (PPh<sub>3</sub>) Au(I) {[Au(abi)PPh<sub>3</sub>]NO<sub>3</sub>}, Malecki [49], p-simen'in Ru(II) {[p-simen)RuCl<sub>2</sub>(abi)]}, Turhan [50], 2,6-piridindikarboksilik asit'in (H<sub>2</sub>dpc) proton transfer tuzu {(Habi)(Hdpc)} ve bunun Fe(III) {(Habi)[Fe(dpc)(SO<sub>4</sub>)(H<sub>2</sub>O)<sub>2</sub>].2H<sub>2</sub>O}, Co(II) {(Habi)<sub>2</sub>[Co(dpc)<sub>2</sub>][Co(dpc)(H<sub>2</sub>O)<sub>3</sub>].2H<sub>2</sub>O}, Ni(II) {(Habi)<sub>2</sub>[Ni(dpc)<sub>2</sub>].3H<sub>2</sub>O} ve Cu(II) {(Habi)<sub>2</sub>[Cu(DPC)<sub>2</sub>].4H<sub>2</sub>O} ve Burgess ve ark. [51], osmiyum karbonil {Os<sub>3</sub>(μ-H)(CO)<sub>10</sub>(abi)} karışık ligandlı metal komplekslerinin yapılarını çeşitli spektroskopik yöntemler ile (ICP-OES, AAS, NMR, tek kristal X-ışını, elemental analiz, IR, termal analiz ve manyetik duyarlılık gibi) aydınlatılmış veya önerilmiştir.

#### 4. SONUÇLAR

2-Aminobenzimidazolün ve türevleri, antibakteriyel, antikanser, antiviral, antiinflamatuvar, antiproliferatif, antifungal, antelmintik ve antihistaminik özelliklere sahip geniş bir ilaç yelpazesinden oluşmakta ve bu özellikleri inceleyen çalışmalar literatürde bulunmaktadır. Bunlardan elde eilecek tuz ve komplekslerinde aynı özellikleri de gösterebileceği beklenmektedir. Bu çalışmada günümüze kadar yapılan 2-aminobenzimidazol ve türevlerinin basit ve karışık ligandlı metal kompleksleri hakkındaki çalışmaları incelenmiştir. 2-Aminobenzimidazol türevleri metal komplekslerinde ya N atomuna proton alarak tamamlayıcı iyon şeklinde yada N atomlarından bağlanmaktadır. Literatürde 2-aminobenzimidazolün sentez ve aktivite çalışmalar bol miktarda yapılmış ancak 2-aminobenzimidazol türevleri ile organik ligandların bir arada bulunduğu metal komplekslerinin biyolojik özellikleri daha az çalışılmıştır.

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