



New Amino Acid Chalcone Conjugates: Synthesis, Characterization and Dielectric Properties

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Abstract: In this study, two novel amino acid chalcone compounds were synthesized through a reaction of Fmoc group-protected L-phenylalanine and two amino chalcone derivatives. Target compounds contain dimethoxy and trimethoxy substitutions. The structures of the synthesized compounds were characterized by elemental analysis, ¹H and ¹³C APT NMR spectroscopy techniques. Dielectric parameters such as dielectric constant, dielectric loss and ac conductivity were measured and the results showed that dielectric constant of trimethoxy conjugate was two times higher than dimethoxy conjugate.

Yeni Amino Asit Kalkon Konjugatları: Sentez, Karakterizasyon ve Dielektrik Özellikler

Anahtar Kelimeler

Dielektrik,
 Kalkonlar,
 Amino asit,
 Organik
 sentez

Öz: Bu çalışmada, Fmoc grubu korumalı L-fenilalanin ve iki amino kalkon türevinin reaksiyonu yoluyla iki yeni amino asit kalkon bileşiği sentezlendi. Hedef bileşikler, dimetoksi ve trimetoksi süstitüe kalkon yapılarını barındırmaktadır. Sentezlenen bileşiklerin yapıları element analiz, ¹H ve ¹³C APT NMR spektroskopisi teknikleri ile aydınlatılmıştır. Bileşiklere ait dielektrik sabiti, dielektrik kayıp ve ac iletkenlik gibi dielektrik parametreler ölçülmüş ve sonuçlar trimetoksi taşıyan konjugatın dielektrik sabitin dimetoksili konjugattan yaklaşık iki kat yüksek olduğunu göstermektedir.

1. INTRODUCTION

Chalcone derivatives are one of the subgroups of compounds called flavonoids in the 15-carbon 1,3-diphenylpropane skeleton with the basic structure of two phenyls and one propane chain combined [1-4]. Different members of flavonoids can be obtained by arranging this 15-carbon skeleton in different ways and by attaching different substituents to the rings. Studies have highlighted chalcone compounds as one of the most important members of flavonoids [5-7]. Chalcone and its derivatives have great importance in the field of chemistry and physics due to their photophysical and photochemical properties [8]. Several compounds containing natural and synthetic chalcone rings have broad fluorescence activity in the visible region. That is why chalcones and their derivatives have been used in several application areas due to their strong fluorescence in the UV and visible regions [9-11].

Amino acid conjugates are the name given to new compounds obtained as a result of the chemical bonding of amino acids with another group of organic compounds

[12-15]. Amino acids are biologically very important compound groups. Therefore, it is aimed to obtain more effective compounds by interacting with compound groups such as vitamins, hormones, heterocyclic compounds, and drugs [16-19]. In addition to their biological importance, they can be used in different application areas by interacting with physically active compounds.

In this study, two new hybrid compounds were obtained by the reaction of Fmoc-protected phenylalanine with chalcones bearing dimethoxy and trimethoxy groups. Dielectric parameters of the target compounds were measured and compared to each other. The results indicate that trimethoxy substituted conjugate has higher dielectric constant than dimethoxy conjugates.

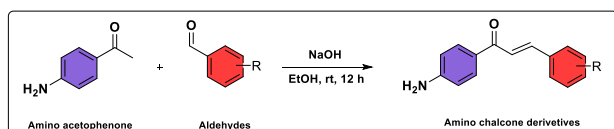
2. MATERIAL AND METHOD

2-chloro-4,6-dimethoxy-1,3,5-triazine (CDMT), N-methyl morpholine (NMM), sodium hydroxide (NaOH), ethanol (EtOH) and acetonitrile (MeCN) were purchased from Sigma-Aldrich used in the synthesis steps, DMSO-d₆ used in NMR analysis were obtained from Merck.

The structures were characterized by using NMR Spectra Bruker Avance III-400. The dielectric analysis was recorded using a QuadTech 7600 LRC impedance analyzer. The elemental analysis data were obtained using a LECO CHNS elemental analyzer.

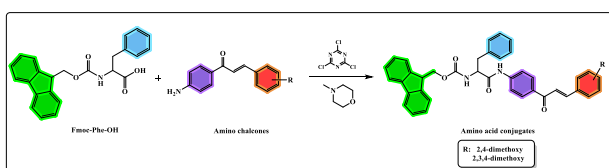
2.1. General Synthesis Method

4-amino acetophenone (1.0 eq) was taken into a reaction flask that contained 50 ml of ethanol and stirred until completely dissolved. 30% of NaOH solution was added to the flask and color change was observed. After 15 minutes, aromatic aldehyde (1.0 eq.) was added to the reaction mixture. The reaction was monitored by thin layer chromatography (TLC) and after the completion of the reaction, the solvent of the mixture was removed and the residue dissolved small amount of acetone (10 ml). The residue was added to water to obtain a precipitate. Yellow color solid was formed, filter and dried [20]. Yields were up to 90%. The general synthesis way was given in Scheme 1.



Scheme 1. General synthesis method of chalcones

Fmoc group protected-amino acid (1.00 mmol), CDMT (1.1 mmol), and the amino chalcone derivative were added to the one-necked reaction flask that contain acetonitrile (80 ml). At room temperature, N-methyl morpholine (1.5 mmol) is added dropwise to the reaction mixture. The reaction is followed by thin layer chromatography. The solvent of the terminated reaction is removed under reduced pressure. Precipitation is observed after the reaction mixture was added in water and in the first stage mixture was completely dissolved. After a while, the precipitation occurred. The target product, which is separated from the mixture by filtration, is left to dry. Yellow color solids were obtained with up to %85 yields [21].



Scheme 2. General synthetic route for amino acid conjugates

(E)-1-(4-aminophenyl)-3-(2,4-dimethoxyphenyl)prop-2-en-1-one

$^1\text{H NMR}$ (400 MHz, DMSO-d_6) δ 3.84 (s, 3H, $-\text{OCH}_3$), 3.90 (s, 3H, $-\text{OCH}_3$), 6.09 (s, 2H), 6.65 – 6.60 (m, 4H), 7.72 – 7.67 (d, $J = 17.0$ Hz, 1H), 7.89 – 7.86 (m, 3H). $^{13}\text{C APT NMR}$: 56.1, 56.6, 99.8, 106.2, 115.6, 118.3, 121.6, 128.2, 130.5, 133.3, 141.2, 143.6, 155.2, 160.1, 188.7. Elemental Analysis: (theoretical) C, 72.07; H, 6.05; N, 4.94, (experimental) C, 72.14; H, 6.12; N, 4.98.

(E)-1-(4-aminophenyl)-3-(2,3,4-trimethoxyphenyl)prop-2-en-1-one

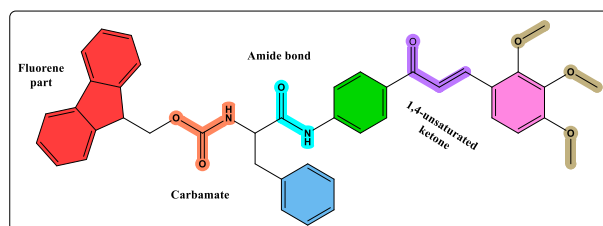
$^1\text{H NMR}$ (400 MHz, DMSO-d_6) δ 3.79 (s, 3H, $-\text{OCH}_3$), 3.86 (s, 3H, $-\text{OCH}_3$), 3.87 (s, 3H, $-\text{OCH}_3$), 6.13 (s, 2H), 6.64 – 6.62 (m, 2H), 6.92 – 6.90 (d, $J = 8.8$ Hz, 1H), 7.79 – 7.72 (m, 3H), 7.91 – 7.89 (m, 2H). $^{13}\text{C APT NMR}$: 56.5, 59.9, 60.1, 104.0, 115.2, 121.6, 122.9, 128.3, 133.1, 134.0, 141.4, 143.3, 149.7, 155.6, 156.0, 188.1. Elemental Analysis: (theoretical) C, 69.00; H, 6.11; N, 4.47; (experimental) C, 69.05; H, 6.16; N, 4.50

(9H-fluoren-9-yl)methyl(E)-1-(1-oxo-3-phenyl-1-((4-(3-(2,3,4-trimethoxyphenyl)acryloyl)phenyl)amino)propan-2-yl)carbamate

$^1\text{H NMR}$ (400 MHz, DMSO-d_6) δ 10.55 (s, 1H), 8.16 (d, $J = 8.4$ Hz, 2H), 7.97 – 7.85 (m, 6H), 7.84 – 7.79 (m, 3H), 7.68 (t, $J = 8.3$ Hz, 2H), 7.45 – 7.37 (m, 4H), 7.31 (t, $J = 6.0$ Hz, 4H), 7.23 (d, $J = 7.5$ Hz, 1H), 6.94 (d, $J = 9.0$ Hz, 1H), 4.48 (td, $J = 9.2, 4.5$ Hz, 1H), 4.21 (q, $J = 6.0, 5.0$ Hz, 2H), 3.88 (d, $J = 3.3$ Hz, 6H), 3.85 (s, 1H), 3.79 (s, 3H), 3.09 (dd, $J = 13.9, 4.6$ Hz, 1H), 2.93 (dd, $J = 13.7, 10.2$ Hz, 1H). $^{13}\text{C NMR}$ (DMSO-d_6) δ 188.01, 171.77, 156.48, 156.16, 154.21, 153.54, 144.22, 143.58, 142.24, 141.15, 138.33, 138.24, 136.26, 133.19, 131.42, 130.24, 129.40, 128.60, 128.11, 127.77, 127.52, 126.91, 125.83, 125.76, 123.86, 121.87, 121.56, 121.34, 120.81, 119.16, 113.19, 108.94, 66.18, 62.01, 60.95, 57.55, 56.55, 47.03, 37.76. Elemental Analysis: (theoretical) C, 73.88; H, 5.61; N, 4.10; (experimental) C, 73.93; H, 5.66; N, 4.15.

(9H-fluoren-9-yl)methyl(E)-1-((4-(3-(2,4-dimethoxyphenyl)acryloyl)phenyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate

$^1\text{H NMR}$ (400 MHz, DMSO-d_6) δ 10.55 (s, 1H), 8.14 (d, $J = 8.3$ Hz, 2H), 8.01 (d, $J = 15.6$ Hz, 1H), 7.95 (dd, $J = 8.3, 4.7$ Hz, 2H), 7.89 (d, $J = 7.6$ Hz, 3H), 7.85 – 7.76 (m, 3H), 7.68 (t, $J = 8.3$ Hz, 2H), 7.43 – 7.37 (m, 3H), 7.30 (dd, $J = 9.6, 4.5$ Hz, 3H), 7.23 (d, $J = 7.3$ Hz, 1H), 6.65 (d, $J = 8.9$ Hz, 2H), 6.21 (d, $J = 67.1$ Hz, 1H), 4.48 (td, $J = 9.6, 4.5$ Hz, 1H), 4.20 (d, $J = 5.4$ Hz, 2H), 3.91 (d, $J = 7.5$ Hz, 3H), 3.85 (d, $J = 6.2$ Hz, 3H), 3.09 (dd, $J = 13.8, 4.6$ Hz, 1H), 2.94 (dd, $J = 13.6, 10.3$ Hz, 1H). $^{13}\text{C NMR}$ (DMSO-d_6) δ 188.08, 171.75, 163.49, 160.39, 156.48, 154.06, 144.23, 144.21, 143.43, 141.15, 138.66, 138.24, 136.62, 133.43, 131.30, 130.50, 130.12, 129.74, 129.40, 128.59, 128.10, 127.52, 126.90, 125.75, 121.86, 120.57, 119.18, 116.51, 113.19, 106.81, 98.78, 66.19, 57.55, 56.31, 56.01, 47.04, 37.79. Elemental Analysis: (theoretical) C, 75.44; H, 5.56; N, 4.29; (experimental) C, 75.49; H, 5.61; N, 4.33.



Scheme 3. General structural representation and functional parts of amino acid-chalcone conjugate

3. RESULTS AND DISCUSSION

3.1. Chemistry

In the ^1H NMR spectrum of the trimethoxy amino chalcone compound in figure 1a, it is seen that the peak of the three methoxy CH_3 protons in the chalcone structure resonates as a singlet at 3.79, 3.86, and 3.87 ppm, and the total number of aromatic and olefinic protons is compatible with the structure. In addition, when the NMR spectrum of the dimethoxy chalcone derivative in Figure 1b is examined, the presence of two methoxy CH_3 protons as a singlet at 3.84 and 3.90 ppm and the compatibility of the number of aromatic protons with the structure can be shown as proof of the formation of compounds. When the ^1H NMR spectrum of the trimethoxy-containing conjugate is evaluated (Figure 2a), first of all, the presence of 9 chalcone methoxy protons in the aliphatic region, diastereotopic CH_2 protons of phenylalanine in the range of 2.90 to 3.11 ppm, and 2 protons of the Fmoc group at 4.18-4.23 ppm indicate that the structure was formed. Therefore, ^{13}C NMR of the same compound is examined, the specific carbonyl of the chalcone compound appeared at 188.01 ppm, the amide carbonyl at 177.77 ppm, and the carbonyl of the Fmoc group appeared at 156.48 ppm. The phenylalanine CH_2 carbon at 37.76 ppm and the CH_2 carbon belonging to the Fmoc group at 66.18 ppm in the aliphatic region indicate that the target structure was formed.

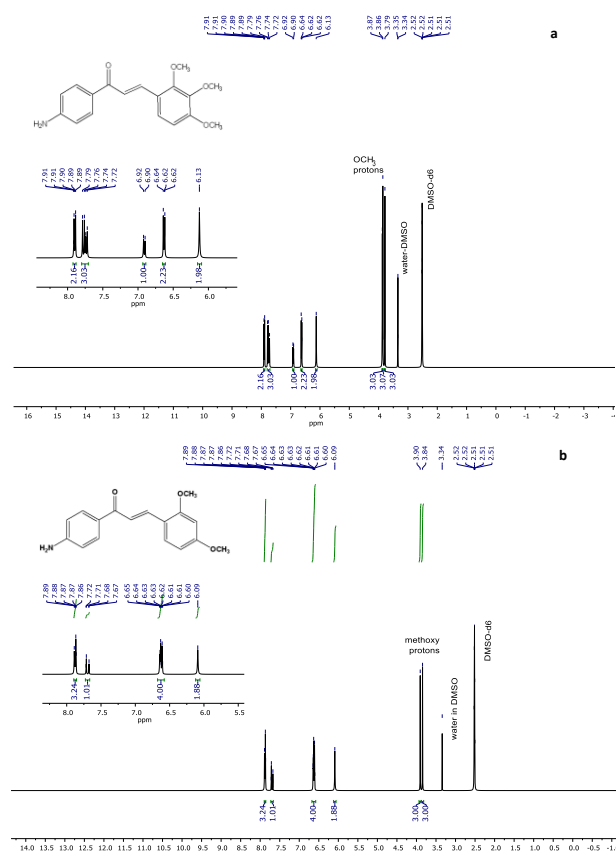


Figure 1. ^1H NMR spectra of dimethoxy amino chalcone (a) and trimethoxy (b) compounds

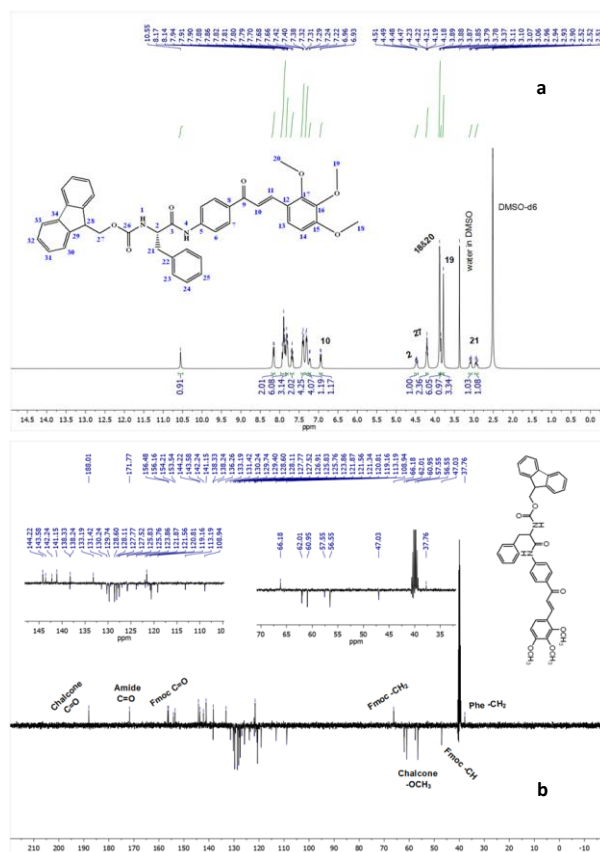


Figure 2. ^1H (a) and ^{13}C APT (b) NMR spectra of trimethoxy chalcone conjugates

3.2. Dielectric Studies

Dielectric is a type of insulating material that can be polarized by placing it in an electric field, but unlike a conductor, the electric charge contained in the dielectric does not flow but causes dielectric polarization to occur. Although the term "insulator" also means low electrical conductivity, the term dielectric is often used for insulating materials with a high level of polarization, the magnitude of which is represented by the dielectric constant. The dielectric coefficient (dielectric constant) can be defined as the ratio of the permittivity of the medium to the permittivity of the free space. The higher the permeability, the more the material tends to reduce the area created. If the polarization created by applying an electric field is high for a dielectric material, the dielectric constant will also be high. This is also true for high resistance to electric current flow [22, 23].

Table 1. Dielectric parameters of conjugates at 1KHz frequency

Entry	Dielectric constant (ϵ')	Dielectric loss (ϵ'')	Conductivity σ_{ac} (S cm^{-1})
<i>Fmoc-Phe-trimethoxy-chalcone</i>	11.93	0.596	6.64×10^{-8}
<i>Fmoc-Phe-dimethoxy-chalcone</i>	5.98	0.392	3.34×10^{-8}

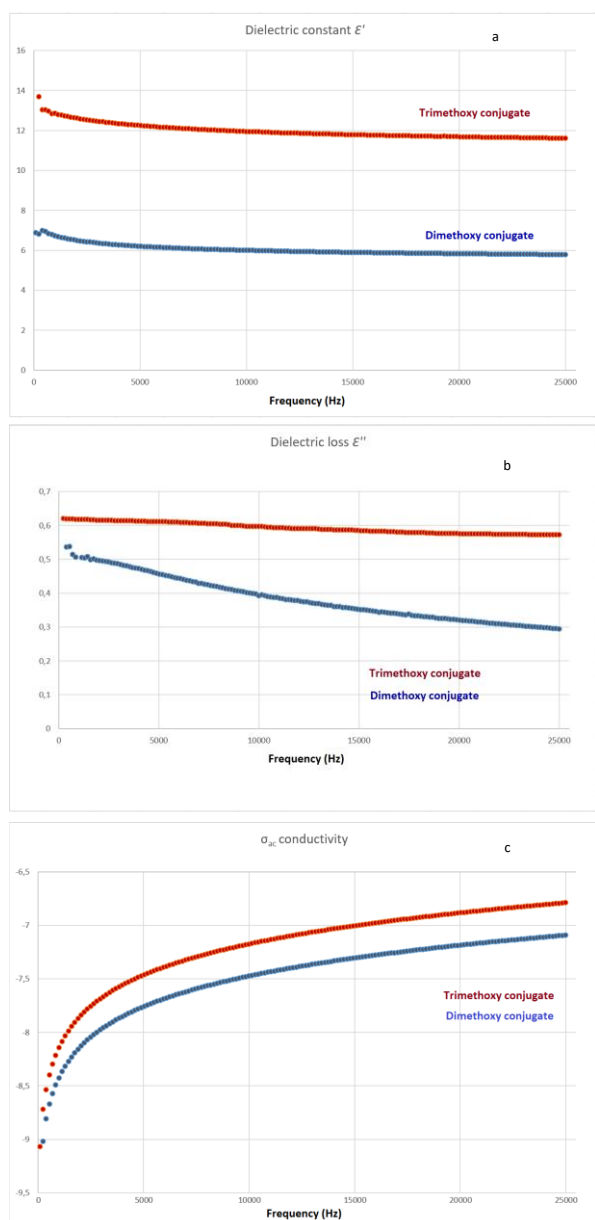


Figure 3. (a) dielectric constant, (b) dielectric loss, (c) ac conductivity results of target compounds

Dielectric parameters of organic and inorganic compounds in which different chalcone structures are substituted were studied. In studies conducted by Koran et al., dielectric constants of methoxy chalcone compounds bonded to phosphazene compounds as hexa-substituted were determined in the range of 1.5 to 2.8. On the other hand, in another study [24], the dielectric properties of methacrylate polymers with chalcone in the side chain were examined and the dielectric constant was found to be 3.33. Compared to the results obtained in other studies [19, 25-31], trimethoxy and dimethoxy conjugates showed considerable dielectric properties. The presence of an extra methoxy group caused extra polarization in the compound and the dielectric constant was higher than the dimethoxy derivative.

4. CONCLUSION

In this work, the synthesis of new amino acid conjugates was successfully completed by following the triazine methodology in high yields. It seems possible that the target compounds have promising dielectric properties and can be used in application areas such as capacitors with various modifications. The obtained compounds have the potential to be used in optical and physical applications.

STATEMENT OF CONFLICT OF INTEREST

The author declared no conflict of interest regarding this article.

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