

Synthesis and Characterization of Novel Schiff's Bases from Ethylenediamine Tetraacetic Acid Derivatives

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Received: 07th July, 19; Revised: 06th August, 19, Accepted: 08th September, 19; Available Online: 25th September, 2019

ABSTRACT

A novel Schiff's base have been synthesized by reaction between ethylenediaminetetraacetic acid (EDTA) derivatives with (2-methoxyaniline, 4-bromoaniline, 4-amino antipyrine) are successfully prepared to obtain six Schiff's base through the reaction of the aldehyde group with compounds containing the amine group as a catalyst glacial acetic acid in ethanol under reflux in good yield (78–92%), the prepared compounds were characterized by were synthesized and characterized by (FT-IR) and ¹HNMR, ¹³C spectroscopy, elemental analysis. The aim of this study is to use cheap EDTA to synthesize Schiff bases, which are thought to have effective biologic and antibacterial properties.

Keywords: 2-methoxyaniline, 4-aminoantipyrine, 4-bromoaniline, Ethylenediaminetetraacetic acid, Schiff base, Synthesis.

International Journal of Pharmaceutical Quality Assurance (2019); DOI: 10.25258/ijpqa.10.3.12

How to cite this article: Aziz, F.S. and Kadem, K.J. (2019). Synthesis and Characterization of Novel Schiff's Bases from Ethylenediamine Tetraacetic Acid Derivatives. International Journal of Pharmaceutical Quality Assurance 10(3): 1-7

Source of support: Nil

Conflict of interest: None

INTRODUCTION

EDTA is considered as a pharmaceutical guide (metal complexing specialist). The corrosive, instead of any salt, is the structure most strong in expelling metals from arrangements. It might be added to attracted blood to avert coagulating and is additionally utilized in the pharmaceutical examination and for the evacuation or inactivation of undesirable particles in the arrangement. EDTA was best in avoiding the oxidation of thiol bunch in medications, for example, captopril. The edetate calcium disodium salt is principally utilized in the determination and treatment of lead harming. It is regulated as implantation containing ¹ O g in 250 or 500 mL of water over a time of 1–2 hours for 3–5 days. The edetate disodium salt is utilized to expel calcium from arrangements, and along these lines, it might be utilized as an anticoagulant.¹ In the 1970's it likewise turned out to be certain that EDTA as FeNa-EDTA could assume a job in battling sickliness in this world through nourishment stronghold. The FeNa-EDTA can be added to numerous nourishment items without prompting undesired taste impacts.² Inorganic ingredients play a vital role in natural and organic curative procedures. Many natural mixtures used in medicine do not have a completely natural way of activity, some of which are biologically modified or modified by the digestion of mineral molecules. Many drugs have changed the toxicological and pharmaceutical properties as a compound of metals and are likely to have flexible C = N (Amin) bases containing mixtures with a wide range of natural movement and metal consolidation in plaque-type showing a level of

antimicrobial and antimicrobial agents and antimicrobial mitigation measures.³ Chef rules are an important category of organic compounds. The Schiff base is the compound that contains the azomethine package (HC = N-). It is the result of the accumulation of ketones (or aldehydes) (aldehydes and ketones) with essential amines, first announced by Hugo Schiff in 1864, and largely based on Schiff's base, largely under acid, base catalysis or with warmth. Schiff's regular base is crystalline solids, which are weakly essential, but there are likely to be some insoluble salts in the structure with solid acids. The Schiff is used as an intermediary for the integration of amino acids or as links to the preparation of mineral rocks that are made in various structures.³ Scented aldehydes, especially with an application framework and structurally fixed chefs, as these aliphatic aldehydes are shaken and polymerized immediately. Legends form the base of aldehydes rather than carbon ketones. Its rules are fully adaptable and varied. There is a wide range of Schiff base mixtures and their perceived behavior on the basis that these mixtures have a completely adaptable and different structure. Schiff rules are mostly a two-tiered, triangular or tetrahedral shale bond and are stable structures with metal particles. Its structural and physical properties in different areas, for example, preparatory uses, identifiable evidence, assurance and confirmation of aldehydes or ketones, and the refinement of mixtures of carbonic or ammonium amino acids or the formation of such mixtures in consideration of puzzling or sensitive responses taken into account by different workers It is also known that Schiff

standards have a wide range of pharmacological activities, for example, antifungal drugs, antiviral drugs,⁴ antimicrobial,⁵ cytotoxic.⁶ Schiff's base is used more in studies in the light of their applications, parasitic and natural,^{4,6}, and antioxidants,⁷ the Schiff scale has been used extensively to date, in addition to countless applications of non-coated,⁸ antimicrobial,⁹ antifungal¹⁰ anti-cancer activity.¹¹ The objective of this study Synthesis and characterization of Schiff bases from EDTA, which is thought to have effective biological aries.¹²

EXPERIMENTAL

All chemicals used in the present study are of analytical grade purchased from Sigma, Aldrich, and Merck chemical co. All the solvents were used after distillation. TLC was run on the silica-coated aluminum sheets (silica gel 60 F254, E Merck, Germany) and visualized in UV light. IR spectra were recorded on the FT-IR Perkin Elmer spectrum BX spectrophotometer.¹ H NMR spectra were obtained by using Bruckner¹H NMR instrument 300 MHz

Synthesis of EDTA derivatives of tetrakis(4-formylphenyl) 2, 2', 2'', 2'''-[ethane-1, 2-diybis(azanetriyl)] tetraacetate(F1)

To solution of EDTA (0.0245mole, 7.17gm) were disintergratedindry N, N-dimethylformamide (DMF) 250Mlsubstituted 4hydroxybenzaldehyde (0.098mole, 12gm) and in a500-mL round-bottomed flask. The blend was mixed for 10 hours. At 98-100⁰CIN, a framework shielded from barometrical dampness and oxygen. The little amount of

the accelerate EDTA kept was evacuated by filtration. The item encouraged at ice bath temperature was recrystallized from10partsof DMF-dioxane(1:2, v/v) to give 4.2 g of unadulterated item, scheme-1: Preparation of(f1).

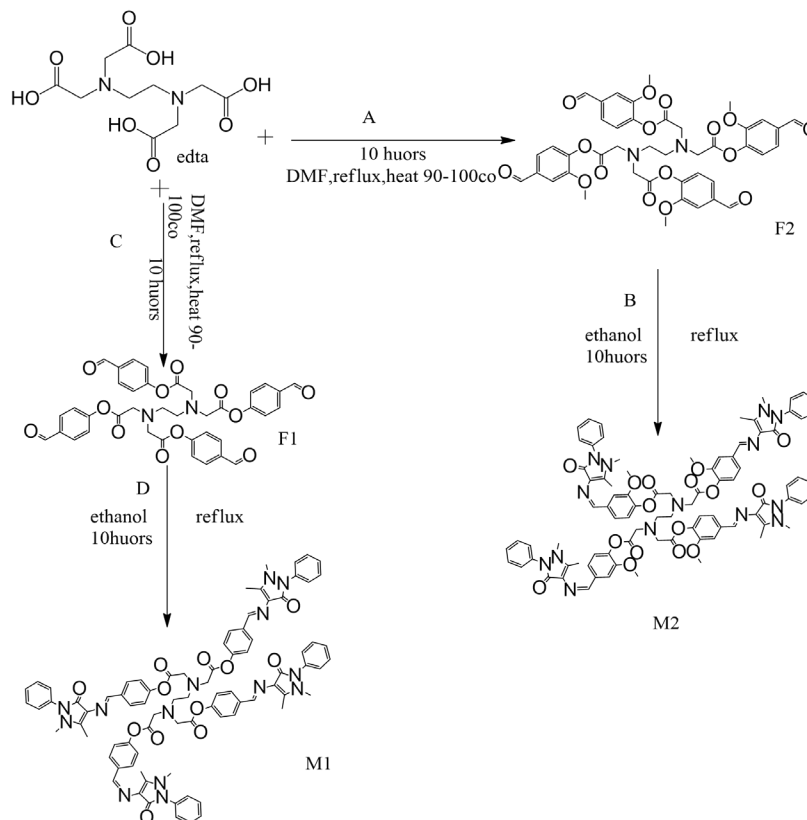
F1: IR (K Br cm⁻¹): 3155(CH as (aromatic), 2960 (Aleph. -CH), 1706 (C = O), 1554 (C = C), 1196 (C-O), ¹HNMR(CDCl₃/ DMSO-d₆, ppm): The aromatic rings give a group of multi signals at 6.82–7.92, (1H, CHO), 9.59, (-C- CH₃) groups3.10–3.19, (2H, CH₂CH₂), 2, 67.¹³C-NMR spectrum of compound (F1) showed signals at (122-136ppm) due to aromatic carbons and at (165-170)ppm due to C = O

Synthesis of EDTA derivatives of tetrakis(4-formyl-2-methoxyphenyl) 2, 2', 2'', 2'''-(ethane-1, 2-diybis(azanetriyl))tetra acetate (F2):

To solution of EDTA (0.0525 mole, 15.366gm) were dissolved in dry N, N-dimethylformamide (250 mL) substituted vanillin (0.2103 mole, 32 gram) and in a 500mL round-bottomed flask. The blend was mixed for 10 hours. At 98-100⁰C in a framework shielded from air dampness and oxygen. The little amount of the hasten (EDTA) kept was expelled by filtration. The item encouraged at ice shower temperature was recrystallized from 10 parts of DMF-dioxane (1:2, v/v) to give 3.6 g of unadulterated item. scheme-1: Preparation of (f2).

F2: IR (K Br cm⁻¹): 3071 (C -H), 1692 (C=O)), 1569 (C=C), 1122 (C-O-C).3165(CH as (aromatic), 2970 (Aleph. -CH).

¹HNMR (CDCl₃/ DMSO-d₆, ppm): 4.41(3H, -OCH₃), 7.10 (1H, Ar-H), 3.28(2H, CH₂CH₂), 9.5(1H, CHO). ¹³C-NMR



Scheme 1: Synthesis of Schiff's bases M1 and M2. A=vanillin, B=4 amino antipyrine, C=4-hydroxybenzaldehyde, D=4-amino antipyrine

spectrum of compound (5) showed signals at (126-133ppm) due to aromatic carbons and at 143ppm due to C=N, showed signal at 55.3ppm due to CH₃ group. and at (165-192)ppm due to C=O.

Synthesis of Schiff base derivatives of bis(4-((E)-((1, 5-dimethyl-3-oxo-2-phenyl-2, 3-dihydro-1H-pyrazol-4-yl)imino)methyl)phenyl) 2, 2'-((2-((2-4-((E)-((1, 5-dimethyl-3-oxo-2-phenyl-2, 3-dihydro-1H-pyrazol-4-yl)imino)methyl)phenoxy)-2-oxoethyl)(2-4-((Z)-((1, 5-dimethyl-3-oxo-2-phenyl-2, 3-dihydro-1H-pyrazol-4-yl)imino)methyl)phenoxy)-2-oxoethyl)amino)ethyl)azanediyl) diacetate(M1)

To a solution of F1(0.002 moles, 2gm) in absolute ethanol (25mL), substituted 4-amino antipyrine (0.00966 moles, 1.9642 gram) and in a 5, 00-mL round-bottomed flask A few drops of glacial acetic acid were included, and the blend is refluxed for around 10 hours. The response blend is cooled and filled 500mL of super cold water, and the hasten got were sifted washed with ethanol and dried and were recrystallized from THF. TLC(chloroform: petroleum ether), (1:1) scheme-1: Preparation of (m1).

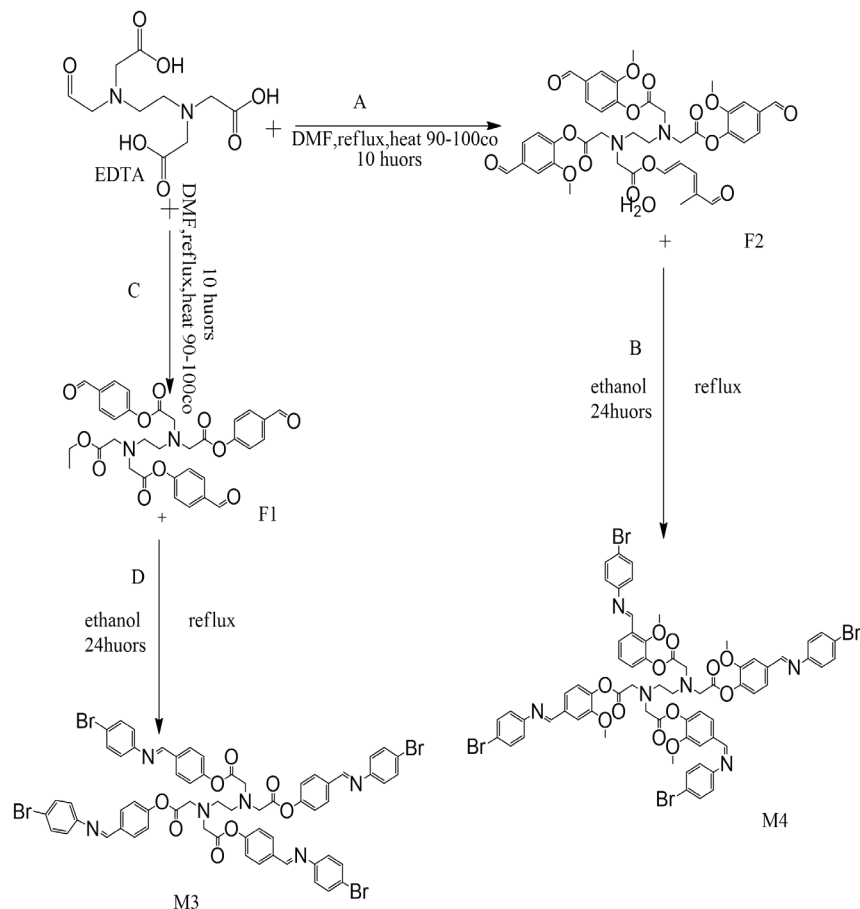
Synthesis of Schiff base derivatives of bis(4-((Z)-((1, 5-dimethyl-3-oxo-2-phenyl-2, 3-dihydro-1H-pyrazol-4-yl)imino)methyl)-2-methoxyphenyl) 2, 2'-((E)-ethane-1, 2-diybis((2-4-((E)-((1, 5-dimethyl-3-oxo-2-

phenyl-2, 3-dihydro-1H-pyrazol-4-yl)imino)methyl)-2-methoxyphenoxy)-2-oxoethyl)azanediyl) diacetate(M2)

To a solution of F2 (0.00988 moles, 7gram) in supreme ethanol (25ml), substituted 4-amino antipyrine (0.0112mol, 8.0354 gram) and in a 500-mL round-bottomed flask a few glacial acetic acids were included, and the blend is refluxed for around 10 hours. The response blend is cooled and filled 500ml of super cold water, and the hasten got were sifted washed with ethanol and dried and were recrystallized from THF. TLC(chloroform: petroleum ether), (1:1), scheme-1: Preparation of (m2).

Synthesis of Schiff base derivatives of bis(4-((E)-((4-bromophenyl) imino)methyl)phenyl)2, 2'-((2(2(4(((4bromophenyl)imino)methyl)phenoxy)2oxoethyl)(2(4((E)-((4bromophenyl) imino)ethyl)phenoxy)2oxoethyl)amintanediyl)diacetate (M3):

To a solution of F1(0.0002822 moles, 0.4854gram) in supreme ethanol (25mL), substituted 4-bromoaniline (0.011288mol, 1.941 gram) and in a 500mL round-bottomed flask a few glacial acetic acids were included, and the blend is refluxed for around 8 hours. The response blend is cooled and filled 500ml of super cold water, and the hasten got were sifted washed with ethanol and dried and were recrystallized from THF. TLC(chloroform: petroleum ether), (1:1), scheme-2: Preparation of (m3).



Scheme 2: Synthesis of Schiff's bases M3 and M4. A=vanillin, B=4-bromoaniline, C=4-hydroxybenzaldehyde, D=4-bromoaniline

Synthesis of Schiff base derivatives of bis(4((Z)((4bromophenyl)imino)methyl)-2-methoxyphenyl)2, 2'((E)ethane1, 2diylbis((2(4((E)((4bromophenyl)imino)methyl)-2-methoxyphenoxy)-2-oxoethyl)azanediyl)diacetate(M4):

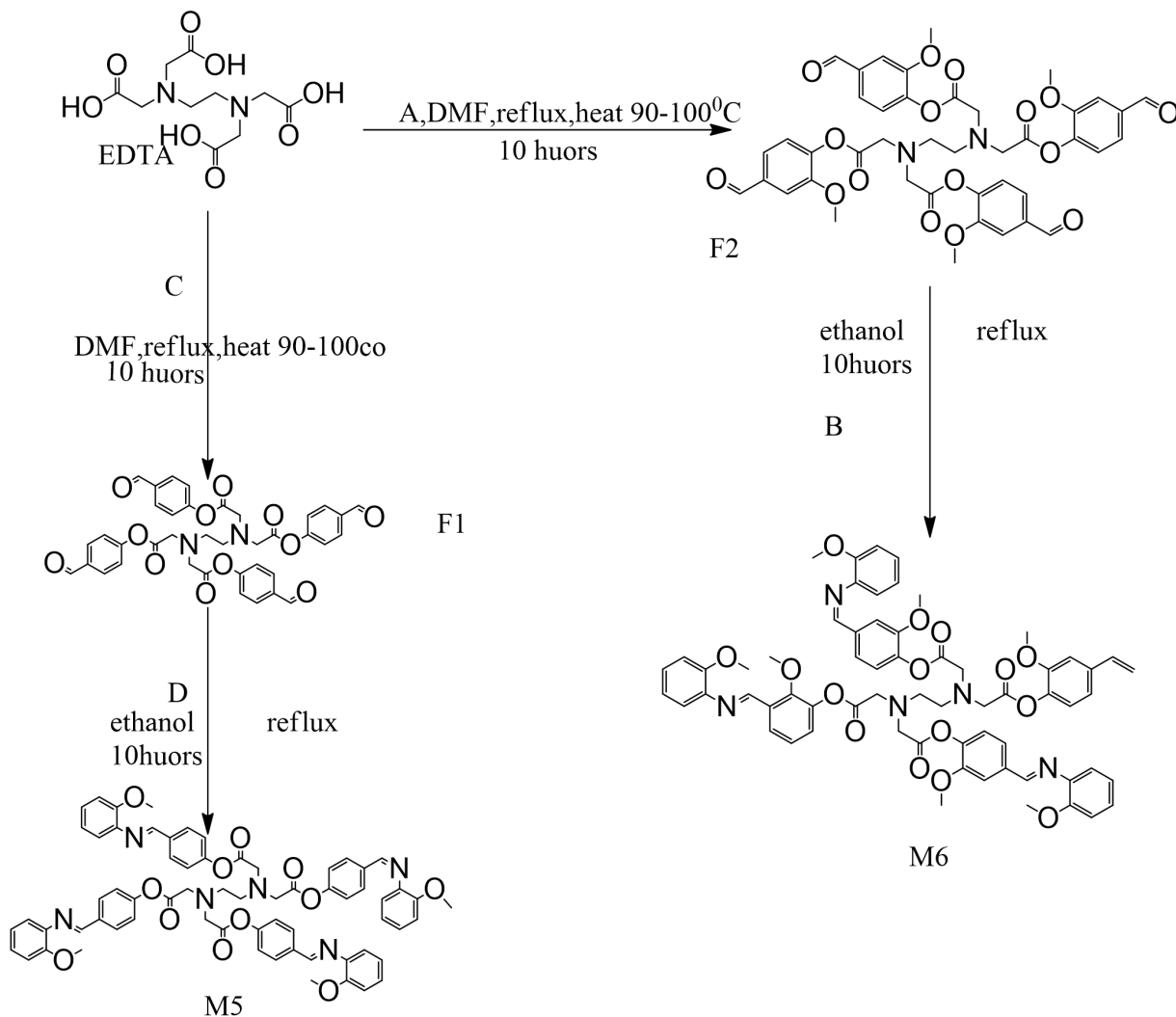
To solution of F2 (0.00024132 mole, 0.4151gram) in supreme ethanol (25ml), substituted 4-bromoaniline (0.0009652mol, 1.6604 gram) and in a 500mL round-bottomed flask a few drops glacial acetic acid were included and the blend is refluxed for around 8 hours. The response blend is cooled and filled 500mL of super cold water and the hasten got were sifted washed with ethanol and dried and were recrystallized from THF. TLC(chloroform: petroleum ether), (1:1), scheme-2: Preparation of(m4).

Synthesis of Schiff base derivatives of bis(4-((E)-((1, 5-dimethyl-3-oxo-2-phenyl-2, 3-dihydro-1H-pyrazol-4-yl)imino)methyl)-2-methoxyphenyl) 2, 2'-((2-((2-(4-(((1, 5-dimethyl-3-oxo-2-phenyl-2, 3-dihydro-1H-pyrazol-4-yl)imino)methyl)-2-methoxyphenoxy)-2-oxoethyl)(2-(4-((E)-((1, 5-dimethyl-3-oxo-2-phenyl-2, 3-dihydro-1H-pyrazol-4-yl)imino)methyl)-2-methoxyphenoxy)-2-oxoethyl)amino)ethyl)azanediyl)diate(M5):

To solution of F1(0.00014mole, 1.0gram) in supreme ethanol (25mL), substituted 2-methoxyaniline(0.00056mol0.69 gram) and in a 500-mL round-bottomed flask a few drops of glacial acetic acid were included and the blend is refluxed for around10 hours. The response blend is cooled and filled 500ml of super cold water and the hasten got were sifted washed with ethanol and dried and were recrystallized from THF. TLC(chloroform: petroleum ether), (1:1), scheme-3: Preparation of(m5).

Synthesis of Schiff base derivatives of bis(4-((E)-((1, 5-dimethyl-3-oxo-2-phenyl-2, 3-dihydro-1H-pyrazol-4-yl)imino)methyl)-2-methoxyphenyl) 2, 2'-((2-((2-(4-(((1, 5-dimethyl-3-oxo-2-phenyl-2, 3-dihydro-1H-pyrazol-4-yl)imino)methyl)-2-methoxyphenoxy)-2-oxoethyl)(2-(4-((E)-((1, 5-dimethyl3oxo2phenyl2, 3dihydro-1H-pyrazol-4-yl)imino)methyl)-2-methoxyphenoxy)-2-Oxo ethyl)amino)ethyl)azanediyl)diate(M6)

To solution of F2(0.00012mole, 1.0gram) in supreme ethanol (25ml), substituted 2-methoxyaniline (0.00048mol, 0.59 gram) and in a 500-mL round-bottomed flask a few drops glacial acetic acid corrosive were included and the blend is



Scheme 3: Synthesis of Schiff's bases M5 and M6. A=vanillin, B=2-methoxybenzylamine, C=4-hydroxybenzaldehyde, D=2-methoxyaniline

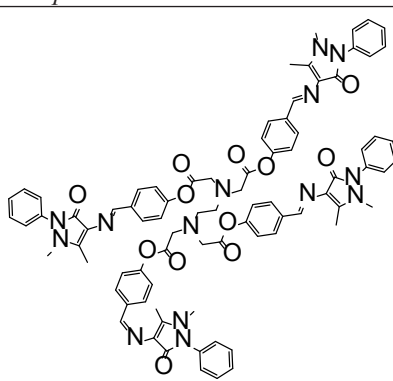
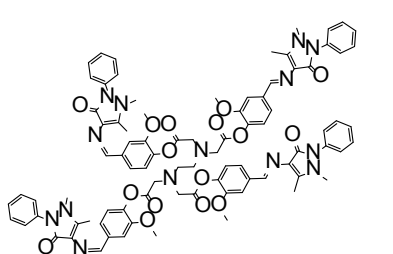
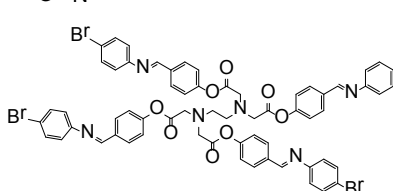
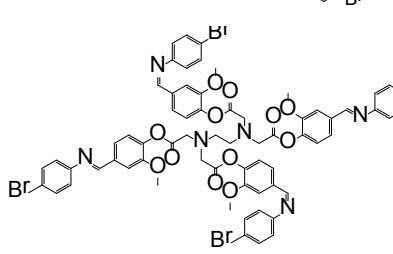
refluxed for around 8 hours. The response blend is cooled and filled 500ml of super cold water and the hasten got were sifted washed with ethanol and dried and were recrystallized from THF. TLC(chloroform: petroleum ether), scheme-3: Preparation of (m6).

RESULTS AND DISCUSSION

New six Schiff bases were synthesized from the reaction EDTA derivatives with (2-methoxyaniline, 4-bromoaniline, 4-amino antipyrine) aldehydes and ketones, shown in scheme (1, 2, 3) Some of these Schiff bases posses' good Physical properties and the % Yield percentage of the prepared Schiff bases were in the range {55-95} % see (Table:1). Such compounds were characterized by different physicochemical techniques like melting point, elemental analysis, and ^1H NMR, ^{13}C NHR spectroscopy show in (Table 1, 2). Compound (M1) showed ^1H NMR $\text{CDCl}_3/\text{DMSO-d}_6$, ppm): 2.35 (3H, -CH₃). The signal of

N-CH₃ was observed at 4.41 ppm (3H). The signals of aryl-H were seen at 7.39–6.83 (3H), 3.28(2H, CH₂CH₂), at 9.48, and 8.27due to the azomethine. ^{13}C -NMR spectrum of compound (M1) showed signals at (122-138ppm) due to aromatic carbons and at 163ppm due to C = N. Show spectrum of compound (M2) ^1H NMR $\text{CDCl}_3/\text{DMSO-d}_6$, ppm): 2.32(3H, -CH₃), The signal of N-CH₃ was observed at 4.43ppm (s, 3H). The signals of aryl-H were seen at 7.41–6.81 (3H), 3.30(2H, CH₂CH₂), at 9.44, and 8.22due to the azomethine. The signal of carbonyl-OCH₃ was observed at 1.32 ppm (3H).¹³ C-NMR spectrum of compound (M2) showed signal at 43-55ppm due to CH₃ group, signals at (122-131ppm) due to aromatic carbons and signal at 163ppm due to C = N. compound (M3) showed ^1H NMR $\text{CDCl}_3/\text{DMSO-d}_6$, ppm): 2.41 (3H, -CH₃), The signal of N-CH₃ was observed at 4.41ppm (3H). The signals of aryl-H were seen at 7.51–6.84 ppm (3H), 3.41 (2H, CH₂CH₂), at 9.39, and 8.27due to the azomethine. The ^{13}C -NMR spectrum of

Table 1: Physical data of the prepared compounds.

Comp. NO.	Compound structure	Elemental analysis, % Found/(calc.) C					Color	Melting Points °C	yield %
		%C	%H	%N	%O	%Br			
M1		67.94	5.28	13.53	13.24		light black	290	55
M2		65.80	5.39	12.49	16.31		dark yellow	305	66
M3		56.21	3.65	6.34	9.66	24.13	light black	270	87
M4		54.87	3.91	5.82	13.29	22.12	Dark yellow	286	95

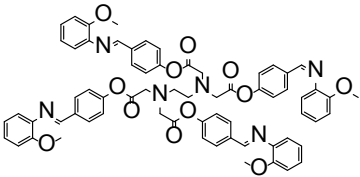
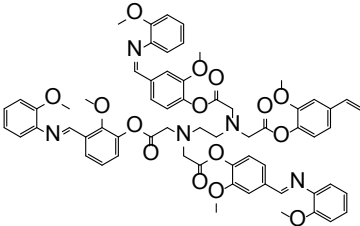
M5		70.20	5.36	7.44	17.00	yellow	295	87
M6		67.30	5.56	6.13	21.01	light yellow	278	77

Table 2: FTIR spectra data, ¹H-NMR, and ¹³C-NMR spectral data for some of the new Schiff bases prepared compounds.

<i>mpd</i>	<i>FTIR spectra data</i>	<i>¹H-NMR spectra data</i>	<i>¹³C-NMR spectra data</i>
M1	3157 cm ⁻¹ (CH) as (aromatic), 2965 cm ⁻¹ (aliphatic.-CH), 1710 cm ⁻¹ (C=O), 1560 cm ⁻¹ (C=C), 1193 cm ⁻¹ (C-O), 1598 cm ⁻¹ (CH=N).	2.41 ppm (3H, -CH ₃), The signal of N-CH ₃ = 4.41ppm (3H). The signals of aryl-H = 7.51–6.84 ppm (3H), 3.41(2H, CH ₂ CH ₂), at 9.39 and 8.27due to the azomethine.	Signals at (122-138ppm) due to aromatic carbons and at 163ppm due to C=N.
M2	3161 cm ⁻¹ (CH) as (aromatic), 2968 cm ⁻¹ (aliphatic.-CH), 1713 cm ⁻¹ (C=O), 1559 cm ⁻¹ (C=C), 1191 cm ⁻¹ (C-O), 1561 cm ⁻¹ (CH=N).	2.32 ppm (3H, -CH ₃), The signal of N-CH ₃ =4.43ppm (s, 3H). The signals of aryl-H = 7.41–6.81 (3H), 3.30(2H, CH ₂ CH ₂), at 9.44 and 8.22due carbonyl-OCH ₃ = 1.32 ppm.	43-55ppm due to CH ₃ group, signals at (122-131ppm) due to aromatic carbons and signal at 163ppm due to C=N.
M3	3168 cm ⁻¹ (CH) as (aromatic), 2971 cm ⁻¹ (aliphatic.-CH), 1711 cm ⁻¹ (C=O), 1559 cm ⁻¹ (C=C), 1191 cm ⁻¹ (C-O), 1561 cm ⁻¹ (CH=N).	2.41 ppm (3H, -CH ₃), The signal of N-CH ₃ = 4.41ppm (3H). The signals of aryl-H=7.51-6.84ppm(3H), 3.41(2H, CH ₂ CH ₂), at 9.39 and 8.27due to the azomethine.	showed signals at (121-129ppm) due to aromatic carbons and signals at (169ppm) due to C=O.
M4	3161 cm ⁻¹ (CH) as (aromatic), 2967 cm ⁻¹ (aliphatic.-CH), 1714 cm ⁻¹ (C=O), 1554 cm ⁻¹ (C=C), 1197 cm ⁻¹ (C-O), 1570 cm ⁻¹ (CH=N).	2.44 ppm (3H, -CH ₃), The signal of N-CH ₃ = 4.39ppm (3H). The signals of aryl-H = 7.53–6.90 ppm (3H), 3.29(2H, CH ₂ CH ₂), at 9.43 and 8.32due to the azomethine, The signal of carbonyl-OCH ₃ = 1.32 ppm (3H).	showed signal at 55.70 ppm due to CH ₃ group, signals at (122-139ppm) due to aromatic carbons and signals at (168ppm) due to C=O .
M5	3233 cm ⁻¹ (CH) as (aromatic), 2965 cm ⁻¹ (aliphatic.-CH), 1722 cm ⁻¹ (C=O), 1566 cm ⁻¹ (C=C), 1207 cm ⁻¹ (C-O), 1602 cm ⁻¹ (CH=N).	2.44 ppm (3H, -CH ₃), the signal of N-CH ₃ = 4.39ppm (3H). The signals of aryl-H=7.63-6.80ppm(3H), 3.31(2H, CH ₂ CH ₂), at 9.39 and 8.42due to the azomethine, the signal of carbonyl-OCH ₃ was observed at 1.42 ppm (3H).	signals at (115-140ppm) due to aromatic carbons and at 161ppm due to C=N, showed signal at (55-58)ppm due to CH ₃ group .
M6	3231 cm ⁻¹ (CH) as (aromatic), 2954 cm ⁻¹ (aliphatic.-CH), 1733 cm ⁻¹ (C=O), 1545 cm ⁻¹ (C=C), 1211 cm ⁻¹ (C-O), 1612 cm ⁻¹ (CH=N).	2.41 ppm (3H, -CH ₃). The signal of N-CH ₃ was observed at 4.32ppm (3H). The signals of aryl-H were seen at 7.53–6.70 ppm (3H), 3.21(2H, CH ₂ CH ₂), at 9.19, and 8.32due to the azomethine, The signal of carbonyl-OCH ₃ was observed at 1.44 ppm (3H).	Signals at (126–133ppm) due to aromatic carbons and at 143ppm due to C = N, showed signal at 30ppm due to CH ₃ group.

compound (3) showed signals at (121-129ppm) due to aromatic carbons and signals at (169ppm) due to C = O. Compound (M4) showed ¹H NMR CDCl₃/ DMSO-d₆, ppm): 2.44(3H, -CH₃), The signal of N-CH₃ was observed at 4.39ppm (3H). The signals of aryl-H were seen at 7.53–6.90 ppm (3H), 3.29(2H, CH₂CH₂), at 9.43, and 8.32due to the azomethine, The signal of carbonyl-OCH₃ was observed at 1.32 ppm (3H). The ¹³C-NMR spectrum of compound (4) showed a signal at 55.70 ppm due

to the CH₃ group signals at (122–139ppm) due to aromatic carbons and signals at (168ppm) due to C = O. Compound (5) showed ¹H NMR CDCl₃/ DMSO-d₆, ppm): 2.44(3H, -CH₃), the signal of N-CH₃ was observed at 4.39ppm (3H). The signals of aryl-H were seen at 7.63–6.80 ppm (3H), 3.31(2H, CH₂CH₂), at 9.39, and 8.42due to the azomethine, the signal of carbonyl-OCH₃ was observed at 1.42 ppm (3H). ¹³C NMR spectrum of compound 5 showed signals at (115–140ppm) due to aromatic

carbons and at 161 ppm due to C = N, showed signal at (55–58) ppm due to CH₃ group. Compound 6 showed ¹H NMR CDCl₃/DMSO-d₆, ppm): 2.41(3H, -CH₃), The signal of N-CH₃ was observed at 4.32 ppm (3H). The signals of aryl-H were seen at 7.53–6.70 ppm (3H), 3.21(2H, CH₂CH₂), at 9.19, and 8.32 due to the azomethine, The signal of carbonyl-OCH₃ was observed at 1.44 ppm (3H). The ¹³C-NMR spectrum of compound 5 showed signals at (126–133 ppm) due to aromatic carbons and at 143 ppm due to C = N, showed signal at 30 ppm due to the CH₃ group. All these results are shown in Table 2.

ACKNOWLEDGMENTS

The authors are grateful to Babylon University, College of Science, Department of chemistry, And Ministry of industry and minerals, Al-Rasheed state.

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