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Article

Synthesis and Biological Activity of Some New Pyrazoline and Pyrimidine Derivatives

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Novas séries de pirazolinas, 3-aril-4,5-diidro-1*H*-pirazol-1-carbaldeídos (**4**-**6**), (aril-4,5-diidro-1*H*-pirazol-1-il)etanonas (**9**-**11**) e 3-aril-4,5-diidro-1*H*-pirazóis (**24** e **25**) foram sintetizadas pela reação de chalconas (**1**-**3**) com hidrato de hidrazina em ácido fórmico, ácido acético ou etanol, respectivamente. Novos derivados de pirimidina 6-arilpirimidina-2-amina (**32**-**34**) também foram sintetizados a partir das mesmas chalconas de partida. As estruturas dos novos compostos sintetizados foram estabelecidas através do estudo dos espectros de IV, ^{1}H RMN, ^{13}C RMN e análise elementar. Todos os compostos foram avaliados quanto as suas atividades antibacteriana e antifúngica. Dentre estes compostos, três mostraram atividade relevante contra *C. albicans* e outros também apresentaram atividade contra *E. coli*.

New series of pyrazoline 3-aryl-4,5-dihydro-1*H*-pyrazole-1-carbaldehydes (**4**-**6**), (aryl-4,5-dihydro-1*H*-pyrazol-1-yl)ethanones (**9**-**11**) and 3-aryl-4,5-dihydro-1*H*-pyrazoles (**24** and **25**) were synthesized by reacting chalcones (**1**-**3**) with hydrazine hydrate in either formic acid, acetic acid or ethanol, respectively. Also, new 6-arylpyrimidin-2-amine derivatives (**32**-**34**) were synthesized from the same chalcones. The structures of the newly synthesized compounds were established on the basis of IR, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analyses. The compounds were evaluated for their antibacterial and antifungal activities. Three heterocycles showed relevant activity against *C. albicans* and some compounds also showed activity against *E. coli*.

Keywords: chalcones, pyrazoline, pyrimidine, antibacterial, antifungal

Introduction

Chalcones are well known intermediates for the synthesis of various heterocyclic compounds. Compounds with the chalcone backbone have been informed to possess various biological activities.[1] Chalcones have been reported to possess antimicrobial,[2] anti-inflammatory,[2,3] antioxidant and anticancer properties.[4] They were also found to exhibit analgesic,[5] platelet antiaggregation,[6] antiulcerative,[7] antimalarial,[8] antiviral,[9] antileishmanial,[10] antitubercular[11] and antihyperglycemic properties,[12] as well as to inhibit the enzymes tyrosinase,[13] and aldose reductase.[9]

Much attention has been paid to the synthesis of heterocyclic compounds bearing nitrogen-containing rings, like pyrazoline and pyrimidine systems, mainly due to their potential pharmacological activity.[14-31]

Pyrazolines are well known and important nitrogen-containing 5-membered heterocycles, which were found to possess a broad spectrum of biological activities such as anti-inflammatory,[14] herbicidal,[15] antimicrobial,[16] antifungal,[17] antidepressant,[18] anticonvulsant,[19] antitumor,[20] antitubercular,[21] insecticidal,[22] antimycobacterial,[23] molluscicidal,[24] and antinociceptive.[25] A classical synthesis of 2-pyrazolines involves the base catalyzed[26] Claisen-Schmidt condensation of appropriate ketones with suitable aldehydes in the presence of potassium hydroxide in aqueous ethanolic solution at room temperature to give chalcones,[27] which undergo a subsequent cyclization reaction with hydrazines.[28] Several alternatives are available for this condensation,[29] including under acidic[28] or basic[30] conditions. On the other hand, pyrimidines have also been reported to show a variety of biological activities.[31]

Based on the interest in the above biological activities exhibited by the pyrazoline and pyrimidine compounds, we report here the synthesis of a new series of pyrazoline and pyrimidine compounds.

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Results and Discussion

Chemistry

The sequence leading to the formation of the title compounds is outlined in Schemes 1 and 2. The desired chalcones (**1**-**3**) were prepared by the reaction of anthracene-9-carbaldehyde with different ketones (*p*-chloro acetophenone, *p*-methyl acetophenone or 2-acetylfuran) in the presence of aqueous ethanolic KOH. The IR spectra of **1**-**3** exhibited a band due to the unsaturated carbonyl group at 1651-1660 cm^{-1}. Their ^1H NMR spectra showed a signal at δ 7.45-7.83 ppm attributed to the =CH-2 proton adjacent to C=O with a coupling constant 16 Hz, and a doublet at the range δ 8.60-8.79 ppm due to the =CH-3 proton with the same coupling constant, which confirmed the presence of chalcones in the *trans* form. The ^{13}C NMR of 3-(anthracen-9-yl)-1-(4-chlorophenyl)prop-2-en-1-one (**1**) as a prototype for the prepared chalcones showed a signal at 188.5 ppm corresponding to the C=O group.

The compounds **1**-**3** were converted into the corresponding 5-(anthracen-9-yl)-3-aryl-4, 5-dihydro-*1H*-pyrazole-1-carbaldehydes (**4**-**6**) by treatment with hydrazine hydrate in formic acid. The IR spectra of aldehydes **4**-**6** showed the C=O band at 1666-1674 cm^{-1}, and their proton NMR spectra showed three signals within the ranges δ 3.28-3.42 , 3.85-4.09, and 6.40-6.96 ppm due to H_4, $H_{4'}$ and H_5 of the pyrazoline ring, respectively, in addition to a singlet signal in the range δ 8.84-9.00 ppm due to the CHO proton.

Reaction of compounds **4** and **5** with benzoyl hydrazine gave rise to the corresponding benzoylhydrazides **7** and **8**, respectively. Their IR spectra showed the NH bands at 3255, 3267, and the carbonyl absorption bands at 1659, 1662 cm^{-1}, respectively. Further, in their proton NMR spectra, it were observed the appearance of signals in the ranges δ 3.38-3.59, 3.85-4.53 and 6.71-7.86 ppm, due to H_4, $H_{4'}$ and H_5 of the pyrazoline ring, respectively, a singlet at δ 8.04 and 8.41 ppm due to the N_1CH=N protons, and a singlet at δ 10.48 and 10.47 ppm, corresponding to the NH protons respectively.

The 1-(5-(anthracen-9-yl)-3-aryl-4, 5-dihydro-1*H*-pyrazol-1-yl)ethanones **9**-**11** were synthesized by cyclization of chalcones **1**-**3** with hydrazine hydrate in acetic acid. Their structures were confirmed by IR spectra, which showed their carbonyl band in the range 1655-1667 cm^{-1}. On the other hand, their proton NMR showed a new singlet in the range δ 2.15-2.37 ppm, attributable to the CH_3 protons, three doublets of doublets in the range δ 3.27-3.48, 3.85-4.03, and 6.66-6.85 ppm corresponding to H_4, $H_{4'}$ and H_5 of the pyrazoline ring, respectively.

Treatment of the methyl ketones **9** and **10** with benzaldehyde in alkaline medium at room temperature afforded the corresponding α,β-unsaturated ketones **12** and **13**, respectively, the IR spectra of which showed the carbonyl group at 1650 and 1652 cm^{-1}. Their proton NMR spectra showed the disappearance of the CH_3 signals and exhibited pairs of signals at δ 7.40, 8.67 and 7.28, 8.70 ppm, respectively, as doublets, due to the olefinic protons ($H_{1'}$, $H_{2'}$).

The desired Schiff's bases **14**-**19** were prepared by heating the methyl ketones **9**-**11** with aryl hydrazines (phenyl hydrazine, *p*-nitrophenyl hydrazine) or hydrazine hydrate in ethanol. Their IR spectra showed a new absorption peak at 3285-3372 cm^{-1} due to the NH group, while their ^1H NMR spectra displayed the CH_3 protons as singlets in the range δ 2.14-2.19 ppm. In addition, a broad singlet was observed in the range δ 9.20-10.61 ppm, corresponding to the NH moiety. In case of compound **19**, the signal of the NH_2 group appeared at δ 7.22 ppm.

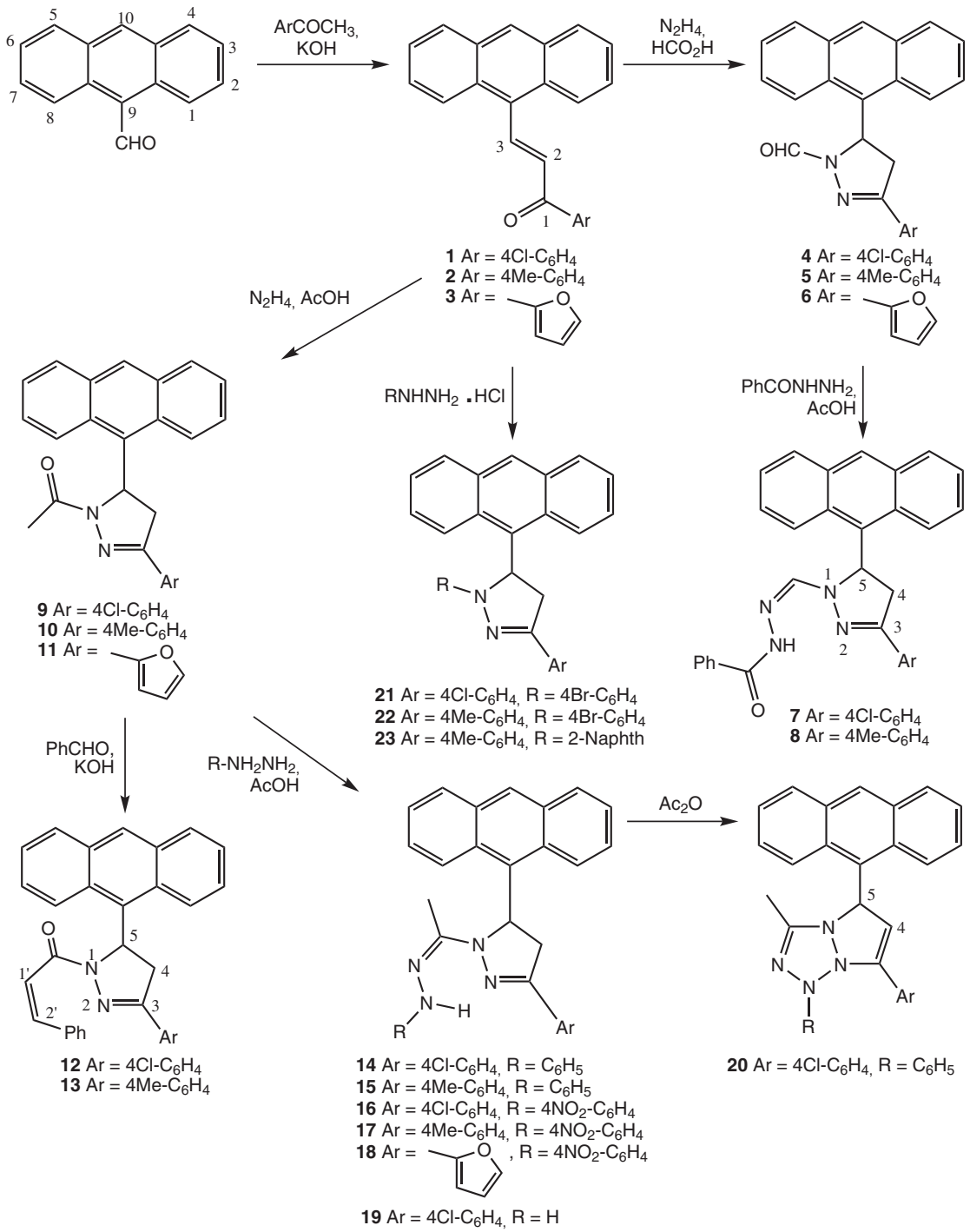
Heating the substituted 4,5-dihydro-1*H*-pyrazole derivative **14** with acetic anhydride afforded the corresponding tetrazole **20**, which evidenced disappearance of NH signals in its IR and proton NMR spectra.

Treatment of the 3-(anthracen-9-yl)-1-arylprop-2-en-1-ones **1** or **2** with *p*-bromophenyl- or 2-naphthyl hydrazine hydrochloride afforded the corresponding 1,3,5-trisubstituted pyrazolines (**21**-**23**). Their ^1H NMR spectra showed three multiplets in the ranges δ 2.99-3.39, 3.78-4.09 and 6.86-6.98 ppm due to the pyrazoline protons, in addition to aromatic protons at δ 7.03-8.54 ppm.

Cyclization of the chalcones **1** and **2** with hydrazine hydrate in ethanol gave the 5-(anthracen-9-yl)-3-aryl-4, 5-dihydro-1*H*-pyrazoles **24** and **25**, respectively. Their IR spectra exhibited a NH absorption peak in the range 3254-3284 cm^{-1}. On other hand, their ^1H NMR showed two multiplets at δ 3.42-4.11 and 6.60-6.74 ppm, due to the pyrazoline protons. The NH protons were observed at δ 8.56 and 9.63 ppm, respectively.

Furthermore, the disubstituted pyrazolines **24** and **25** were allowed to react with sodium nitrite, phenylisothiocyanate, and *p*-toluenesulfonyl chloride to correspondingly furnish 5-(anthracen-9-yl)-3-aryl-1-nitroso-4,5-dihydro-1*H*-pyrazoles **26** and **27**, 5-(anthracen-9-yl)-3-aryl-*N*-phenyl-4,5-dihydro-1*H*-pyrazole-1-carbothioamides **28** and **29** and 5-(anthracen-9-yl)-3-aryl-1-tosyl-4,5-dihydro-1*H*-pyrazoles **30** and **31**, respectively, in 74-89% yield.

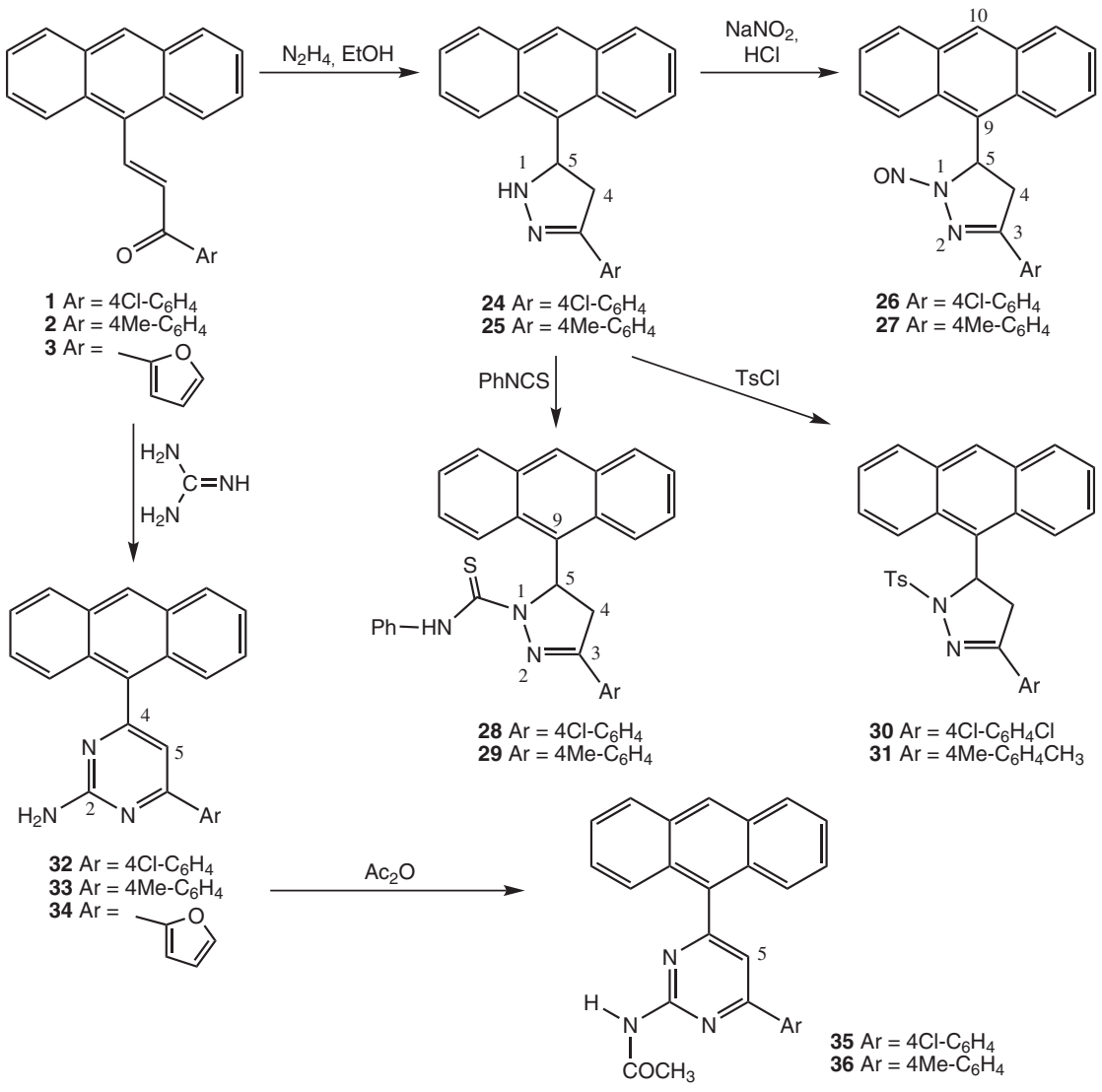
On the other hand, the reaction of chalcones **1**-**3** with an alcoholic solution of guanidine carbonate containing aqueous NaOH produced the corresponding 2-amino-4, 6-diarylpyrimidines **32**-**34** (Scheme 2). This transformation might proceed either by 1,4-addition or 1,2-addition of the



Scheme 1.

guanidine to the chalcones, followed by cyclization of the intermediate, which undergoes proton shift and aromatization to yield the 2-aminopyrimidines.[32] The infrared spectra of the products showed two bands in the ranges 3054-3147 and 3323-3366 cm^{-1} corresponding to the NH_2 group. Furthermore, their ^1H NMR showed a D_2O exchangeable signal at δ 5.97-6.26 ppm due to the NH_2 protons. A singlet at δ 7.35-7.91 ppm was observed due to the pyrimidine-H_5.

Acetylation of the 2-aminopyrimidines **32** and **33** with Ac_2O yielded the monoacetylated compounds **35** and **36**, respectively. Their infrared spectra showed peaks at 3260 and 3218 cm^{-1} corresponding to the NH group and strong sharp peaks at 1667 and 1669 cm^{-1}, respectively, due to the C=O group. On the other hand, their ^1H NMR showed the CH_3 protons as singlets at δ 2.25 and 2.29 ppm, in addition to the NH protons at δ 10.77 and 10.47 ppm respectively.



Scheme 2.

Evaluation of the biological activity

Four test organisms representing different groups of microorganisms were used to evaluate the bioactivity of the designed products. The inhibition zone and minimal inhibitory concentration results are given in Table 1.

From the data, it stems that compounds **1**, **3**, **7**, **20**, **23**, **31** and **34** were the most active against *E. coli*, while compounds **18**, **28** and **30** were found to be active against *C. albicans*. Some chlorinated compounds exhibited activity against *C. albicans* (**28** and **30**) and against *E. coli* (**1**, **7** and **20**). In addition, some sulfur-containing compounds exhibited activity against *C. albicans* (**28** and **30**) and against *E. coli* (**31**). It was noticed that furan derivatives also showed activity against *C. albicans* (**18**), and against *E. coli* (**3** and **34**). No systematic variation was observed in the antibacterial and antifungal activities for the rest of the compounds. All tested compounds showed poor biological activity against *P. aeruginosa* and *S. aureus*.

Conclusions

In summary, new series of anthracenylpyrazolines and anthracenylpyrimidines were synthesized from 3-(anthracen-9-yl)-1-aryl-prop-2-en-1-one derivatives, and spectroscopically characterized. The biological activity of the compounds was evaluated against *E. coli*, *P. aeruginosa*, *S. aureus* and *C. albicans* by the agar diffusion method. The potency of compounds **18**, **28** and **30** as antifungics against *C. albicans* is about 50% of that of Clotrimazole. On the other hand, the potency of compounds **1**, **3**, **7**, **20**, **23**, **31** and **34** as antibacterials against *E. coli* is about 50% of that of Ampicillin.

Table 1. *In vitro* antimicrobial activity of the test compounds and evaluation of their antimicrobial activity of the inhibition zone (IZ) and the minimal inhibitory concentration (MIC)

Compound / Microorganism	*E. coli*		*S. aureus*		*C. albicans*		*P. aeruginosa*	
	IZ	MIC	IZ	MIC	IZ	MIC	IZ	MIC
Ampicillin 10 μg *per* disc	18	25	22	12.5	-----	------	-----	-----
Ciprofloxacin 5 μg *per* disc	28	12.5	30	25	-----	------	38	25
Clotrimazole 100 μg *per* disc	----	-----	-----	------	40	12.5	-----	------
Imipenem 10 μg *per* disc	26	-----	30	------	-----	----	30	------
1	20	50	14	200	15	100	22	200
2	20	100	14	100	13	100	22	100
3	15	50	10	200	13	100	18	200
4	21	100	14	100	12	100	22	200
5	20	100	14	200	12	50	22	100
6	15	100	12	200	12	100	16	200
7	15	50	10	200	12	100	17	100
8	21	100	13	200	15	100	22	200
9	20	100	14	200	12	50	22	200
10	20	100	14	100	12	100	22	100
11	15	100	12	200	14	100	17	200
12	22	100	14	100	12	100	22	100
13	20	100	13	100	12	100	22	100
14	20	100	13	100	12	100	22	200
15	20	100	13	200	13	100	22	200
16	20	100	14	100	12	100	22	2000
17	20	100	13	100	16	100	22	200
18	16	100	13	200	13	25	17	100
19	15	100	13	200	15	100	20	200
20	15	50	11	100	13	100	17	200
21	20	100	14	200	11	100	22	100
22	22	100	14	100	12	100	22	200
23	22	50	13	100	19	100	22	200
24	20	100	14	200	15	100	22	100
25	20	100	13	100	12	100	22	200
26	16	100	12	200	13	100	17	100
27	16	100	12	100	14	100	17	200
28	15	100	11	200	13	25	17	100
29	15	100	12	200	13	100	17	200
30	16	100	12	200	14	25	19	100
31	15	50	12	100	14	100	17	100
32	15	100	13	200	15	100	20	100
33	16	100	13	100	15	100	20	200
34	16	50	14	200	15	100	20	200
35	15	100	13	100	15	100	20	200
36	16	100	13	200	15	50	20	200

Experimental

Chemistry

General experimental considerations

Reagent quality solvents were used without purification. Melting points were obtained in open capillary tubes by using a MEL-Temp II melting point apparatus and are uncorrected. Infrared spectra (IR) were recorded on a Perkin-Elmer 1600 series Fourier transform instrument with the samples as KBr pellets. ^{1}H NMR and ^{13}C NMR spectra were recorded on JEOL 500 MHz spectrometers at ambient temperature using tetramethylsilane as an internal reference. Mass spectra were recorded on a JEOL JMS AX-500 spectrometer by using electron impact ionization at 70 eV. Elemental analyses were carried out by the University of Cairo Microanalytical Laboratories. The antimicrobial tests were carried out at the Pharmaceutical Department, Faculty of Pharmacy, Alexandria University. ChemDraw-Ultra-11.0 has been used for the nomenclature of the prepared compounds.

*General procedure for the preparation of compounds **1-3***

An equimolar mixture of anthracene-9-carbaldehyde (2.06 g, 0.01 mol) and the substituted ketone (1.54 g 4-chloro acetophenone, 1.34 g 4-methyl acetophenone or 1.10 g 2-acetylfuran) in 2% ethanolic KOH (20 mL) was stirred at r.t. for 4 h. The solid product was cooled, collected by filtration, washed with ethanol, dried and recrystallized from chloroform/ethanol.

*3-(Anthracen-9-yl)-1-(4-chlorophenyl)prop-2-en-1-one (**1**)*

Yield: 90%, orange-yellow crystals, mp 124-125 ºC. IR (KBr) ν_{max}/cm^{-1}: 1593 (C_2=C_3), 1656 (C=O); ^{1}H NMR ($CDCl_3$) δ 7.45-7.51 (m, 7H, =CH-2 and 6 ArH), 8.00 (d, 4H, *J* 8 Hz, ArH), 8.27 (d, 2H, *J* 8 Hz, ArH), 8.42 (s,1H, $H_{anth\text{-}10}$), 8.79 (d, 1H, *J* 16 Hz, =CH-3); ^{13}C NMR (DMSO-d_6) δ 125.2, 125.4, 125.5, 125.6, 126.6, 126.7, 128.7, 128.8, 129.0, 129.2, 129.3, 129.5, 129.7, 130.0, 130.1, 130.3, 130.6, 131.4, 136.3, 139.7, 142.5, 142.6, 188.5 (C=O). Anal. Calc. for $C_{23}H_{15}ClO$ (342.08): C, 80.58; H, 4.41. Found: C, 80.63; H, 4.57%.

*3-(Anthracen-9-yl)-1-p-tolylprop-2-en-1-one (**2**)*

Yield: 86%, yellow crystals, mp 111-112 ºC. IR (KBr) ν_{max}/cm^{-1}: 1601 (C_2=C_3), 1660 (C=O); ^{1}H NMR (DMSO-d_6) δ 2.19 (3H, s, *p*-CH_3), 6.94 (d, 2H, *J* 8.0 Hz, ArH), 7.31 (d, 2H, *J* 8.0 Hz, ArH;), 7.49-7.54 (m, 4H, ArH), 7.83 (d, 1H, *J* 16 Hz, =CH-2), 8.03 (t, 2H, *J* 7.0 Hz, ArH;), 8.31 (d, 2H, *J* 7.0 Hz, ArH), 8.47 (s, 1H, $H_{anth\text{-}10}$), 8.79 (d, 1H, *J* 16 Hz, =CH-3). Anal. Calc. for $C_{24}H_{18}O$ (322.40): C, 89.41; H, 5.63. Found: C, 89.60; H, 5.70%.

*3-(Anthracen-9-yl)-1-(furan-2-yl)prop-2-en-1-one (**3**)*

Yield: 87%, yellow crystals, mp 140-141 ºC. IR (KBr) ν_{max}/cm^{-1}: 1594 (C_2=C_3), 1651 (C=O); ^{1}H NMR (DMSO-d_6) δ 6.75 (t, 1H, *J* 8.0 Hz, ArH), 7.50-7.58 (m, 5H, =CH-2 + 4 ArH), 7.74 (d, 1H, *J* 3.0 Hz, ArH), 8.12 (d, 3H, *J* 8.0 Hz, ArH) 8.20 (d, 2H, *J* 8.0 Hz, ArH), 8.60 (d, 1H, *J* 16 Hz, =CH-3), 8.66 (s, 1H, $H_{anth\text{-}10}$). Anal. Calc. for $C_{21}H_{14}O_2$ (298.33): C, 84.54; H, 4.73. Found: C, 84.65; H, 4.81%.

*General procedure for the preparation of compounds **4-6***

A mixture of 3-(anthracen-9-yl)-1-(aryl)prop-2-en-1-one (**1**-**3**, 0.001 mol) and hydrazine hydrate (3 mL) in formic acid (15 mL) was heated under reflux for 8 h. The reaction mixture was poured onto crushed ice, the precipitated product was filtered, washed with water, dried and recrystallized from chloroform/ethanol.

*5-(Anthracen-9-yl)-3-(4-chlorophenyl)-4, 5-dihydro-1H-pyrazole-1-carbaldehyde (**4**)*

Yield: 85%, buff crystals, mp 225-226 ºC. IR (KBr) ν_{max}/cm^{-1}: 1674 (C=O); ^{1}H NMR (DMSO-d_6) δ 3.36-3.39 (m, 1H, pyrazoline-H_4), 3.85-4.09 (m, 1H, pyrazoline-$H_{4'}$), 6.86-6.96 (dd, 1H, $J_{1,2}$ 13, $J_{1,3}$ 18 Hz, pyrazoline-H_5), 7.48 (dd, 2H, *J* 3, 7.0 Hz, ArH), 7.56 (d, 2H, *J* 7.6 Hz, ArH), 7.69 (d, 2H, *J* 7.0 Hz, ArH), 7.91(d, 2H, *J* 7.0 Hz, ArH), 8.05 (dd, 2H, *J* 3.0, 7.0 Hz, ArH), 8.11 (d, 2H, *J* 7.6 Hz, ArH), 8.53 (s, 1H, $H_{anth\text{-}10}$), 8.84 (s, 1H, CHO). Anal. Calc. for $C_{24}H_{17}ClN_2O$ (384.86): C, 74.90; H, 4.45; N, 7.28. Found: C, 74.65; H, 4.23; N, 7.49%.

*5-(Anthracen-9-yl)-3-p-tolyl-4,5-dihydro-1H-pyrazole-1-carbaldehyde (**5**)*

Yield: 81%, brown crystals, mp 199-200 ºC. IR (KBr) ν_{max}/cm^{-1}: 1666 (C=O); ^{1}H NMR (DMSO-d_6) δ 2.19 (3H, s, *p*-CH_3), 3.15-3.30 (1H, m, pyrazoline-H_4), 4.08 (dd, 1H, $J_{1,2}$ 13, $J_{1,3}$ 18 Hz, pyrazoline-$H_{4'}$), 6.88 (t, 1H, *J* 7.0, 12 Hz, pyrazoline-H_5), 7.37-7.58 (m, 6H, ArH), 7.67 (d, 1H, *J* 8.0 Hz, ArH), 7.86 (d, 2H, *J* 7.6 Hz, ArH), 8.00 (d, 2H, *J* 8.0 Hz, ArH), 8.56-8.58 (m, 2H, ArH), 9.00 (s, 1H, CHO). Anal. Calc. for $C_{25}H_{20}N_2O$ (364.44): C, 82.39; H, 5.53; N, 7.69. Found: C, 82.15; H, 5.33; N, 7.90%.

*5-(Anthracen-9-yl)-3-(furan-2-yl)-4, 5-dihydro-1H-pyrazole-1-carbaldehyde (**6**)*

Yield: 78%, buff crystals, mp 204-205 ºC. IR (KBr) ν_{max}/cm^{-1}: 1670 (C=O); ^{1}H NMR (DMSO-d_6) δ 3.28-3.42

(m, 1H, pyrazoline-H_4), 3.98-4.07 (m, 1H, pyrazoline-$H_{4'}$), 6.40-6.48 (m, 1H, pyrazoline-H_5), 6.54 (d, 1H, *J* 3.0 Hz, ArH), 6.70 (t, 1H, *J* 8.0 Hz, ArH), 6.86 (d, 2H, *J* 7.0 Hz, ArH), 7.05 (d, 2H, *J* 7.0 Hz, ArH), 7.20 (d, 1H, *J* 8.0 Hz, ArH), 7.44 (dd, 2H, *J* 3.0, 7.0 Hz, ArH), 8.03 (dd, 2H, *J* 3.0, 7.0 Hz, Ar-H), 8.52 (s, 1H, $H_{anth\text{-}10}$), 8.59 (s, 1H, CHO). Anal. Calc. for $C_{22}H_{16}N_2O_2$ (340.37): C, 77.63; H, 4.74; N, 8.23. Found: C, 77.69; H, 4.83; N, 8.04%.

*General procedure for the preparation of compounds **7** and **8***

To a solution of 5-(anthracen-9-yl)-3-aryl-4, 5-dihydro-1*H*-pyrazole-1-carbaldehyde **4** (3.84 g, 0.01 mol) or **5** (3.64 g, 0.01 mol) in ethanol (30 mL) was added benzoyl hydrazine (1.63 g, 0.012 mol) and two drops of acetic acid. The reaction mixture was heated under reflux for 6 h, partially concentrated and cooled. The separated solid product was filtered, washed with ethanol, dried and crystallized from ethanol.

*N'-((5-(Anthracen-9-yl)-3-(4-chlorophenyl)-4,5-dihydro-1H-pyrazole-1-yl)methylene) benzoylhydrazide (**7**)*

Yield: 77%, buff crystals, mp 207-208 ºC. IR (KBr) ν_{max}/cm^{-1}: 1659 (C=O), 3255 (NH); ^{1}H NMR (DMSO-d_6) δ 3.38-3.59 (m, 1H, pyrazoline-H_4), 4.51-4.53 (m, 1H, pyrazoline-$H_{4'}$), 6.71-6.86 (m, 1H, pyrazoline-H_5), 7.31-7.37 (m, 4H, ArH), 7.47-7.62 (m, 2H, ArH), 7.71-7.83 (m, 5H, ArH), 7.89-7.96 (m, 4H, ArH), 8.04 (s, 1H, N_1CH=N), 8.17-8.32 (m, 2H, ArH), 8.52 (s, 1H, $H_{anth\text{-}10}$), 10.48 (s, 1H, NH; D_2O exchangeable). Anal. Calc. for $C_{31}H_{23}ClN_4O$ (502.99): C, 74.02; H, 4.61; N, 11.14. Found: C, 74.24; H, 4.85; N, 11.00%.

*N'-((5-(Anthracen-9-yl)-3-p-tolyl-4,5-dihydro-1H-pyrazole-1-yl)methylene)benzoylhydrazide (**8**)*

Yield: 74%, buff crystals, mp 181-182 ºC. IR (KBr) ν_{max}/cm^{-1}: 1662 (C=O), 3267 (NH); ^{1}H NMR ($CDCl_3$) δ 2.18 (3H, s, *p*-CH_3), 3.46 (dd, 1H, $J_{1,2}$ 9, $J_{1,3}$ 18 Hz, pyrazoline-H_4), 3.85 (dd, 1H, $J_{1,2}$ 13, $J_{1,3}$ 18 Hz, pyrazoline-$H_{4'}$), 6.86 (dd, 1H, $J_{1,2}$ 9, $J_{1,3}$ 13 Hz, pyrazoline-H_5), 7.34-7.46 (m, 10H, ArH), 7.73-7.81 (m, 4H, ArH), 8.00-8.10 (m, 3H, ArH), 8.41 (s, 1H, N_1CH=N), 8.50 (s, 1H, $H_{anth\text{-}10}$), 10.47 (s, 1H, NH; D_2O exchangeable). Anal. Calc. for $C_{32}H_{26}N_4O$ (482.58): C, 79.64; H, 5.43; N, 11.61. Found: C, 79.41; H, 5.60; N, 11.83%.

*General procedure for the preparation of compounds **9**-**11***

A mixture of 3-(anthracen-9-yl)-1-(aryl)prop-2-en-1-one (**1-3**, 0.001 mol) and hydrazine hydrate (3 mL) in acetic acid (15 mL) was heated under reflux for 8 h. The reaction mixture was poured onto crushed ice, the precipitated product was filtered, washed with water, dried and recrystallized from chloroform/ethanol.

*1-(5-(Anthracen-9-yl)-3-(4-chlorophenyl)-4,5-dihydro-1H-pyrazol-1-yl)ethanone (**9**)*

Yield: 84%, buff crystals, mp 239-240 ºC. IR (KBr) ν_{max}/cm^{-1}: 1655 (C=O); ^{1}H NMR ($CDCl_3$) δ 2.35 (s, 3H, $COCH_3$), 3.46 (dd, 1H, $J_{1,2}$ 9, $J_{1,3}$ 18 Hz, pyrazoline-H_4), 3.85 (dd, 1H, $J_{1,2}$ 13, $J_{1,3}$ 18 Hz, pyrazoline-$H_{4'}$), 6.85 (dd, 1H, $J_{1,2}$ 9, $J_{1,3}$ 13 Hz, pyrazoline-H_5), 7.33-7.48 (m, 5H, ArH), 7.55 (t, 1H, *J* 7.6 Hz, ArH), 7.74 (dd, 3H, *J* 2, 9 Hz, ArH), 8.01 (dd, 2H, *J* 3, 7.6 Hz, ArH), 8.41 (s, 1H, $H_{anth\text{-}10}$), 8.49 (d, 1H, *J* 9 Hz, ArH). Anal. Calc. for $C_{25}H_{19}ClN_2O$ (398.88): C, 75.28; H, 4.80; N, 7.02. Found: C, 75.08; H, 4.65; N, 7.21%.

*1-(5-(Anthracen-9-yl)-3-p-tolyl-4,5-dihydro-1H-pyrazol-1-yl)ethanone (**10**)*

Yield: 78%, buff crystals, mp 194-195 ºC. IR (KBr) ν_{max}/cm^{-1}: 1667 (C=O); ^{1}H NMR ($CDCl_3$) δ 2.37 (s, 3H, $COCH_3$), 2.43 (s, 3H, *p*-CH_3), 3.48 (dd, 1H, $J_{1,2}$ 9, $J_{1,3}$ 18 Hz, pyrazoline-H_4), 3.89 (dd, 1H, $J_{1,2}$ 13, $J_{1,3}$ 18 Hz, pyrazoline-$H_{4'}$) 6.85 (dd, 1H, $J_{1,2}$ 9, $J_{1,3}$ 13 Hz, pyrazoline-H_5), 7.27 (t, 2H, *J* 7.6 Hz, ArH), 7.32-7.41 (m, 2H, ArH), 7.49 (t, 1H, *J* 7.6 Hz, ArH), 7.54-7.57 (m, 1H, ArH), 7.72 (d, 2H, *J* 7.6 Hz, ArH), 7.79 (d, 1H, *J* 8 Hz, ArH), 8.01 (d, 2H, *J* 8.0 Hz, ArH), 8.42 (s, 1H, $H_{anth\text{-}10}$), 8.52 (d, 1H, *J* 8.0 Hz, ArH). Anal. Calc.for $C_{26}H_{22}N_2O$ (378.47): C, 82.51; H, 5.86; N, 7.40. Found: C, 82.72; H, 5.98; N, 7.19%.

*1-(5-(Anthracen-9-yl)-3-(furan-2-yl)-4,5-dihydro-1H-pyrazol-1-yl)ethanone (**11**)*

Yield: 80%, buff crystals, mp 200-201 ºC. IR (KBr) ν_{max}/cm^{-1}: 1657 (C=O); ^{1}H NMR (DMSO-d_6) δ 2.15 (3H, s, $COCH_3$), 3.27 (dd, 1H, $J_{1,2}$ 9, $J_{1,3}$ 18 Hz, pyrazoline-H_4), 4.03 (dd, 1H, $J_{1,2}$ 13, $J_{1,3}$ 18 Hz, pyrazoline-$H_{4'}$), 6.66-6.67 (m, 1H, ArH), 6.84 (dd, 1H, $J_{1,2}$ 9, $J_{1,3}$ 13 Hz pyrazoline-H_5), 6.99 (d, 1H, *J* 3.0 Hz, ArH), 7.42 (t, 2H, *J* 8.0 Hz, ArH), 7.51 (t, 1H, *J* 7.0 Hz, ArH), 7.56 (t, 1H, *J* 7.0 Hz, ArH), 7.68 (d, 1H, *J* 3.0 Hz, ArH),7.90 (s, 1H, $H_{anth\text{-}10}$), 8.07 (d, 2H, *J* 7.0 Hz, ArH), 8.55-8.56 (m, 2H, ArH). Anal. Calc. for $C_{23}H_{18}N_2O_2$ (354.40): C, 77.95; H, 5.12; N, 7.90. Found: C, 77.73; H, 5.32; N, 7.99%.

*General procedure for the preparation of compounds **12** and **13***

An equimolar mixture of 1-(5-(anthracen-9-yl)-3-aryl-4, 5-dihydro-1*H*-pyrazol-1-yl)ethanone **9** (3.98 g,

0.01 mol) or **10** (3.78 g, 0.01 mol) and benzaldehyde (1.06 g, 0.01 mol) in 2% ethanolic KOH (20 mL) was stirred at r.t. for 4 h. The solid product was cooled, collected by filtration, washed with ethanol, dried, and recrystallized from chloroform/ethanol.

*1-(5-(Anthracen-9-yl)-3-(4-chlorophenyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenyl-prop-2-en-1-one (**12**)*

Yield: 71%, off white needles, mp 259-260 ºC. IR (KBr) ν_{max}/cm^{-1}: 1650 (C=O); ^{1}H NMR (DMSO-d_6) δ 3.33-3.37 (m, 1H, pyrazoline-H$_4$), 4.07 (dd, 1H, $J_{1,2}$ 13, $J_{1,3}$ 18 Hz, pyrazoline-H$_4$'), 6.88 (dd, 1H, $J_{1,2}$ 9, $J_{1,3}$ 13 Hz, pyrazoline-H$_5$), 7.40 (d, 1H, *J* 6.0 Hz, =CH-1.), 7.42-7.47 (m, 4H, ArH), 7.50-7.58 (m, 5H, ArH), 7.67 (d, 2H, *J* 8 Hz, ArH), 7.86 (d, 2H, *J* 7.6 Hz, ArH), 7.96 (d, 2H, *J* 8 Hz, ArH), 8.08 (d, 2H, *J* 7.6 Hz, ArH), 8.55 (s, 1H, H$_{anth\text{-}10}$), 8.67 (d, 1H, *J* 6.0 Hz, =CH-2). Anal. Calc. for $C_{32}H_{23}ClN_2O$ (486.99): C, 78.92; H, 4.76; N, 5.75. Found: C, 79.00; H, 4.82; N, 5.58%.

*1-(5-(Anthracen-9-yl)-3-p-tolyl-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylprop-2-en-1-one (**13**)*

Yield: 73%, off white needles, mp 225-226 ºC. IR (KBr) ν_{max}/cm^{-1}: 1652 (C=O); ^{1}H NMR (DMSO-d_6) δ 2.33 (3H, s, *p*-CH$_3$), 3.27-3.38 (m, 1H, pyrazoline-H$_4$), 4.07 (dd, 1H, $J_{1,2}$ 13, $J_{1,3}$ 18 Hz, pyrazoline-H$_4$'), 6.86 (dd, 1H, $J_{1,2}$ 9, $J_{1,3}$ 13 Hz, pyrazoline-H$_5$), 7.28 (d, 1H, *J* 6 Hz, =CH-1), 7.35 (t, 2H, *J* 7.6 Hz, ArH), 7.41 (t, 2H, *J* 7.0 Hz, ArH), 7.50-7.58 (m, 5H, ArH), 7.70 (d, 2H, *J* 7.0 Hz, ArH), 7.77 (d, 2H, *J* 7.6 Hz, ArH), 8.08 (d, 2H, *J* 8.0 Hz, ArH), 8.55 (s, 1H, H$_{anth\text{-}10}$), 8.58 (d, 2H, *J* 8.0 Hz, ArH), 8.70 (d, 1H, *J* 6.0 Hz, =CH-2). Anal. Calc. for $C_{33}H_{26}N_2O$ (466.57): C, 84.95; H, 5.62; N, 6.00. Found: C, 84.70; H, 5.90; N, 6.27%.

*General procedure for the preparation of compounds **14-19***

To a solution of 1-(5-(anthracen-9-yl)-3-aryl-4, 5-dihydro-1*H*-pyrazol-1-yl)ethanone (**9-11**, 0.01 mol) in ethanol (25 mL) was added hydrazine hydrate or aryl hydrazine (0.012 mol) and two drops of acetic acid. The reaction mixture was heated under reflux for 8 h, partially concentrated and cooled. The separated solid product was filtered, washed with ethanol, dried and crystallized from ethanol.

*5-(Anthracen-9-yl)-3-(4-chlorophenyl)-1-(1-(2-phenylhydrazono)ethyl)-4,5-dihydro-1H-pyrazole (**14**)*

Yield: 77%, buff crystals, mp 270-271 ºC. IR (KBr) ν_{max}/cm^{-1}: 3295 (NH); ^{1}H NMR (DMSO-d_6) δ 2.19 (3H, s, N=C-CH$_3$), 3.22-3.40 (m, 1H, pyrazoline-H$_4$), 4.07 (m, 1H, pyrazoline-H$_4$'), 6.89 (dd, 1H, $J_{1,2}$ 9, $J_{1,3}$ 13 Hz, pyrazoline-H$_5$), 7.37 (t, 2H, *J* 8 Hz, ArH), 7.42 (t, 2H, *J* 7.0 Hz, ArH), 7.52-7.58 (m, 5H, ArH), 7.66 (d, 2H, *J* 8.0 Hz, ArH), 7.87 (d, 4H, *J* 8.0 Hz, ArH), 8.06 (d, 2H, *J* 7.0 Hz, ArH), 8.56 (s, 1H, H$_{anth\text{-}10}$), 9.58 (s, 1H, NH; D$_2$O exchangeable). Anal. Calc.for $C_{31}H_{25}ClN_4$ (489.01): C, 76.14; H, 5.15; N, 11.46. Found: C, 76.31; H, 5.26; N, 11.19%.

*5-(Anthracen-9-yl)-1-(1-(2-phenylhydrazono)ethyl)-3-p-tolyl-4,5-dihydro-1H-pyrazole (**15**)*

Yield: 78%, reddish brown crystals, mp 89-90 ºC. IR (KBr) ν_{max}/cm^{-1}: 3297 (NH); ^{1}H NMR (DMSO-d_6) δ 2.19 (3H, s, N=C-CH$_3$), 2.34 (3H, s, *p*-CH$_3$), 3.33-3.39 (m, 1H, pyrazoline-H$_4$), 4.08 (m, 1H, pyrazoline-H$_4$'), 6.87 (dd, 1H, $J_{1,2}$ 9, $J_{1,3}$ 13 Hz, pyrazoline-H$_5$), 7.21-7.77 (m, 12H, ArH), 8.09 (d, 2H, *J* 8.0 Hz, ArH), 8.18-8.20 (m, 2H, ArH), 8.56-8.60 (m, 2H, ArH), 10.61 (s, 1H, NH; D$_2$O exchangeable). Anal. Calc.for $C_{32}H_{28}N_4$ (468.59): C, 82.02; H, 6.02; N, 11.96. Found: C, 82.25; H, 5.88; N, 12.20%.

*5-(Anthracen-9-yl)-3-(4-chlorophenyl)-1-(1-(2-(4-nitrophenyl)hydrazono)ethyl)-4,5-dihydro-1H-pyrazole (**16**)*

Yield: 79%, pale brown crystals, mp 180-181 ºC. IR (KBr) ν_{max}/cm^{-1}: 3285 (NH); ^{1}H NMR (DMSO-d_6) δ 2.19 (s, 3H, N=C-CH$_3$), 3.26-3.33 (m, 1H, pyrazoline-H$_4$), 4.08 (dd, 1H, $J_{1,2}$ 13, $J_{1,3}$ 18 Hz, pyrazoline-H$_4$'), 6.88 (dd, 1H, $J_{1,2}$ 9, $J_{1,3}$ 13 Hz, pyrazoline-H$_5$),7.43-7.52 (m, 4H, ArH), 7.55 (d, 2H, *J* 9.0 Hz, ArH), 7.66 (d, 2H, *J* 9.0 Hz, ArH), 7.69-7.74 (m, 2H, ArH), 7.87 (d, 2H, *J* 8.0 Hz, ArH;), 7.97 (d, 2H, *J* 7.6 Hz, ArH), 8.08 (d, 2H, *J* 7.6 Hz, ArH), 8.57 (s, 1H, H$_{anth\text{-}10}$), 9.22 (s, 1H, NH; D$_2$O exchangeable). Anal. Calc. for $C_{31}H_{24}ClN_5O_2$ (534.01): C, 69.72; H, 4.53; N, 13.11. Found: C, 69.79; H, 4.80; N, 12.97%.

*5-(Anthracen-9-yl)-1-(1-(2-(4-nitrophenyl)hydrazono) ethyl)-3-p-tolyl-4,5-dihydro-1H-pyrazole (**17**)*

Yield: 80%, pale brown crystals, mp 85-86 ºC. IR (KBr) ν_{max}/cm^{-1}: 3300 (NH); ^{1}H NMR (DMSO-d_6) δ 2.19 (3H, s, N=C-CH$_3$), 2.33 (3H, s, *p*-CH$_3$), 3.30-3.40 (m, 1H, pyrazoline-H$_4$), 4.08 (dd, 1H, $J_{1,2}$ 13, $J_{1,3}$ 18 Hz, pyrazoline-H$_4$'), 6.86 (dd, 1H, $J_{1,2}$ 9, $J_{1,3}$ 13 Hz, pyrazoline-H$_5$), 7.28 (d, 2H, *J* 8.0 Hz, ArH), 7.34-7.43 (m, 3H, ArH), 7.50-7.58 (m, 3H, ArH), 7.69-7.82 (m, 4H, ArH), 8.12 (d, 2H, *J* 8.0 Hz, ArH), 8.55 (s, 1H, H$_{anth\text{-}10}$), 8.58 (d, 2H, *J* 8.0 Hz, ArH), 9.20 (s, 1H, NH; D$_2$O exchangeable), MS *m/z*: 513 (M). Anal. Calc.for $C_{32}H_{27}N_5O_2$ (513.59): C, 74.83; H, 5.30; N, 13.64. Found: C, 74.60; H, 5.09; N, 13.85%.

*5-(Anthracen-9-yl)-3-(furan-2-yl)-1-(1-(2-(4-nitrophenyl) hydrazono)ethyl)-4,5-dihydro-1H-pyrazole (**18**)*

Yield: 81%, brown crystals, mp 120-121 ºC. IR (KBr) ν_{max}/cm^{-1}: 1323, 1502 (NO_2), 3372 (NH); ^{1}H NMR (DMSO-d_6) δ 2.14 (3H, s, N=C-CH_3), 3.26 (dd, 1H, $J_{1,2}$ 9, $J_{1,3}$ 18 Hz, pyrazoline-H_4), 4.03 (dd, 1H, $J_{1,2}$ 13, $J_{1,3}$ 18 Hz, pyrazoline-$H_{4'}$), 6.84 (dd, 1H, $J_{1,2}$ 9, $J_{1,3}$ 13 Hz pyrazoline-H_5), 6.98 (d, 1H, *J* 3.0 Hz, ArH), 7.42 (t, 3H, *J* 3.8 Hz, ArH), 7.50-7.56 (m, 4H, ArH), 7.67 (d, 1H, *J* 10 Hz, ArH), 7.93 (s, 1H, $H_{anth\text{-}10}$), 8.07 (d, 4H, *J* 7.6 Hz, ArH), 8.54-8.56 (m, 2H, ArH), 9.20 (s, 1H, NH; D_2O exchangeable). Anal. Calc. for $C_{29}H_{23}N_5O_3$ (489.52): C, 71.15; H, 4.74; N, 14.31. Found: C, 71.33; H, 4.51; N, 14.05%.

*5-(Anthracen-9-yl)-3-(4-chlorophenyl)-1-(1-hydrazonoethyl)-4, 5-dihydro-1H-pyrazole (**19**)*

Yield: 85%, pale yellow needles, mp 275-276 ºC. ^{1}H NMR (DMSO-d_6) δ 2.19 (3H, s, N=C-CH_3), 3.38 (m, 1H, pyrazoline-H_4), 4.08 (dd, 1H, $J_{1,2}$ 13, $J_{1,3}$ 18 Hz, pyrazoline-$H_{4'}$), 6.91 (dd, 1H, $J_{1,2}$ 9, $J_{1,3}$ 13 Hz, pyrazoline-H_5), 7.22 (s, 2H, NH_2; D_2O exchangeable), 7.37-7.43 (m, 2H, ArH), 7.51-7.57 (m, 4H, ArH), 7.67 (d, 2H, *J* 7.0 Hz, ArH), 7.88 (d, 2H, *J* 8.0 Hz, ArH), 8.09 (d, 2H, *J* 8.0 Hz, ArH), 8.57 (s, 1H, $H_{anth\text{-}10}$). Anal. Calc. for $C_{25}H_{21}ClN_4$ (412.91): C, 72.72; H, 5.13; N, 13.57. Found: C, 72.63; H, 4.95; N, 13.73%.

*5-(Anthracen-9-yl)-7-(4-chlorophenyl)-3-methyl-1-phenyl-1, 5-dihydropyrazolo[1,2-a]tetrazole (**20**)*

A mixture of 4,5-dihydro-1*H*-pyrazole derivative **14** (0.49 g, 0.001 mol) and acetic anhydride (10 mL) was heated on a boiling water bath for 5 h. The reaction mixture was poured onto crushed ice, the precipitated product was filtered, washed with water, dried and recrystallized from ethanol/chloroform, furnishing **20**.

Yield: 65%, buff crystals, mp 169-170 ºC. ^{1}H NMR (DMSO-d_6) δ 2.32 (3H, s, CH_3), 4.34-4.38 (m, 1H, pyrazoline-H_4), 4.50-4.53 (m, 1H, pyrazoline-H_5), 7.27 (t, 2H, *J* 7.6 Hz, ArH), 7.37-7.51 (m, 3H, ArH), 7.68 (d, 2H, *J* 8.0 Hz, ArH), 7.90-7.91 (m, 2H, ArH), 7.99 (d, 2H, *J* 8.0 Hz, ArH), 8.04 (d, 2H, *J* 7.6 Hz, ArH), 8.12 (d, 2H, *J* 7.6 Hz, ArH), 8.17-8.19 (m, 2H, ArH), 8.68 (s, 1H, $H_{anth\text{-}10}$). ^{13}C NMR (DMSO) δ 22.16, 56.88, 122.93, 123.11, 124.36, 126.79, 127.04, 128.07, 128.30, 128.95, 129.11, 129.47, 129.69, 130.07, 130.38, 130.51, 130.58, 131.44, 131.95, 132.94, 135.62, 154.09. Anal. Calc. for $C_{31}H_{23}ClN_4$ (486.99): C, 76.46; H, 4.76; N, 11.50. Found: C, 76.53; H, 4.81; N, 11.41%.

*General procedure for the preparation of compounds **21-23***

To a solution of 3-(anthracen-9-yl)-1-(aryl)prop-2-en-1-one (**1**, 0.34 g, 0.001 mol or **2**, 0.32 g, 0.001 mol) in absolute ethanol (20 mL) was added the proper aryl hydrazine hydrochloride (0.0012 mol). The reaction mixture was heated under reflux for 4 h. A solid product was obtained after concentration and cooling. The precipitated product was filtered, washed with ethanol, dried, and recrystallized from ethanol/chloroform.

*5-(Anthracen-9-yl)-1-(4-bromophenyl)-3-(4-chlorophenyl)-4, 5-dihydro-1H-pyrazole (**21**)*

Yield: 70%, buff crystals, mp 299-300 ºC. ^{1}H NMR (DMSO-d_6) δ 3.12-3.39 (1H, m, pyrazoline-H_4), 3.94-4.06 (1H, m, pyrazoline-$H_{4'}$), 6.86-6.94 (1H, m, pyrazoline-H_5), 7.03-7.15 (m, 4H, ArH), 7.30 (d, 2H, *J* 7.6 Hz, ArH), 7.41 (t, 2H, *J* 7.6 Hz, ArH), 7.48 (t, 2H, *J* 7 Hz, Ar-H), 7.71 (d, 2H, *J* 8.0 Hz, ArH), 7.91 (d, 2H, *J* 8.0 Hz, ArH), 8.05 (d, 2H, *J* 8.0 Hz, ArH), 8.53 (s, 1H, $H_{anth\text{-}10}$). Anal. Calc. for $C_{29}H_{20}BrClN_2$ (511.84): C, 68.05; H, 3.94; N, 5.47. Found: C, 68.27; H, 4.09; N, 5.22%.

*5-(Anthracen-9-yl)-1-(4-bromophenyl)-3-p-tolyl)-4,5-dihydro-1H-pyrazole (**22**)*

Yield: 73%, brown crystals, mp 130-131 ºC. ^{1}H NMR (DMSO-d_6) δ 2.17 (s, 3H, *p*-CH_3), 3.34 (dd, 1H, $J_{1,2}$ 9, $J_{1,3}$ 18 Hz, pyrazoline-H_4), 4.09 (dd, 1H, $J_{1,2}$ 13, $J_{1,3}$ 18 Hz, pyrazoline-$H_{4'}$), 6.86 (dd, 1H, $J_{1,2}$ 9, $J_{1,3}$ 13 Hz, pyrazoline-H_5), 7.34 (t, 2H, *J* 7.6 Hz, ArH), 7.41 (t, 2H, *J* 7.6 Hz, ArH), 7.49-7.58 (m, 5H, Ar-H), 7.62 (d, 2H, *J* 9.0 Hz, ArH), 7.85 (d, 2H, *J* 8.0 Hz, ArH), 8.08 (d, 2H, *J* 8.0 Hz, ArH), 8.54-8.56 (m, 1H, ArH). Anal. Calc. for $C_{30}H_{23}BrN_2$ (491.42): C, 73.32; H, 4.72; N, 5.70. Found: C, 73.59; H, 4.61; N, 5.51%.

*5-(Anthracen-9-yl)-1-(naphthalene-2-yl)-3-p-tolyl-4, 5-dihydro-1H-pyrazole (**23**)*

Yield: 77%, pale brown crystals, mp 160-161 ºC. ^{1}H NMR (DMSO-d_6) δ 2.44 (3H, s, *p*-CH_3), 2.99-3.39 (m, 1H, pyrazoline-H_4), 3.78-4.04 (m, 1H, pyrazoline-$H_{4'}$), 6.92-6.98 (m, 1H, pyrazoline-H_5), 7.21-7.27 (m, 4H, ArH), 7.29 (dd, 2H, *J* 7.6, 13 Hz, ArH), 7.39-7.43 (m, 2H, ArH), 7.57-7.79 (m, 4H, ArH), 7.81 (dd, 1H, *J* 3.0, 5.0 Hz, ArH), 7.97 (dd, 2H, *J* 7.6, 13 Hz), 8.20-8.28 (m, 2H, ArH), 8.31 (dd, 1H, *J* 3.0, 5.0 Hz, ArH), 8.50 (s, 1H, ArH), 8.52 (s, 1H, ArH). Anal. Calc. for $C_{34}H_{26}N_2$ (462.58): C, 88.28; H, 5.57; N, 6.06. Found: C, 88.05; H, 5.43; N, 6.24%.

*General procedure for the preparation of compounds **24** and **25***

A mixture of 3-(anthracen-9-yl)-1-(aryl)prop-2-en-1-one (**1**, 0.34 g, 0.001 mol or **2**, 0.32 g, 0.001 mol) and hydrazine hydrate (3 mL) in ethanol (20 mL) was heated under reflux for 4 h. The solid product was obtained after concentration and cooling, the precipitated product was filtered, washed with ethanol, dried and recrystallized from ethanol.

*5-(Anthracen-9-yl)-3-(4-chlorophenyl)-4, 5-dihydro-1H-pyrazole (**24**)*

Yield: 74%, pale brown crystals, mp 230-231 ºC. IR (KBr) ν_{max}/cm^{-1}: 3254 (NH); ^{1}H NMR (DMSO-d_6) δ 3.60-4.11 (m, 2H, pyrazoline-H_4,$H_{4'}$), 6.71-6.74 (m, 1H, pyrazoline-H_5), 7.01-7.11 (m, 2H, ArH), 7.25-7.40 (m, 2H, ArH), 7.50-7.71 (m, 4H, ArH), 7.83-7.91 (m, 4H, ArH), 8.18 (s, 1H, $H_{anth\text{-}10}$), 8.56 (s, 1H, NH; D_2O exchangeable), MS *m/z*: 356, 358 (M). Anal. Calc. for $C_{23}H_{17}ClN_2$ (356.85): C, 77.41; H, 4.80; N, 7.85. Found: C, 77.60; H, 4.60; N, 7.63%.

*5-(Anthracen-9-yl)-3-p-tolyl-4, 5-dihydro-1H-pyrazole (**25**)*

Yield: 71%, reddish brown crystals, mp 145-146 ºC. IR (KBr) ν_{max}/cm^{-1}: 3284 (NH); ^{1}H NMR (DMSO-d_6) δ 2.44 (s, 3H, *p*-CH_3), 3.42-4.08 (m, 2H, pyrazoline-H_4,$H_{4'}$), 6.60-6.73 (m, 1H, pyrazoline-H_5), 7.17 (d, 2H, *J* 8.0 Hz, ArH), 7.64 (d, 2H, *J* 7.6 Hz, ArH), 7.70 (d, 2H, *J* 7.6 Hz, ArH), 7.90 (dd, 2H, *J* 3.0, 5.0 Hz, ArH), 8.12 (d, 2H, *J* 8.0 Hz, ArH), 8.18 (dd, 2H, *J* 3.0, 5.0 Hz, ArH), 8.47 (s, 1H, $H_{anth\text{-}10}$), 9.63 (s, 1H, NH; D_2O exchangeable). Anal. Calc. for $C_{24}H_{20}N_2$ (336.43): C, 85.68; H, 5.99; N, 8.33. Found: C, 85.60; H, 5.79; N, 8.52%.

*General procedure for the preparation of compounds **26** and **27***

To an ice cold solution of 5-(anthracen-9-yl)-3-aryl-4,5-dihydro-1*H*-pyrazole **24** (0.35 g, 0.001 mol) or **25** (0.33 g, 0.001 mol) in hydrochloric acid (50%, 15 mL) was added $NaNO_2$ (0.07 g, 0.001 mol) and the reaction mixture was stirred for 3 h. The separated solid product was filtered, washed with ethanol, dried and recrystallized from ethanol.

*5-(Anthracen-9-yl)-3-(4-chlorophenyl)-1-nitroso-4,5-dihydro-1H-pyrazole (**26**)*

Yield: 89%, pale brown crystals, mp 150-151 ºC. ^{1}H NMR (DMSO-d_6) δ 3.28 (dd, 1H, $J_{1,2}$ 13.8, $J_{1,3}$ 16.8 Hz, pyrazoline-H_4), 3.67 (dd, 1H, $J_{1,2}$ 13.8, $J_{1,3}$ 16.8 Hz, pyrazoline-$H_{4'}$), 6.39 (t, 1H, *J* 13.8 Hz, pyrazoline-H_5), 7.43-7.52 (m, 6H, ArH), 7.69 (d, 2H, *J* 8.0 Hz, ArH), 8.06 (d, 2H, *J* 7.6 Hz, ArH), 8.41 (d, 2H, *J* 8.0 Hz, ArH), 8.55 (s, 1H, $H_{anth\text{-}10}$). Anal. Calc. for $C_{23}H_{16}ClN_3O$ (385.85): C, 71.59; H, 4.18; N, 10.89. Found: C, 71.70; H, 4.32; N, 10.70%.

*5-(Anthracen-9-yl)-1-nitroso3-p-tolyl-4,5-dihydro-1H-pyrazole (**27**)*

Yield: 84%, buff crystals, mp 129-130 ºC. ^{1}H NMR (DMSO-d_6) δ 2.43 (3H, s, *p*-CH_3), 3.25-3.44 (m, 1H, pyrazoline-H_4), 3.69-4.09 (m, 1H, pyrazoline-$H_{4'}$), 7.00-7.24 (m, 1H, pyrazoline-H_5), 7.18 (d, 2H, *J* 9 Hz, ArH), 7.39 (d, 2H, *J* 9.0 Hz, ArH), 7.59 (t, 2H, *J* 8.0 Hz, ArH), 7.69 (d, 2H, *J* 8.0 Hz, ArH), 7.82 (t, 2H, *J* 8 Hz, ArH), 7.88 (d, 2H, *J* 8.0 Hz, ArH), 8.17 (s, 1H, $H_{anth\text{-}10}$). Anal. Calc. for $C_{24}H_{19}N_3O$ (365.43): C, 78.88; H, 5.24; N, 11.50. Found: C, 78.75; H, 4.98; N, 11.74%.

*General procedure for the preparation of compounds **28** and **29***

To a solution of 5-(anthracen-9-yl)-3-aryl-4,5-dihydro-1*H*-pyrazole (**24**, 0.35 g, 0.001 mol or **25**, 0.33 g, 0.001 mol) in dry ether (20 mL) was added an equal amount of phenylisothiocyanate (0.14 g) and the reaction mixture was stirred for 6 h. The solid product obtained was filtered, washed with ethanol, dried and recrystallized from ethanol.

*5-(Anthracen-9-yl)-3-(4-chlorophenyl)-N-phenyl-4,5-dihydro-1H-pyrazole-1-carbothioamide (**28**)*

Yield: 82%, pale grey crystals, mp 250-251 ºC. IR (KBr) ν_{max}/cm^{-1}: 949, 1143, 1346, 1552 (NCS amide I, II, III, IV respectively), 3260 (NH); ^{1}H NMR (DMSO-d_6) δ 3.29-3.31 (m, 1H, pyrazoline-H_4), 3.82-3.95 (m, 1H, pyrazoline-$H_{4'}$), 7.10-7.25 (m, 1H, pyrazoline-H_5), 7.30-7.35 (m, 2H, ArH), 7.39-7.45 (m, 3H, ArH), 7.48-7.54 (m, 2H, ArH), 7.58-7.64 (m, 2H, ArH), 7.69-7.73 (d, 2H, *J* 8.0 Hz, ArH), 7.78-7.86 (d, 2H, *J* 7.0 Hz, ArH), 7.90-7.97 (m, 2H, ArH), 8.08-8.17 (m, 2H, ArH), 8.17 (s, 1H, $H_{anth\text{-}10}$), 11.10 (s, 1H, NH; D_2O exchangeable). Anal. Calc. for $C_{30}H_{22}ClN_3S$ (492.03): C, 73.23; H, 4.51; N, 8.54. Found: C, 73.40; H, 4.62; N, 8.30%.

*5-(Anthracen-9-yl)-N-phenyl-3-p-tolyl-4,5-dihydro-1H-pyrazole-1-carbothioamide (**29**)*

Yield: 85%, buff crystals, mp 215-216 ºC. IR (KBr) ν_{max}/cm^{-1}: 938, 1168, 1327, 1588 (NCS amide I, II, III, IV respectively), 3243 (NH); ^{1}H NMR (DMSO-d_6) δ 2.44 (s, 3H, *p*-CH_3), 3.34-3.69 (m, 1H, pyrazoline-H_4), 3.80-4.03 (m, 1H, pyrazoline-$H_{4'}$), 7.28-7.33 (m, 2H, ArH), 7.36-7.41 (m, 2H, ArH), 7.44-7.49 (m, 3H, ArH), 7.51-7.58 (m, 1H,

pyrazoline-H_5), 7.62-7.68 (d, 2H, *J* 9 Hz, ArH) 7.70-7.75 (m, 2H, ArH), 7.79-7.83 (d, 2H, *J* 8.0 Hz, ArH), 7.86-7.90 (m, 2H, ArH), 8.04-8.10 (m, 2H, ArH), 8.39 (s, 1H, $H_{anth\text{-}10}$), 11.15 (s, 1H, NH; D_2O exchangeable). Anal. Calc. for $C_{31}H_{25}N_3S$ (471.62): C, 78.95; H, 5.34; N, 8.91. Found: C, 78.76; H, 5.12; N, 9.00%.

*General procedure for the preparation of compounds **30** and **31***

To a solution of 5-(anthracen-9-yl)-3-aryl-4, 5-dihydro-1*H*-pyrazole **24** (0.35 g, 0.001 mol) or **25** (0.33 g, 0.001 mol) in dry pyridine (10 mL) was added an equivalent amount of *p*-tosyl chloride (0.19 g). The reaction mixture was heated on a boiling water bath for 3 h, cooled and then poured onto crushed ice. The solid product separated was filtered, washed with water, dried and recrystallized from ethanol.

*5-(Anthracen-9-yl)-3-(4-chlorophenyl)-1-tosyl-4,5-dihydro-1H-pyrazole (**30**)*

Yield: 76%, buff crystals, mp 135-136 ºC. ^{1}H NMR (DMSO-d_6) δ 2.44 (3H, s, CH_3), 3.42-4.02 (m, 2H, pyrazoline-H_4, $H_{4'}$), 6.60-6.67 (m, 1H, pyrazoline-H_5), 7.35 (d, 2H, *J* 7.6 Hz, ArH), 7.43 (d, 2H, *J* 8 Hz, ArH), 7.56 (t, 2H, *J* 8.0 Hz, ArH), 7.76 (d, 2H, *J* 8.0 Hz, ArH), 7.91 (t, 2H, *J* 8.0 Hz, ArH), 8.01 (m, 2H, ArH), 8.13 (d, 2H, *J* 7.6 Hz, ArH), 8.51 (m, 2H, ArH), 8.57 (s, 1H, $H_{anth\text{-}10}$). Anal. Calc. for $C_{30}H_{23}ClN_2O_2S$ (511.03): C, 70.51; H, 4.54; N, 5.48. Found: C, 70.32; H, 4.45; N, 5.69%.

*5-(Anthracen-9-yl)-3-p-tolyl-1-tosyl-4,5-dihydro-1H-pyrazole (**31**)*

Yield: 74%, buff crystals, mp 200-201 ºC. ^{1}H NMR (DMSO-d_6) δ 2.41 (s, 3H, CH_3), 2.44 (s, 3H, CH_3), 3.40-4.00 (m, 2H, pyrazoline-H_4, $H_{4'}$), 6.60-6.64 (m, 1H, pyrazoline-H_5), 7.05 (d, 2H, *J* 3 Hz, ArH), 7.22 (d, 2H, *J* 8 Hz, ArH), 7.29 (t, 2H, *J* 8 Hz, ArH), 7.33 (d, 2H, *J* 7.0 Hz, ArH), 7.38 (d, 2H, *J* 15.0 Hz, ArH), 7.67 (d, 2H, *J* 7.0 Hz, ArH), 7.89 (d, 2H, *J* 15.0 Hz, ArH), 7.90 (t, 2H, *J* 3.0 Hz ArH), 8.47 (s, 1H, $H_{anth\text{-}10}$). Anal. Calc. for $C_{31}H_{26}N_2O_2S$ (490.62): C, 75.89; H, 5.34; N, 5.71. Found: C, 75.70; H, 5.22; N, 5.89%.

*General procedure for the preparation of compounds **32**-**34***

A mixture of 3-(anthracen-9-yl)-1-(aryl)prop-2-en-1-one **1**-**3** (0.01 mol) and guanidine carbonate (1.21 g, 0.01 mol) in ethanol (50 mL) was heated under reflux, while a 5 mol L^{-1} solution of sodium hydroxide (10 mL) was added portion-wise during one hour. Refluxing was continued for a further 10 h, when the reaction mixture was concentrated, diluted with water and extracted with benzene. The solid product was obtained after concentration and cooling; the precipitated product was filtered, dried and recrystallized from chloroform.

*4-(Anthracen-9-yl)-6-(4-chlorophenyl)pyrimidin-2-amine (**32**)*

Yield: 83%, buff crystals, mp 310-311 ºC. IR (KBr) ν_{max}/cm^{-1}: 3054, 3358 (NH_2); ^{1}H NMR (DMSO-d_6) δ 5.97 (s, 2H, NH_2; D_2O exchangeable), 7.17 (d, 2H, *J* 8.0 Hz, ArH;), 7.35 (s, 1H, pyrimidine-H_5), 7.44 (t, 2H, *J* 8.0 Hz, ArH), 7.59 (t, 2H, *J* 8 Hz, ArH), 7.98 (d, 2H, *J* 8.0 Hz, ArH), 8.05 (d, 2H, *J* 9.0 Hz, ArH), 8.18 (d, 2H, *J* 9.0 Hz, ArH), 8.68 (s, 1H, $H_{anth\text{-}10}$). Anal. Calc. for $C_{24}H_{16}ClN_3$ (381.86): C, 75.49; H, 4.22; N, 11.00. Found: C, 75.21; H, 4.00; N, 11.26%.

*4-(Anthracen-9-yl)-6-p-tolylpyrimidin-2-amine (**33**)*

Yield: 81%, buff crystals, mp 210-211 ºC. IR (KBr) ν_{max}/cm^{-1}: 3142, 3366 (NH_2); ^{1}H NMR (DMSO-d_6) δ 2.25 (s, 3H, *p*-CH_3), 6.07 (s, 2H, NH_2; D_2O exchangeable), 7.46-7.52 (m, 4H, ArH), 7.57-7.59 (m, 4H, ArH), 7.63-7.65 (d, 2H, *J* 9.0 Hz, ArH), 7.71-7.86 (d, 2H, *J* 8.0 Hz, ArH), 7.91 (s, 1H, pyrimidine-H_5), 8.18 (s, 1H, $H_{anth\text{-}10}$). Anal. Calc. for $C_{25}H_{19}N_3$ (361.44): C, 83.08; H, 5.30; N, 11.63. Found: C, 83.29; H, 5.56; N, 11.42%.

*4-(Anthracen-9-yl)-6-(furan-2-yl)pyrimidin-2-amine (**34**)*

Yield:78%, buff crystals, mp 263-264 ºC. IR (KBr) ν_{max}/cm^{-1}: 3147, 3323 (NH_2); ^{1}H NMR (DMSO-d_6) δ 6.26 (s, 2H, NH_2; D_2O exchangeable), 7.53 (s, 1H, pyrimidine-H_5), 7.60-7.64 (m, 1H, ArH), 7.73-7.80 (m, 1H, ArH), 7.85-7.89 (m, 1H, ArH), 7.98 (dd, 2H, *J* 3.0, 6.0 Hz, ArH), 8.06-8.08 (m, 4H, ArH), 8.17 (dd, 2H, *J* 3.0, 6.0 Hz, ArH), 8.33 (s, 1H, $H_{anth\text{-}10}$). Anal. Calc. for $C_{22}H_{15}N_3O$ (337.37): C, 78.32; H, 4.48; N, 12.46. Found: C, 78.56; H, 4.27; N, 12.25%.

*General procedure for the preparation of compounds **35** and **36***

A mixture of 4-(anthracen-9-yl)-6-arylpyrimidin-2-amine (**32**, 0.38 g, 0.001 mol or **33**, 0.36 g, 0.001 mol) and acetic anhydride (10 mL) was heated on boiling water bath for 2 h. The reaction mixture was poured onto cold water and the precipitated product was filtered, washed with water, dried and recrystallized from ethanol/chloroform.

*N-(4-(Anthracen-9-yl)-6-(4-chlorophenyl)pyrimidin-2-yl) acetamide (**35**)*

Yield: 83%, buff crystals, mp 130-131 ºC. IR (KBr) ν_{max}/cm^{-1}: 1667 (C=O), 3260 (NH); ^{1}H NMR (DMSO-d_6)

δ 2.25 (s, 3H, $NCOCH_3$), 7.28 (t, 2H, *J* 8.0 Hz, ArH), 7.47 (t, 2H, *J* 6.0 Hz, ArH), 7.61 (d, 2H, *J* 7.6 Hz, ArH), 7.89 (d, 2H, *J* 6.0 Hz, ArH), 8.00 (s, 1H, pyrimidine-H_5), 8.06 (d, 2H, *J* 8.0 Hz, ArH), 8.17 (d, 2H, *J* 7.6 Hz, ArH), 8.70 (s, 1H, $H_{anth\text{-}10}$), 10.77 (s, 1H, NH; D_2O exchangeable). Anal. Calc. for $C_{26}H_{18}ClN_3O$ (423.89): C, 73.67; H, 4.28; N, 9.91. Found: C, 73.89; H, 4.01; N, 9.75%.

*N-(4-(Anthracen-9-yl)-6-p-tolylpyrimidin-2-yl)acetamide (**36**)*

Yield: 78%, buff crystals, mp 119-120 ºC. IR (KBr) ν_{max}/cm^{-1}: 1669 (C=O), 3218 (NH); ^1H NMR (DMSO-d_6) δ 2.29 (s, 3H, $NCOCH_3$), 2.36 (s, 3H, *p*-CH_3), 7.30-7.63 (m, 4H, ArH), 7.90-7.92 (m, 4H, ArH), 8.17-8.19 (m, 4H, ArH), 8.37 (s, 1H, pyrimidine-H_5), 8.74 (s, 1H, $H_{anth\text{-}10}$), 10.47 (s, 1H, NH; D_2O exchangeable). Anal. Calc. for $C_{27}H_{21}N_3O$ (403.48): C, 80.37; H, 5.25; N, 10.41. Found: C, 80.56; H, 5.01; N, 10.23%.

Biological activity assay

Measurement of the inhibition zone (IZ)

Compounds **1**-**36** were evaluated *in vitro* for antimicrobial activity against *Escherichia coli* ATCC8739 and *Pseudomonas aeruginosa* ATCC 9027 as gram-negative bacteria, *Staphylococcus aureus* ATCC 6538P as an example of gram-positive bacteria and *Candida albicans* ATCC 2091 as yeast-like fungus. The agar-diffusion method[33] was used for the determination of antibacterial and antifungal activity. From 1 mg mL^{-1} solutions of each of the test compounds in *N,N*-dimethylformamide (DMF), 75 µL was placed in a 6 mm diameter well in an agar plate seeded with the appropriate test organism in triplicates. Ampicillin trihydrate (10 µg *per* disc), Ciprofloxacin (5 µg *per* disc), Imipenem (10 µg *per* disc) and Clotrimazole (100 µg *per* disc) were used as standard antibacterial and antifungal agents, respectively. The plates were incubated at 37 °C for 24 h. The results were recorded for each tested compounds as the average diameter of inhibition zone of bacterial growth in mm (Table 1). DMF alone (control) showed no inhibition zone.

Minimal inhibitory concentration (MIC)

The microdilution susceptibility test in Muller-Hinton broth (oxoid) and Sabouraud liquid medium (oxoid) were used for the determination of antibacterial and antifungal activity with the same test organisms. The MIC measurements[34] were carried out for compounds that showed significant inhibition zones using the two-fold serial dilution technique with solutions in the concentration range 500-15.63 µg mL^{-1}. Suspensions of the microorganisms at 10^6 CFU mL^{-1} (Colony Forming Units mL^{-1}) were used to inoculate the prepared test compounds in the above mentioned serial dilution broth. The culture tubes were incubated at 37 ºC for 24-48 h. At the end of the incubation period the growth of bacteria was observed in the form of turbidity. The MIC is defined as the lowest concentration that showed no bacterial growth (Table 1).

Supplementary Information

Supplementary data are available free of charge at http://jbcs.sbq.org.br as PDF file.

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Supplementary Information

Synthesis and Biological Activity of Some New Pyrazoline and Pyrimidine Derivatives

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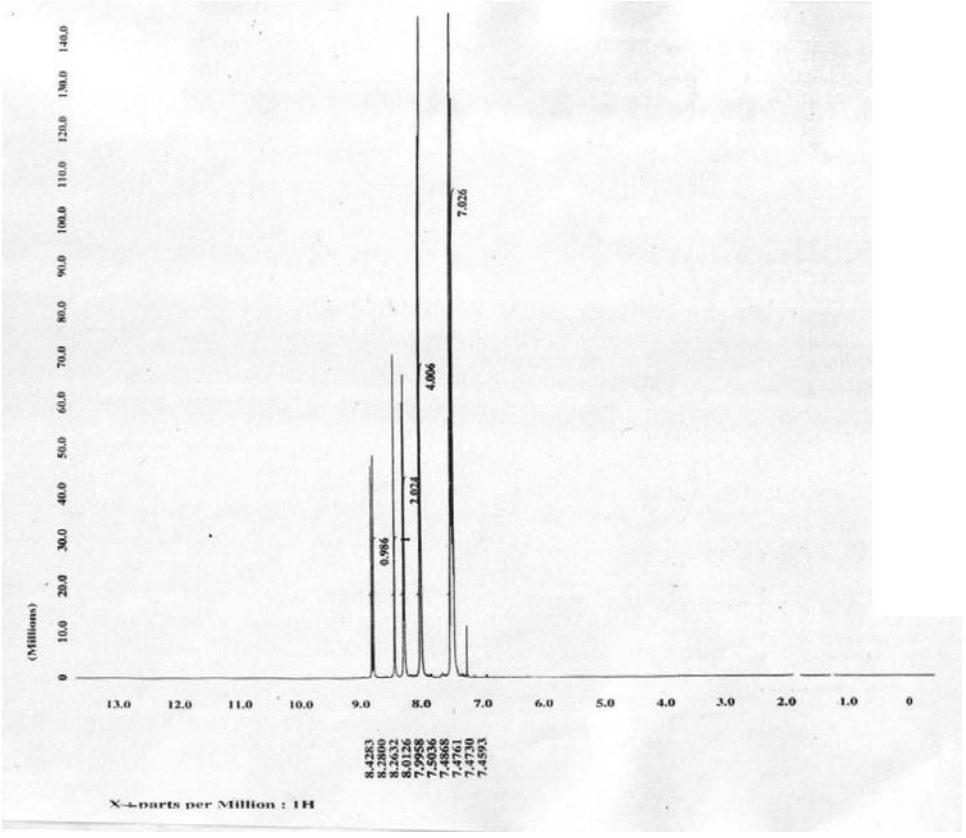

Figure S1. ^{1}H NMR spectrum of compound **1**.

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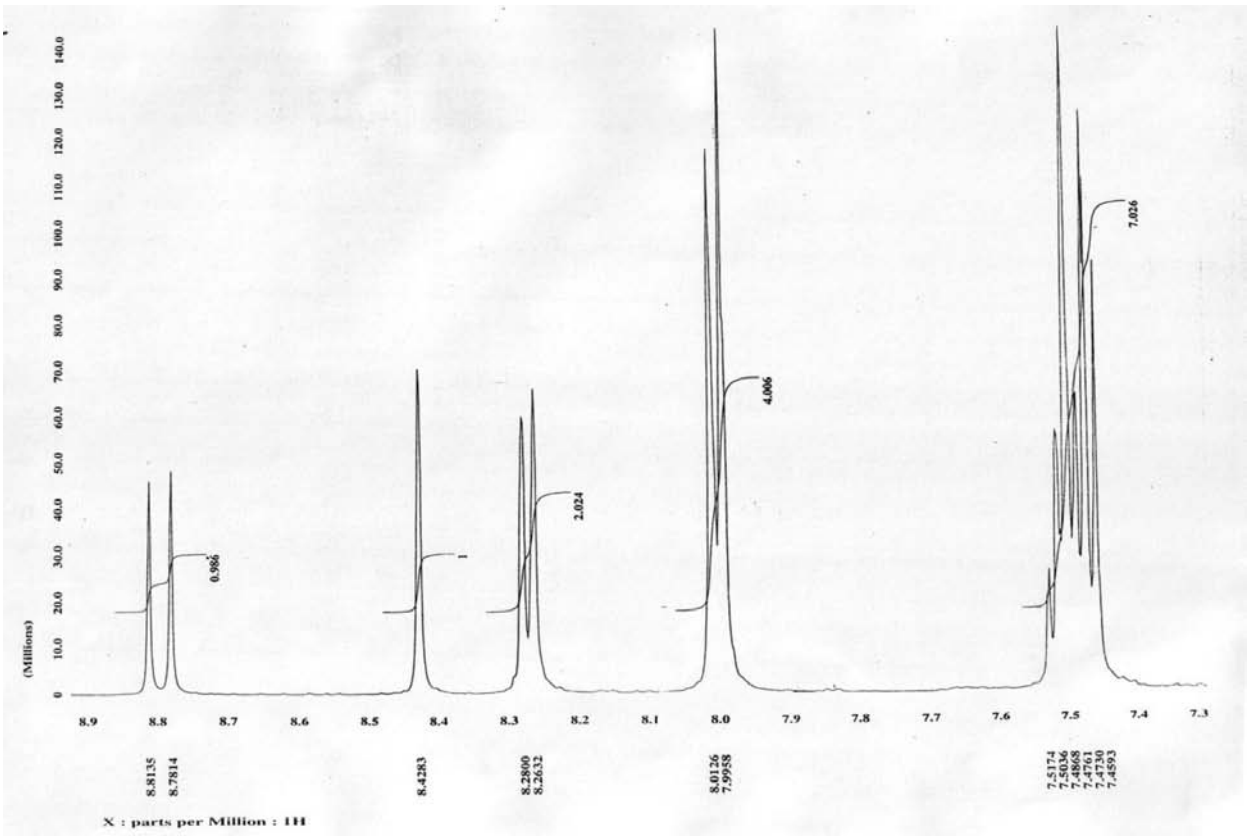

Figure S2. ^{1}H NMR spectrum of compound **1**.

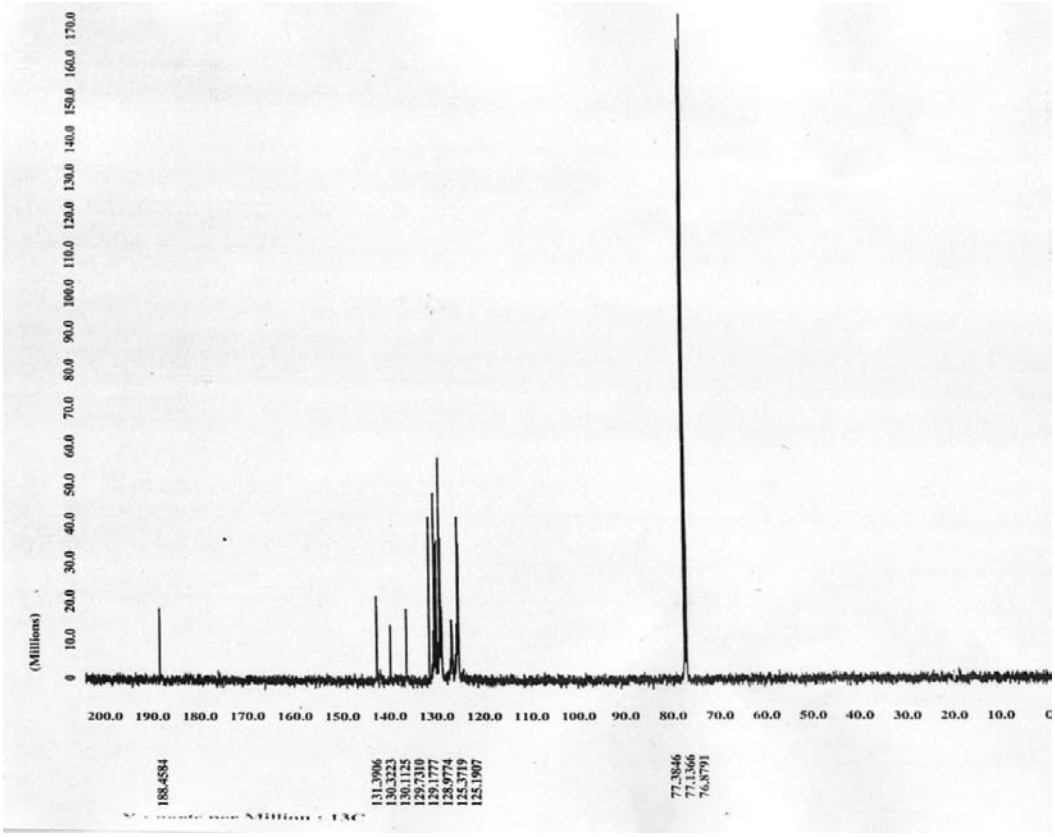

Figure S3. ^{13}C NMR spectrum of compound **1**.

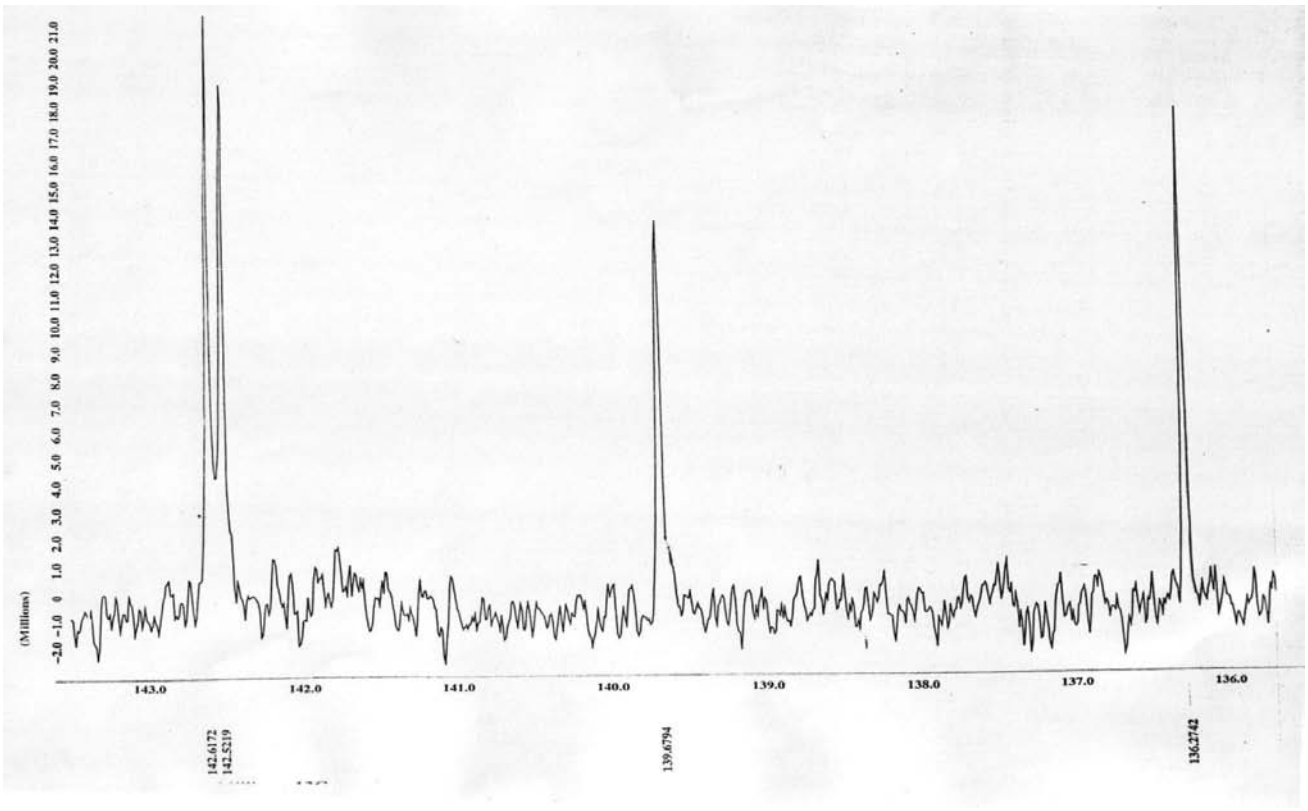

Figure S4. ^{13}C NMR spectrum of compound **1**.

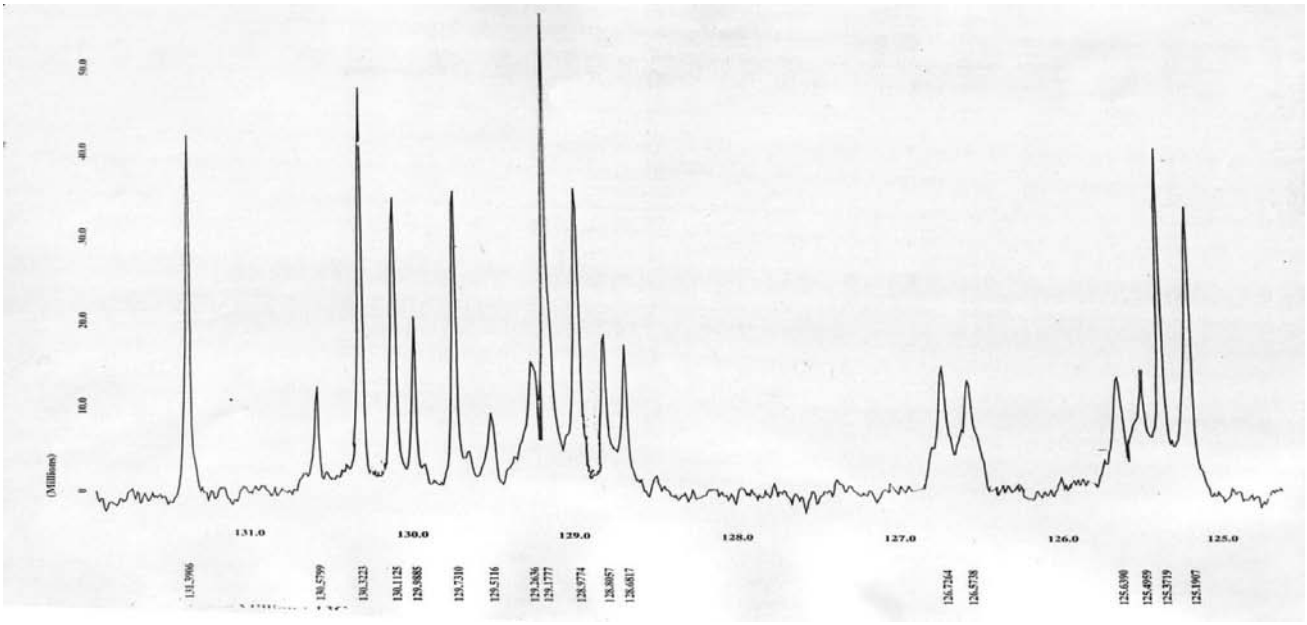

Figure S5. ^{13}C NMR spectrum of compound **1**.

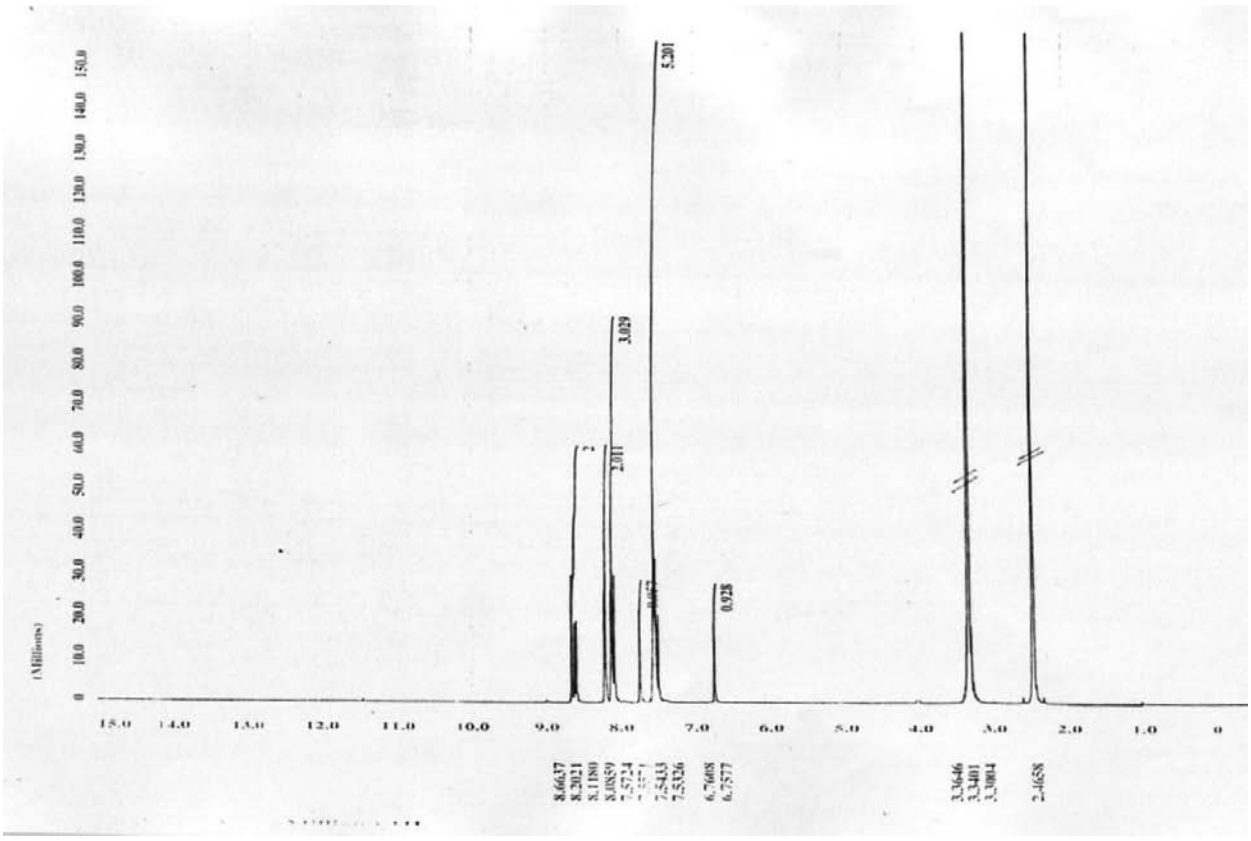

Figure S6. ^{1}H NMR spectrum of compound **3**.

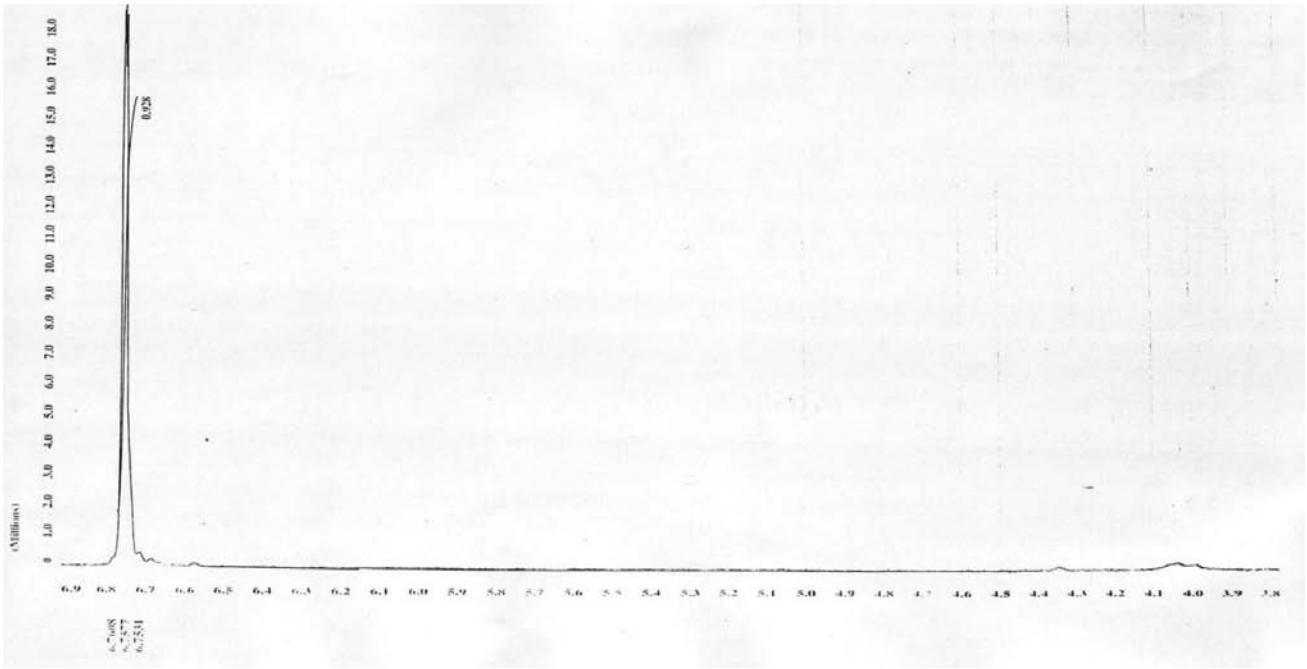

Figure S7. ^{1}H NMR spectrum of compound **3**.

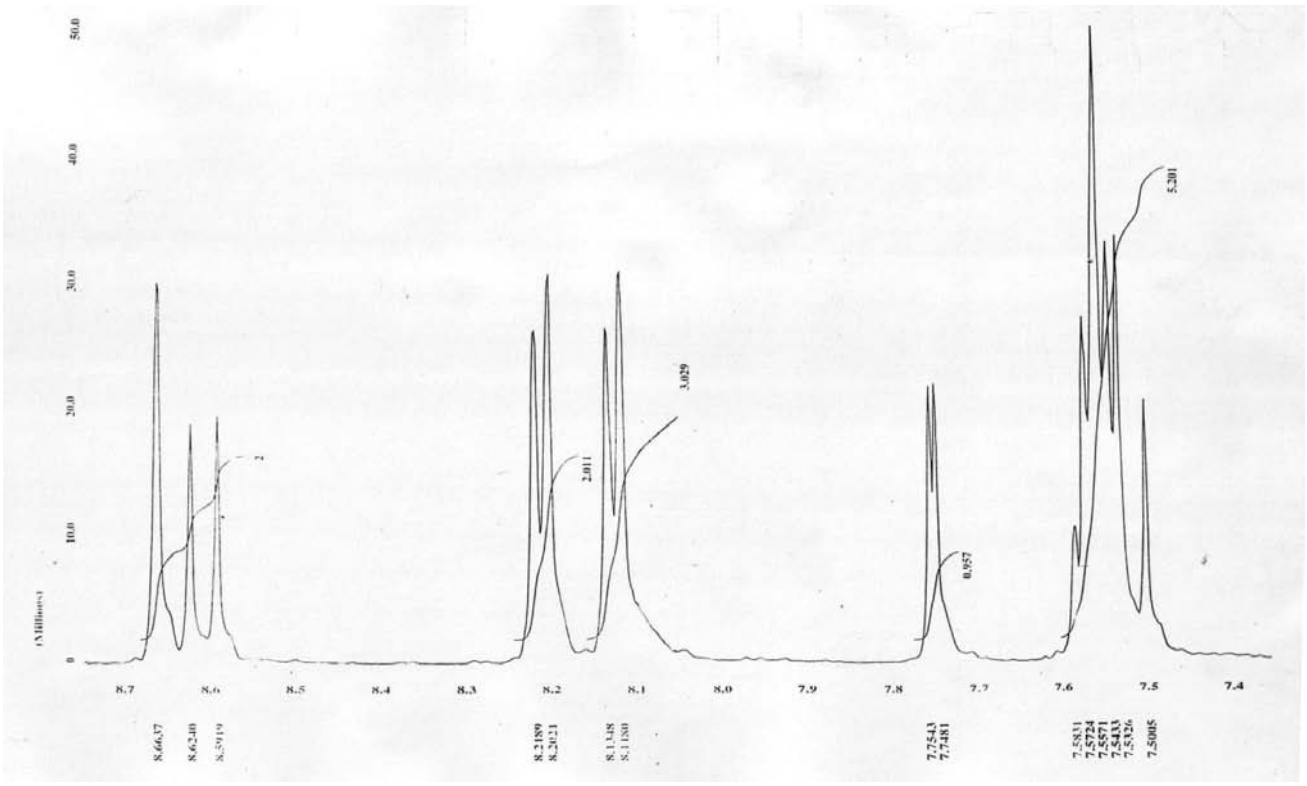

Figure S8. [1]H NMR spectrum of compound **3**.

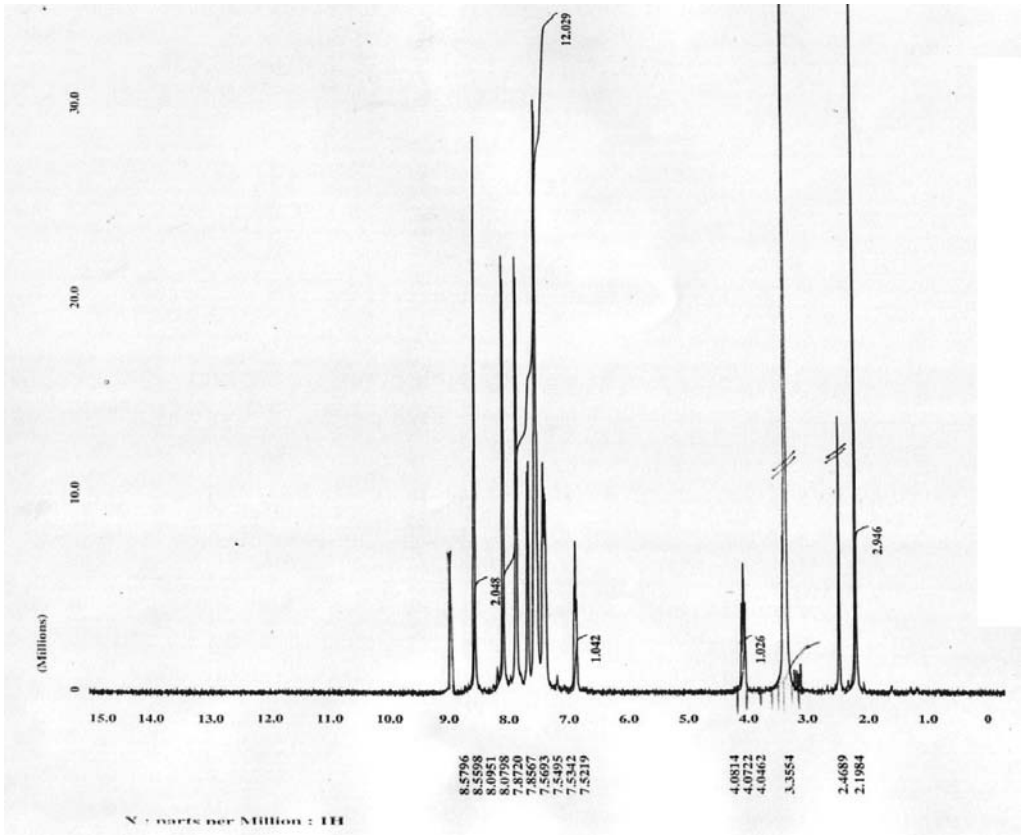

Figure S9. [1]H NMR spectrum of compound **5**.

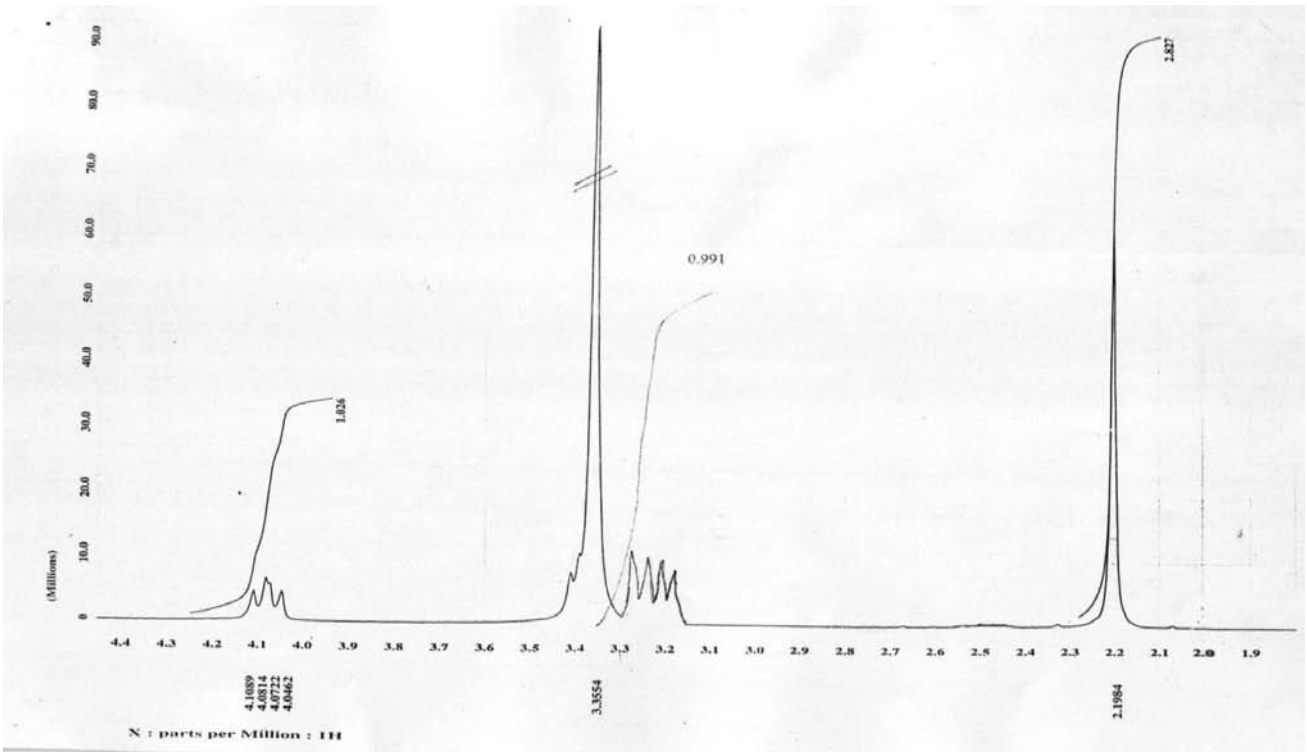

Figure S10. ^{1}H NMR spectrum of compound **5**.

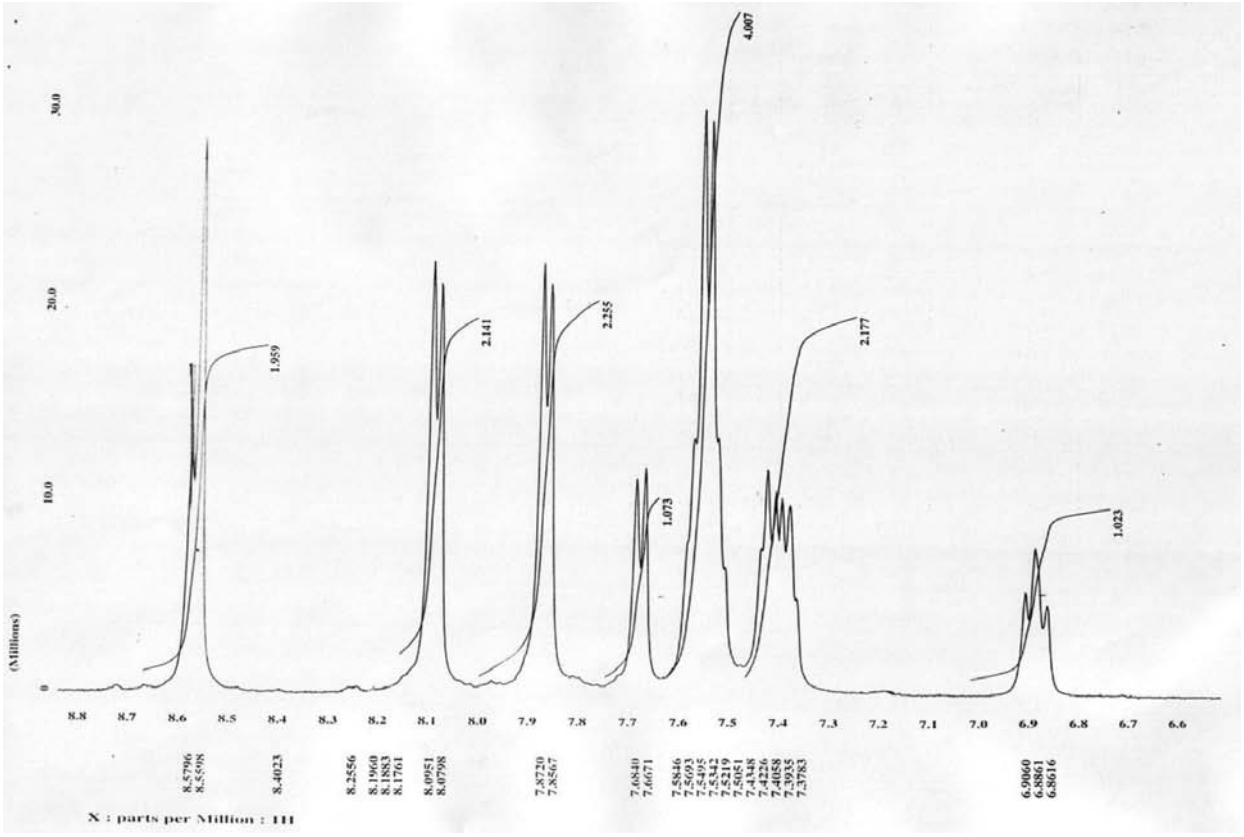

Figure S11. ^{1}H NMR spectrum of compound **5**.

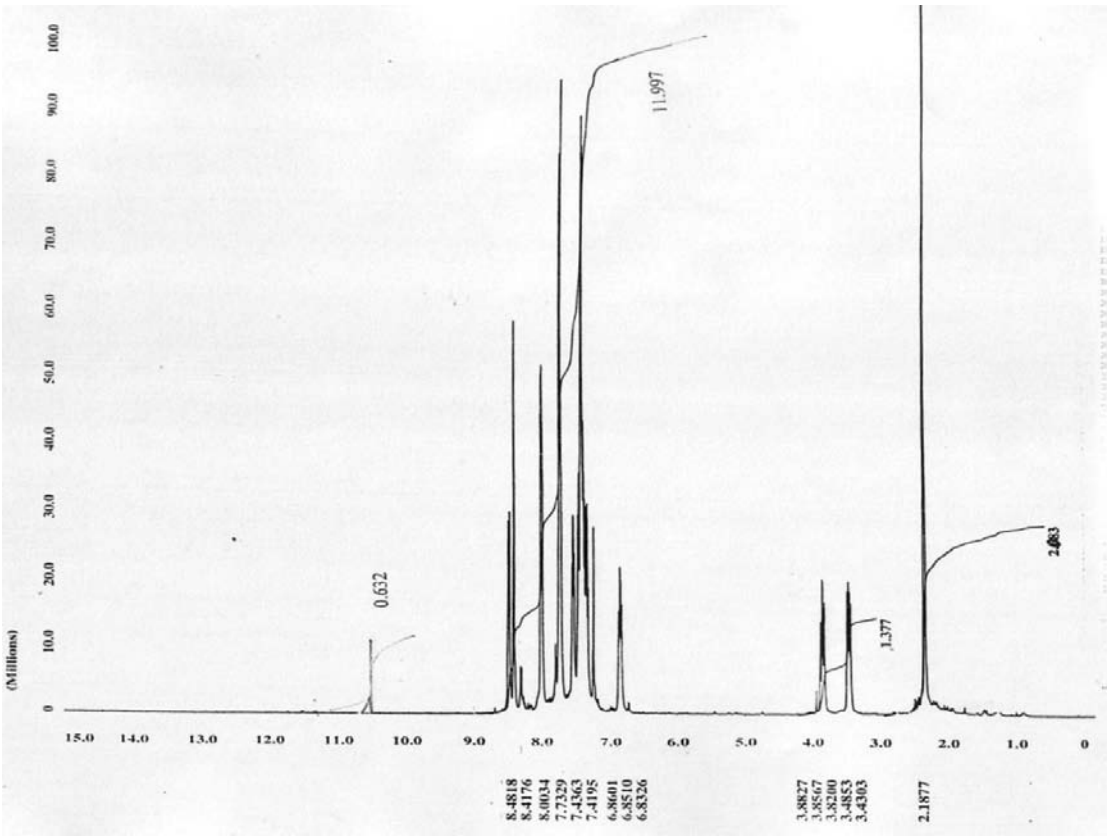

Figure S12. [1]H NMR spectrum of compound **8**.

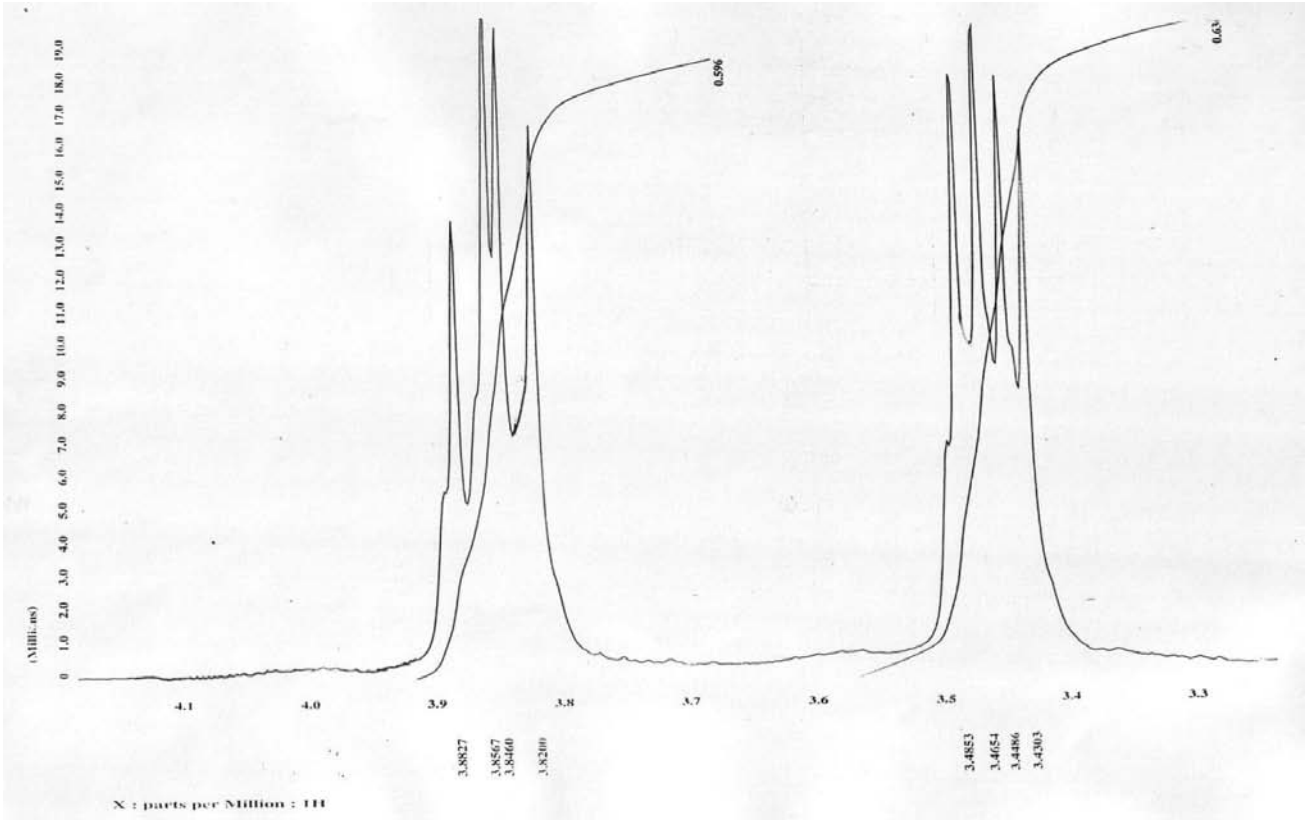

Figure S13. [1]H NMR spectrum of compound **8**.

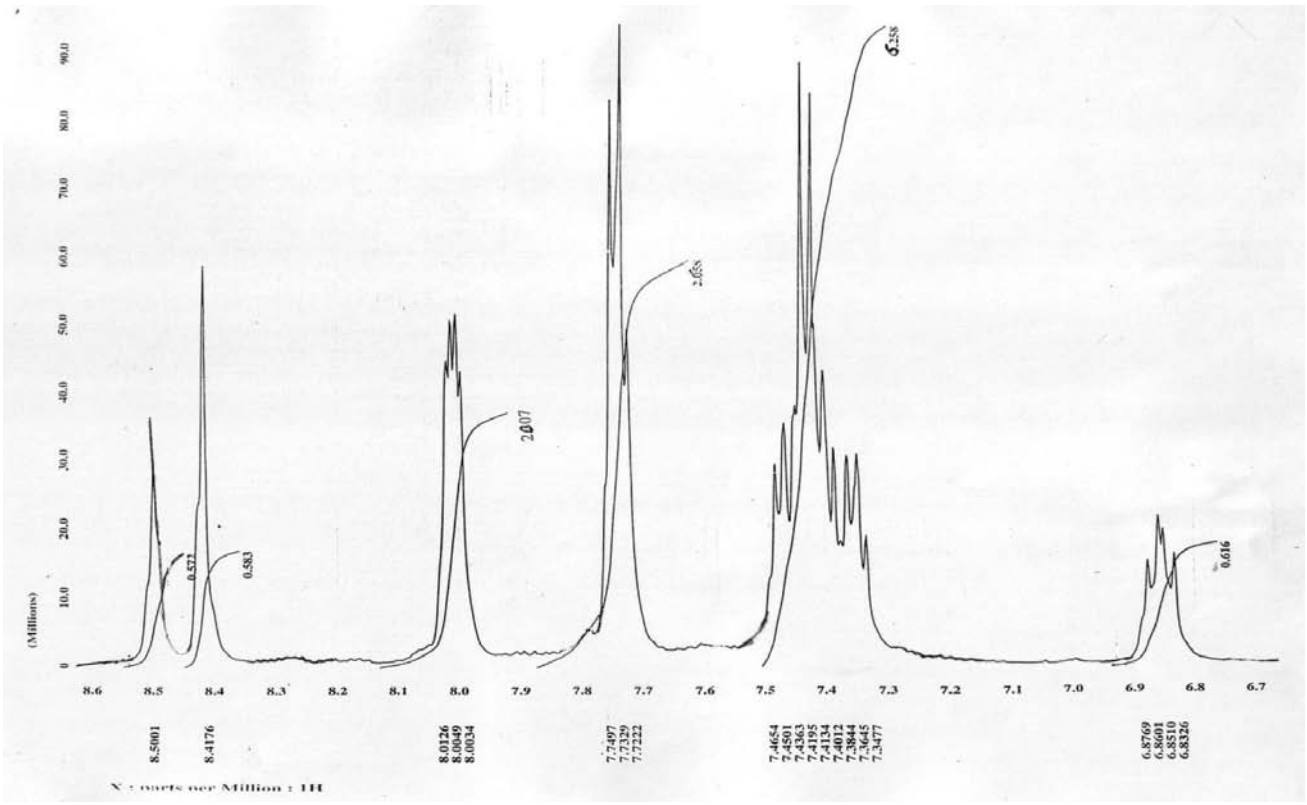

Figure S14. [1]H NMR spectrum of compound **8**.

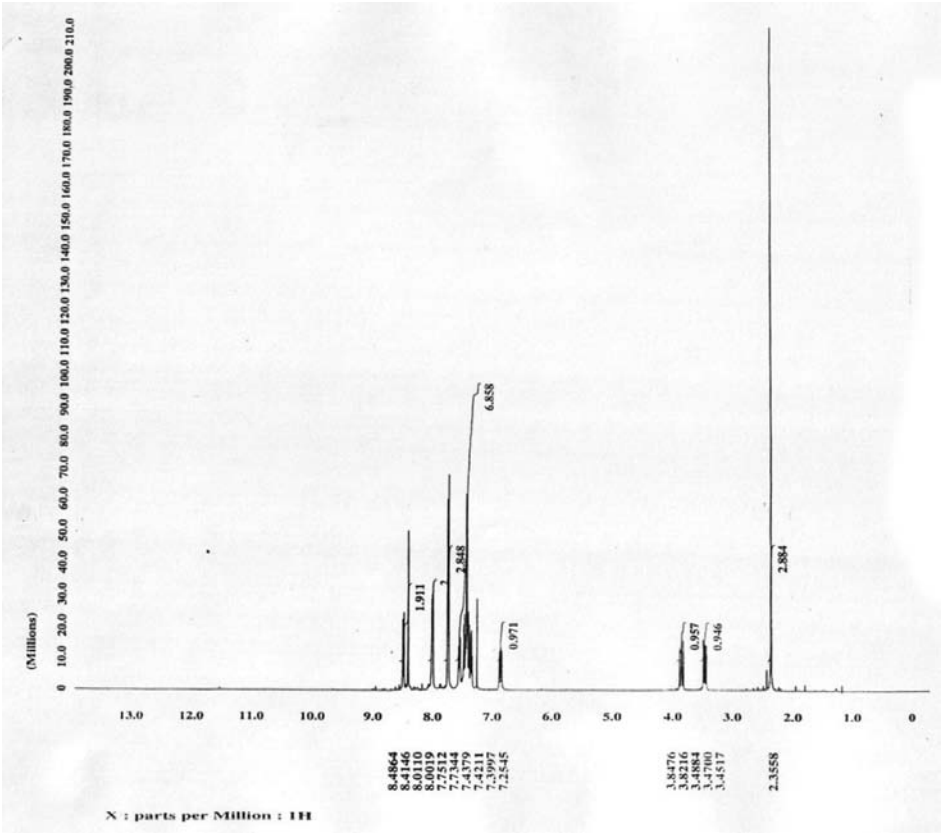

Figure S15. [1]H NMR spectrum of compound **9**.

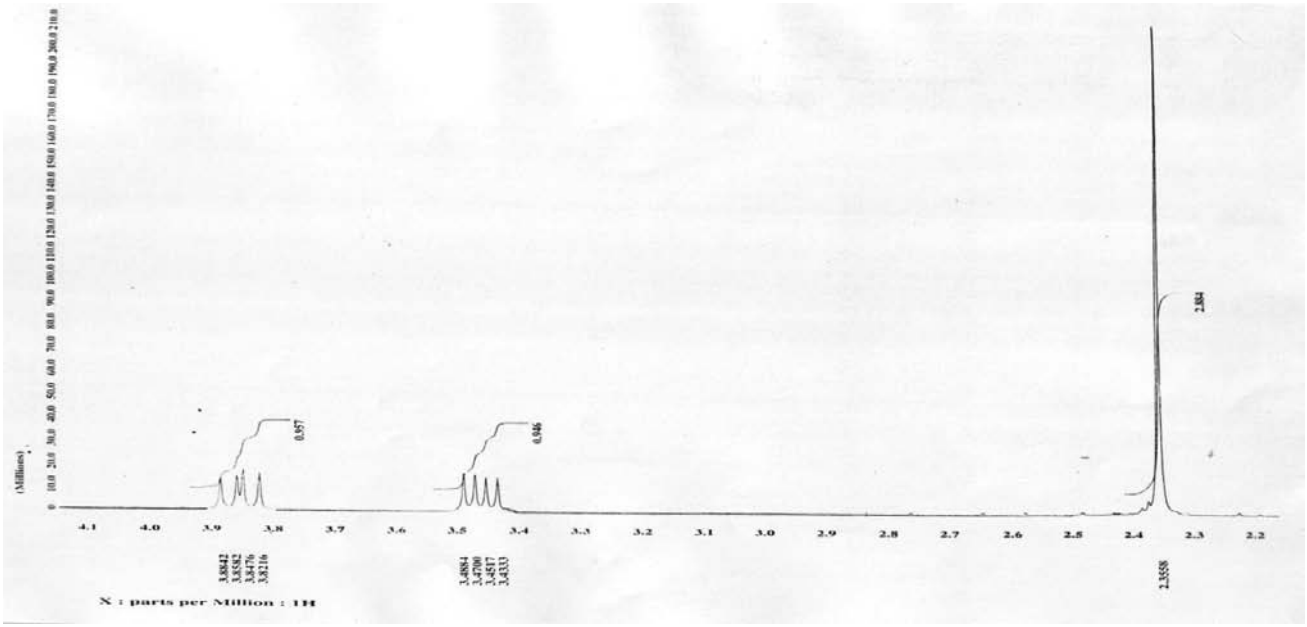

Figure S16. [1]H NMR spectrum of compound **9**.

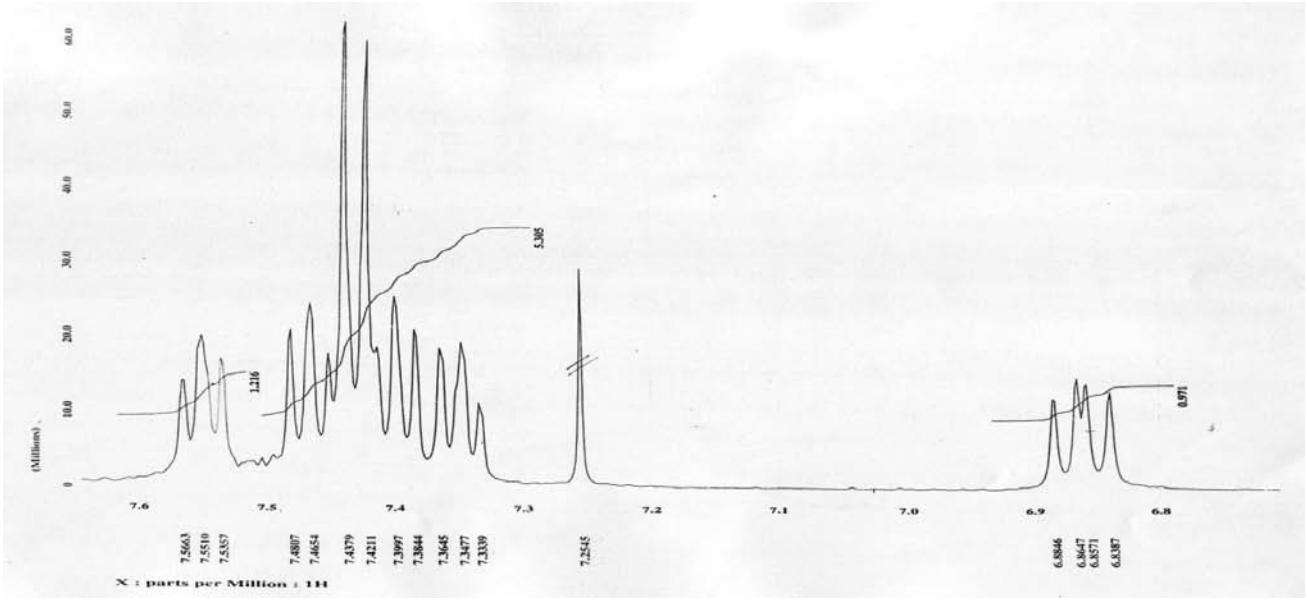

Figure S17. [1]H NMR spectrum of compound **9**.

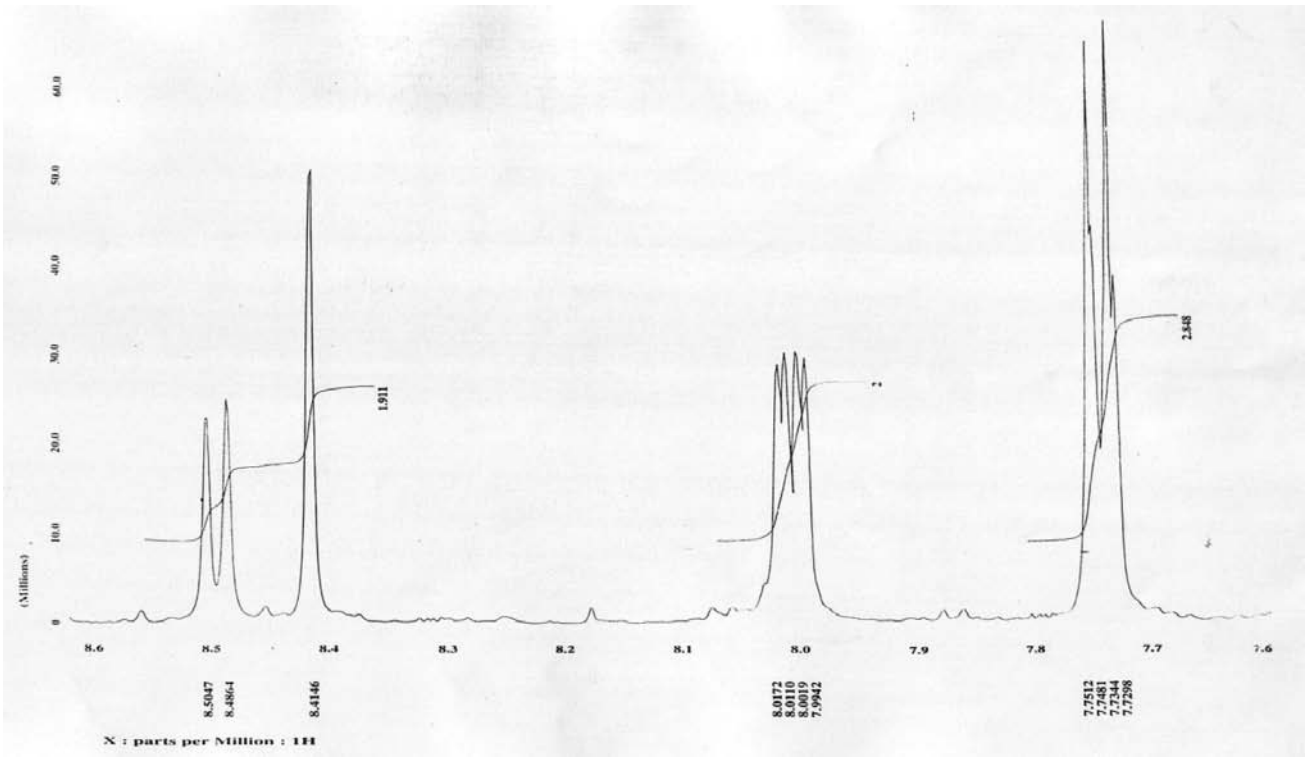

Figure S18. ^{1}H NMR spectrum of compound **9**.

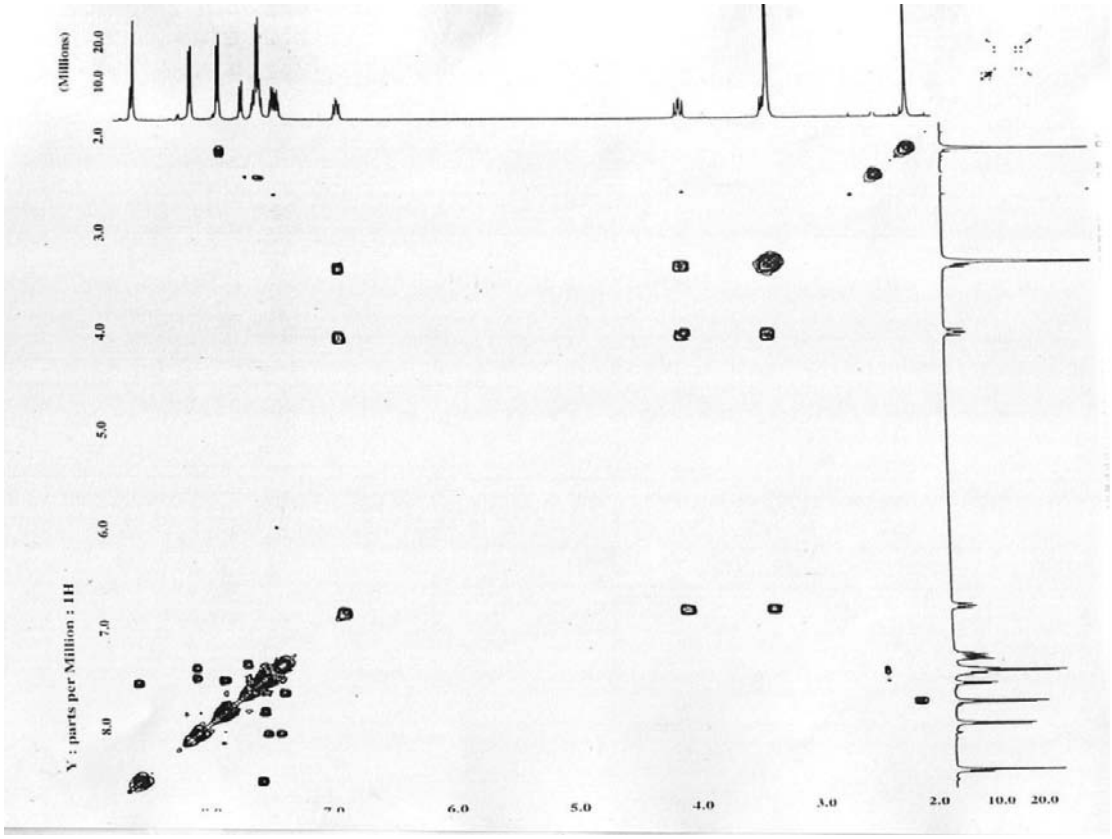

Figure S19. 2D NMR spectrum of compound **9**

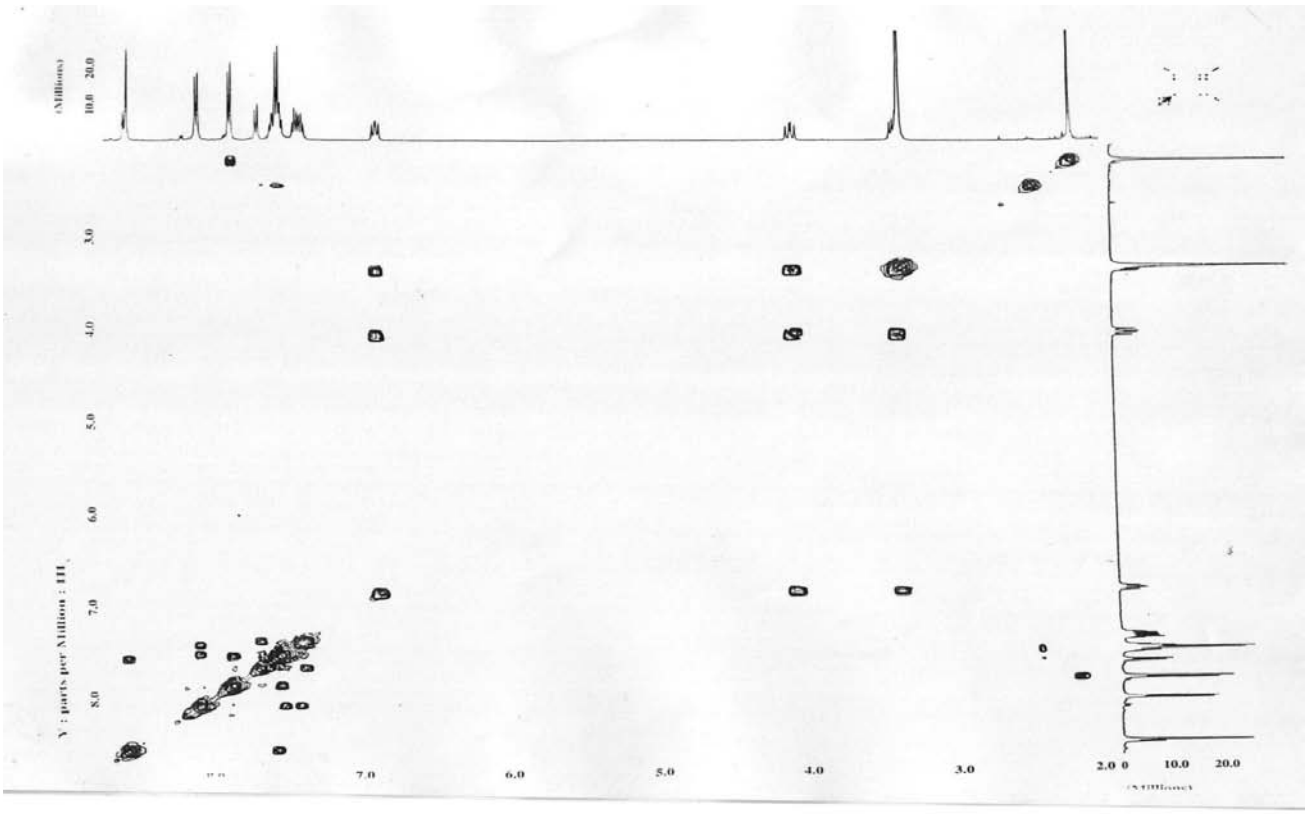

Figure S20. 2D NMR spectrum of compound **9**.

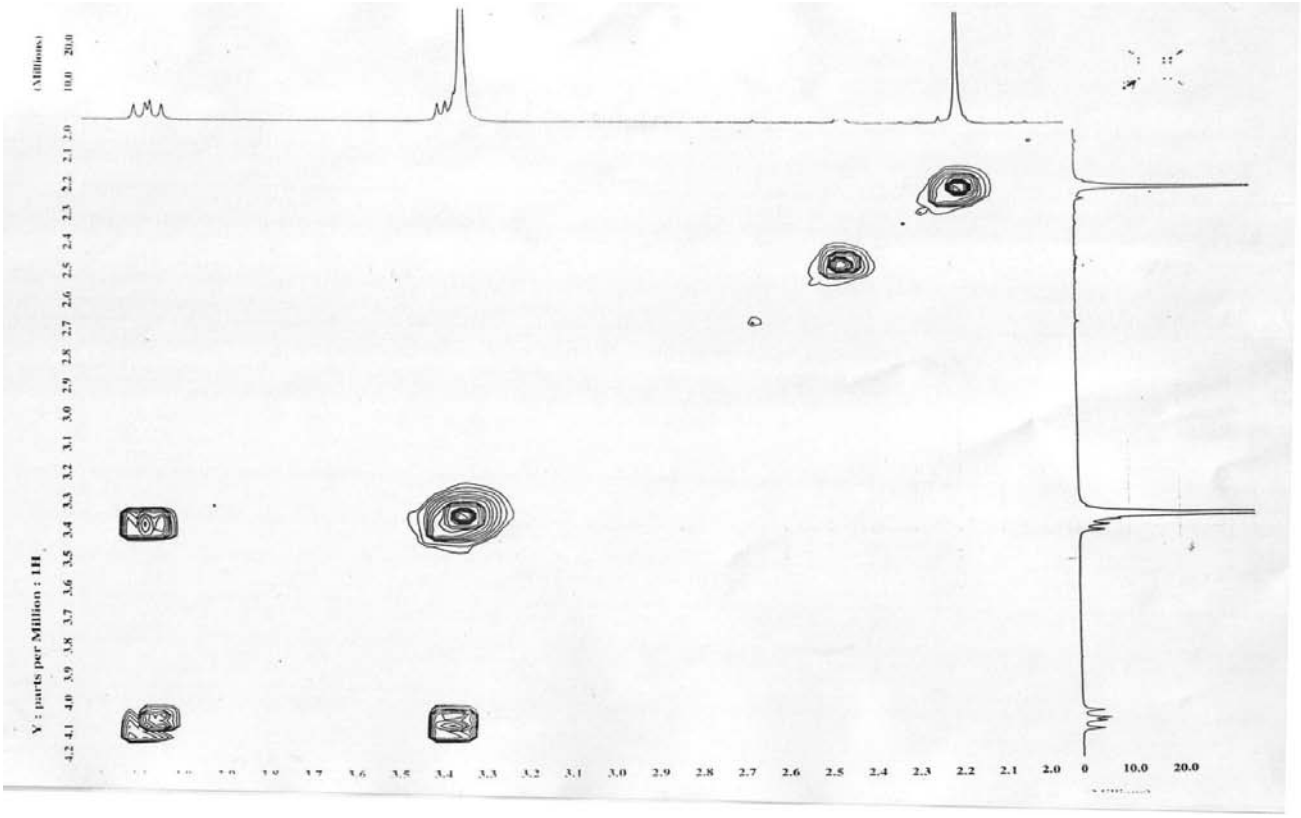

Figure S21. 2D NMR spectrum of compound **9**.

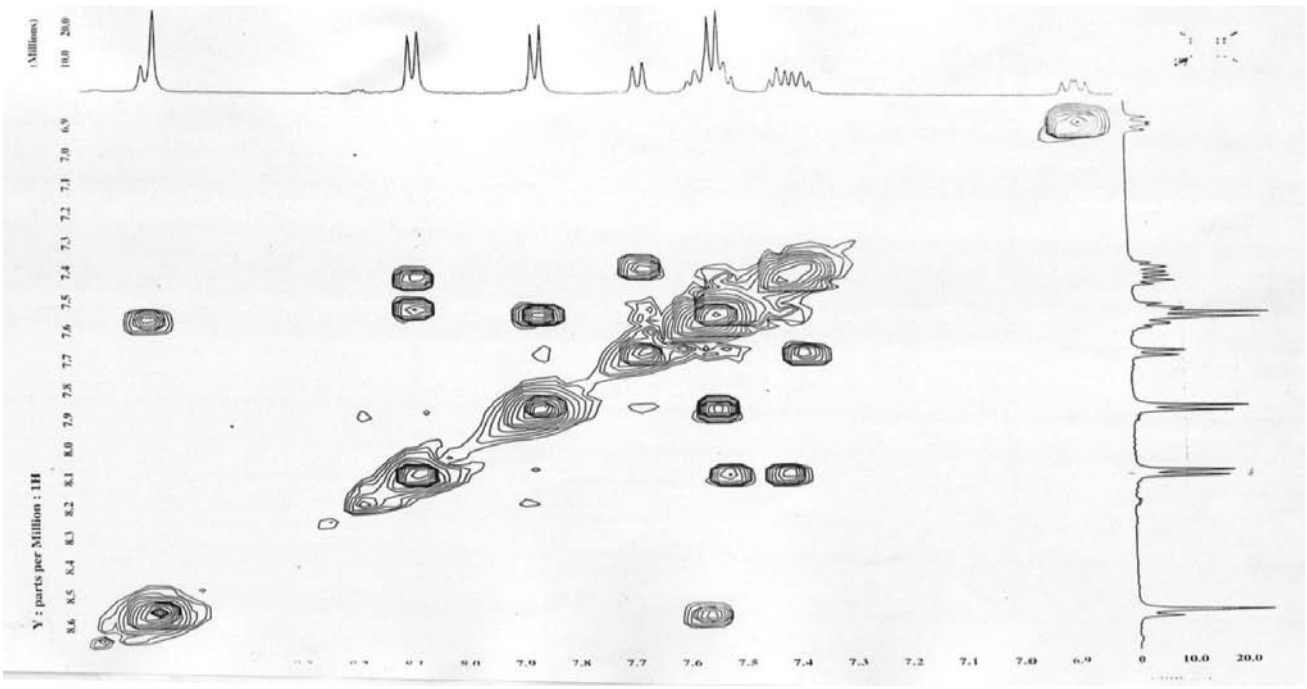

Figure S22. 2D NMR spectrum of compound **9**.

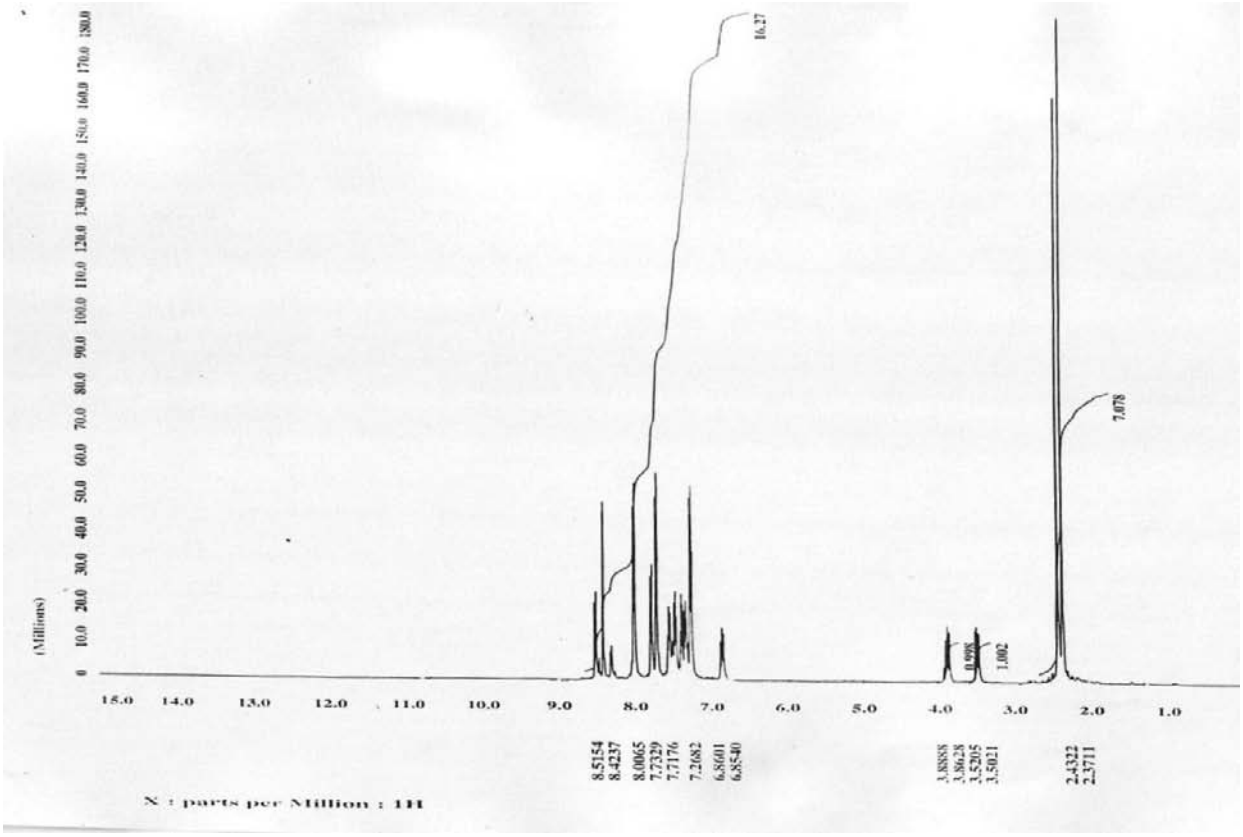

Figure S23. ^{1}H NMR spectrum of compound **10**.

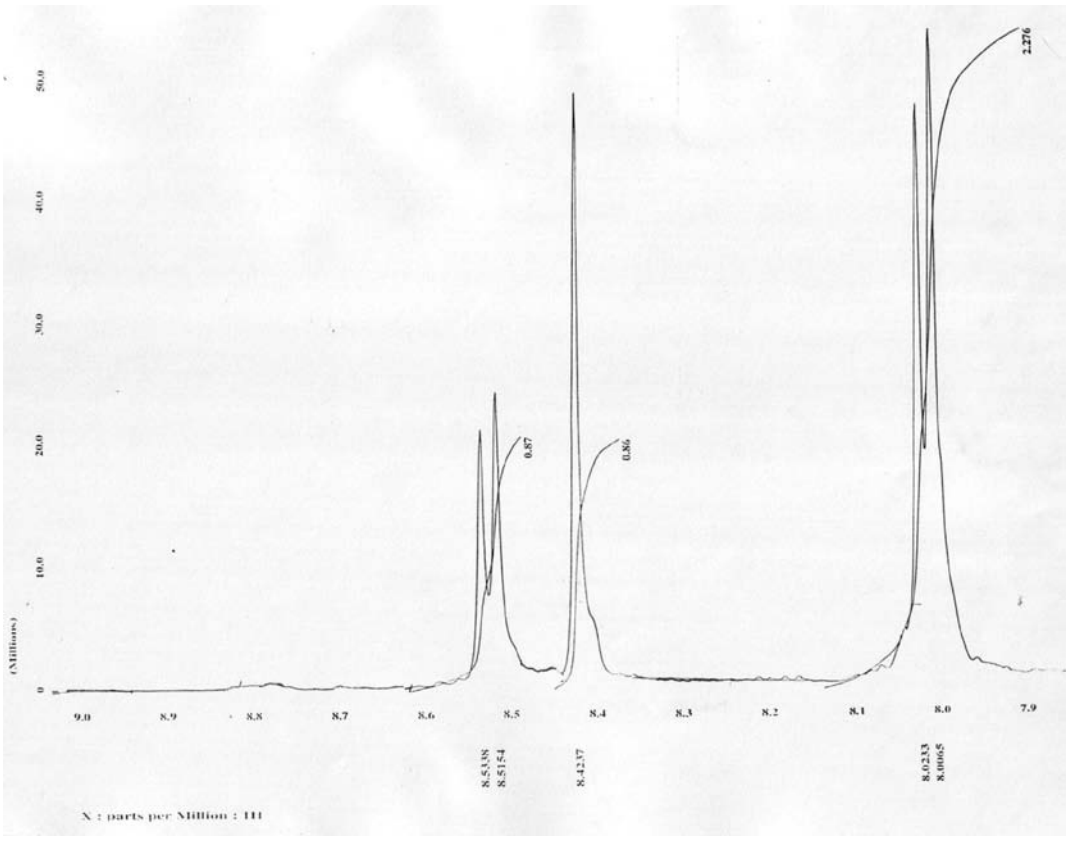

Figure S24. [1]H NMR spectrum of compound **10**.

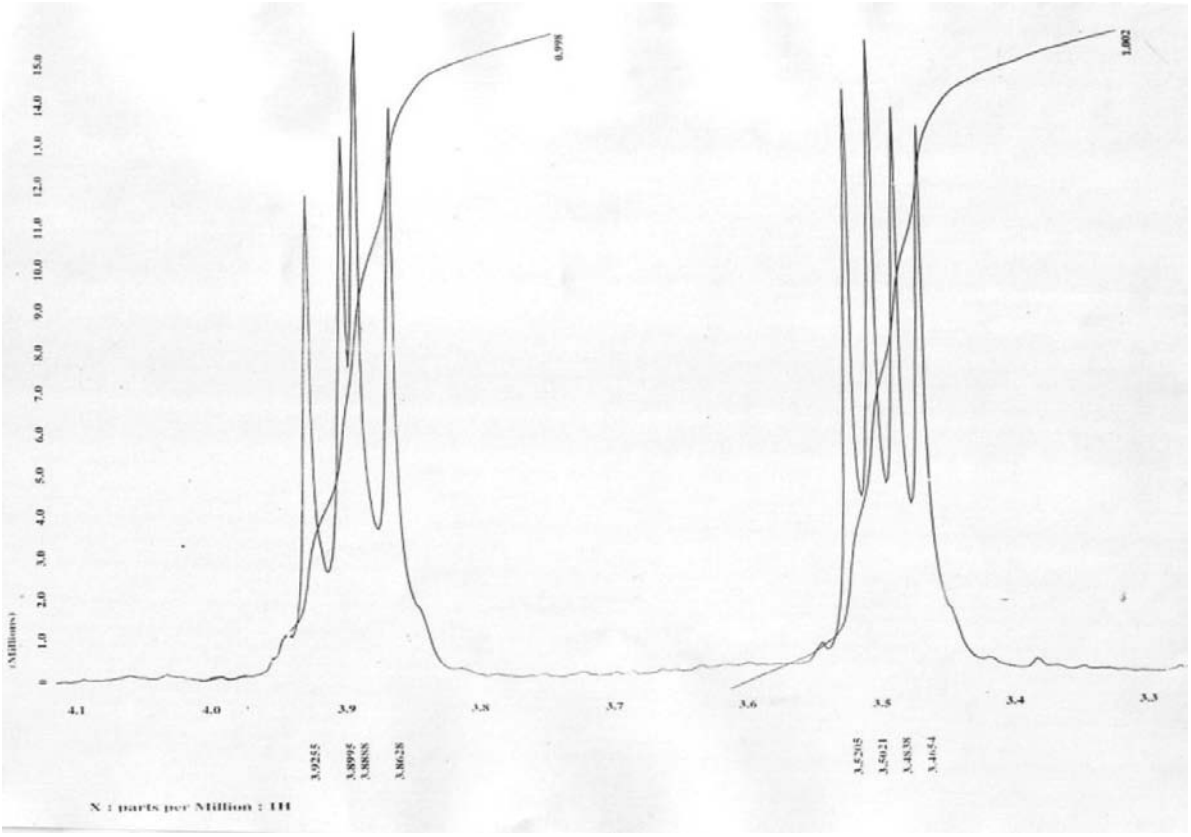

Figure S25. [1]H NMR spectrum of compound **10**.

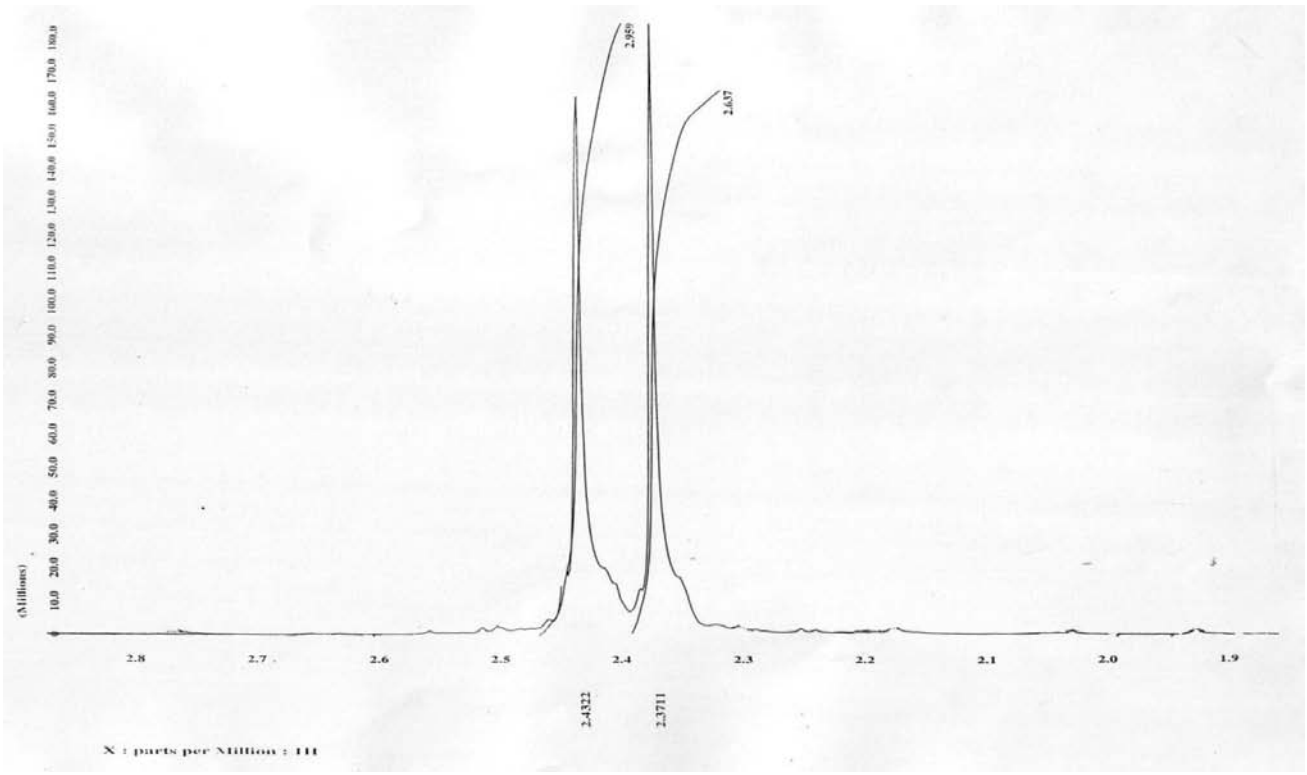

Figure S26. [1]H NMR spectrum of compound **10**.

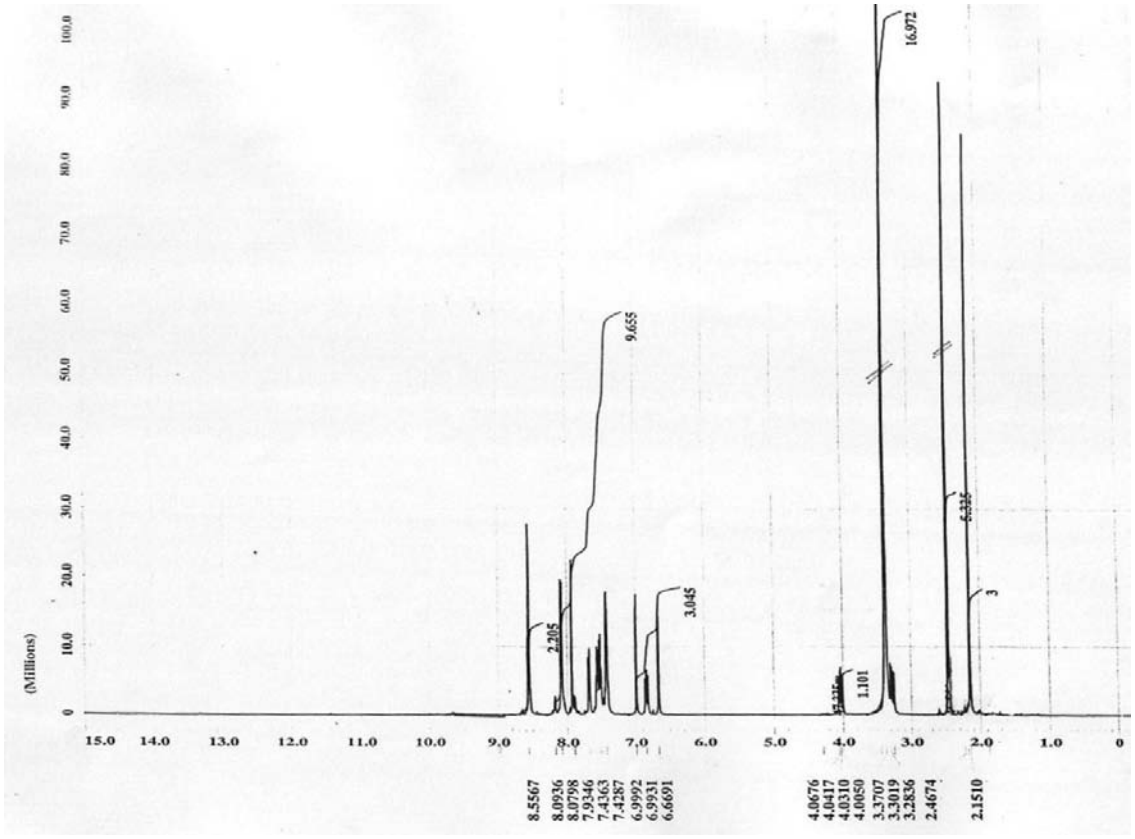

Figure S27. [1]H NMR spectrum of compound **11**.

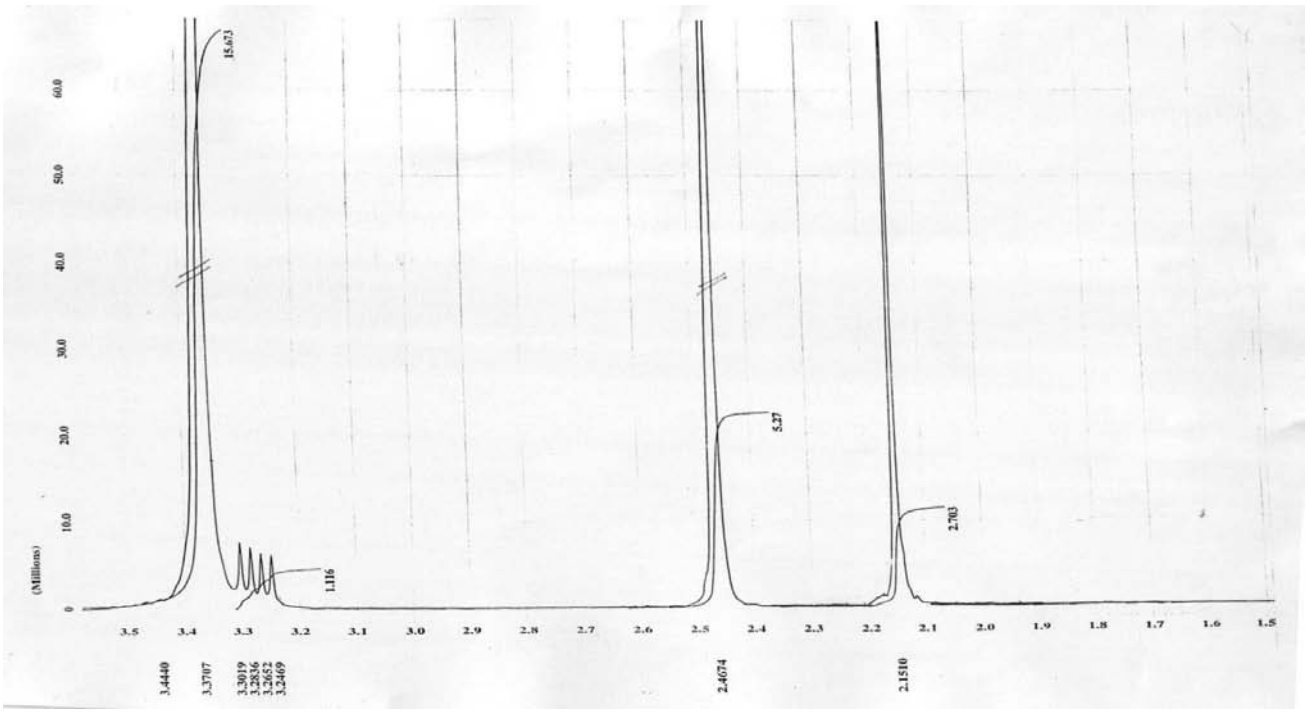

Figure S28. [1]H NMR spectrum of compound **11**.

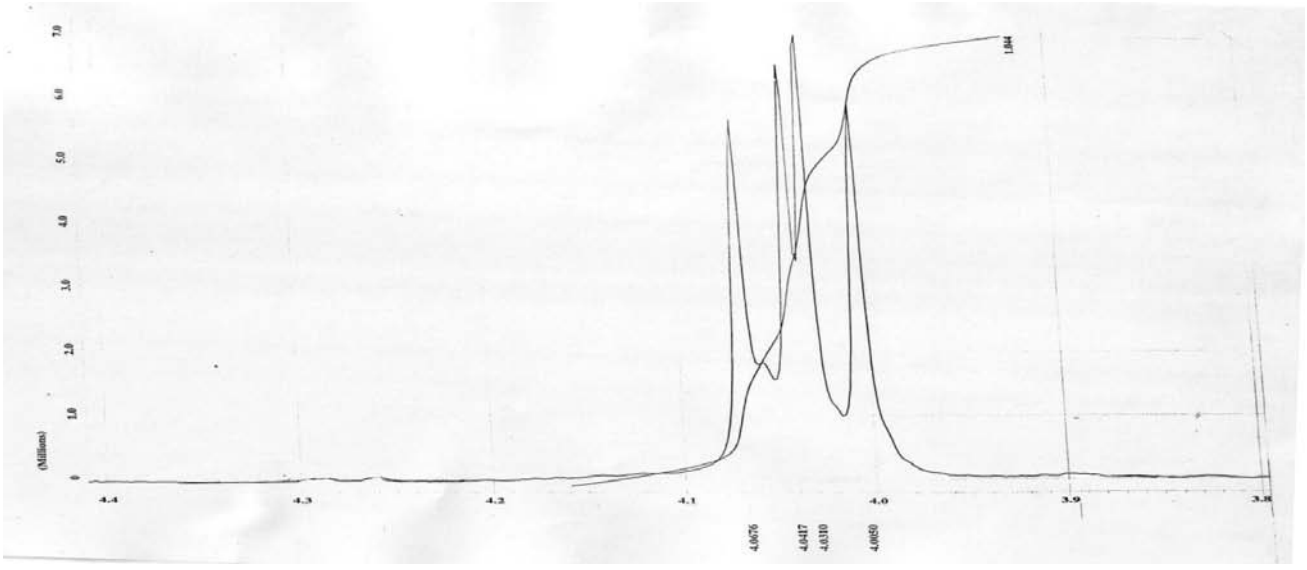

Figure S29. [1]H NMR spectrum of compound **11**.

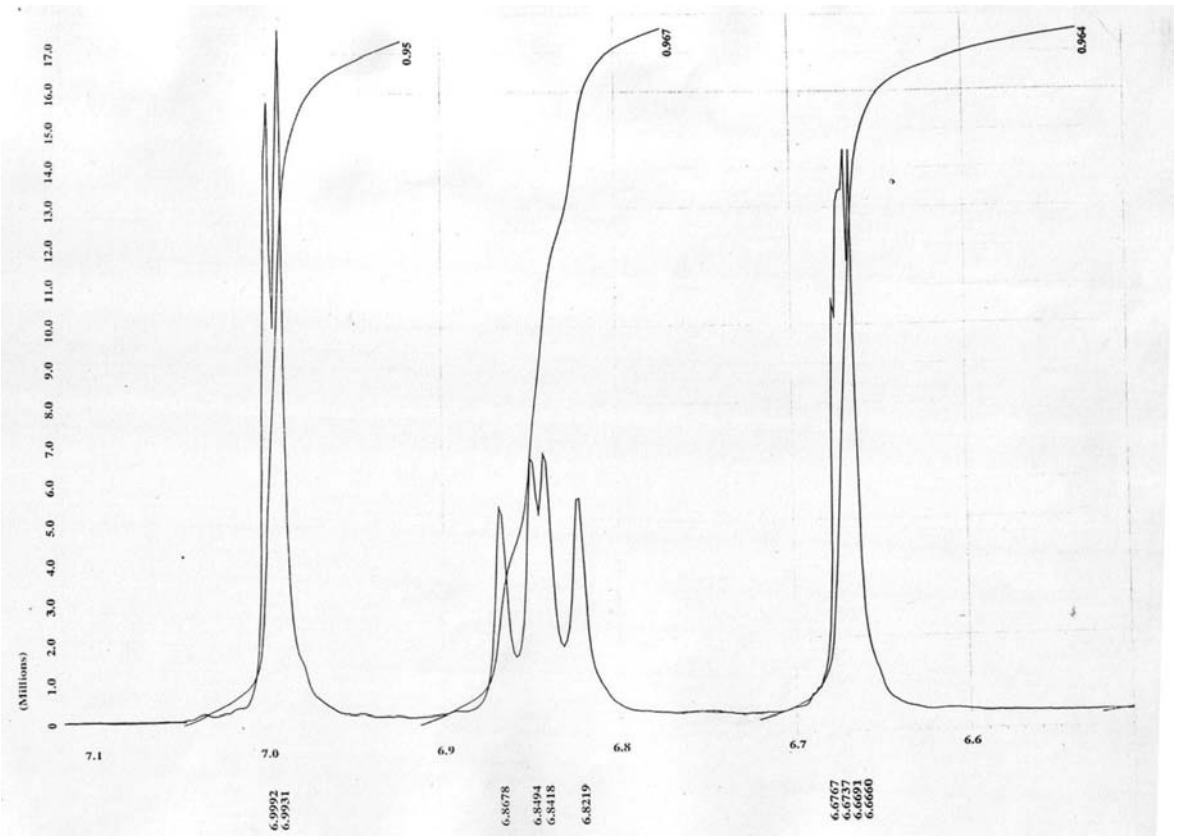

Figure S30. [1]H NMR spectrum of compound **11**.

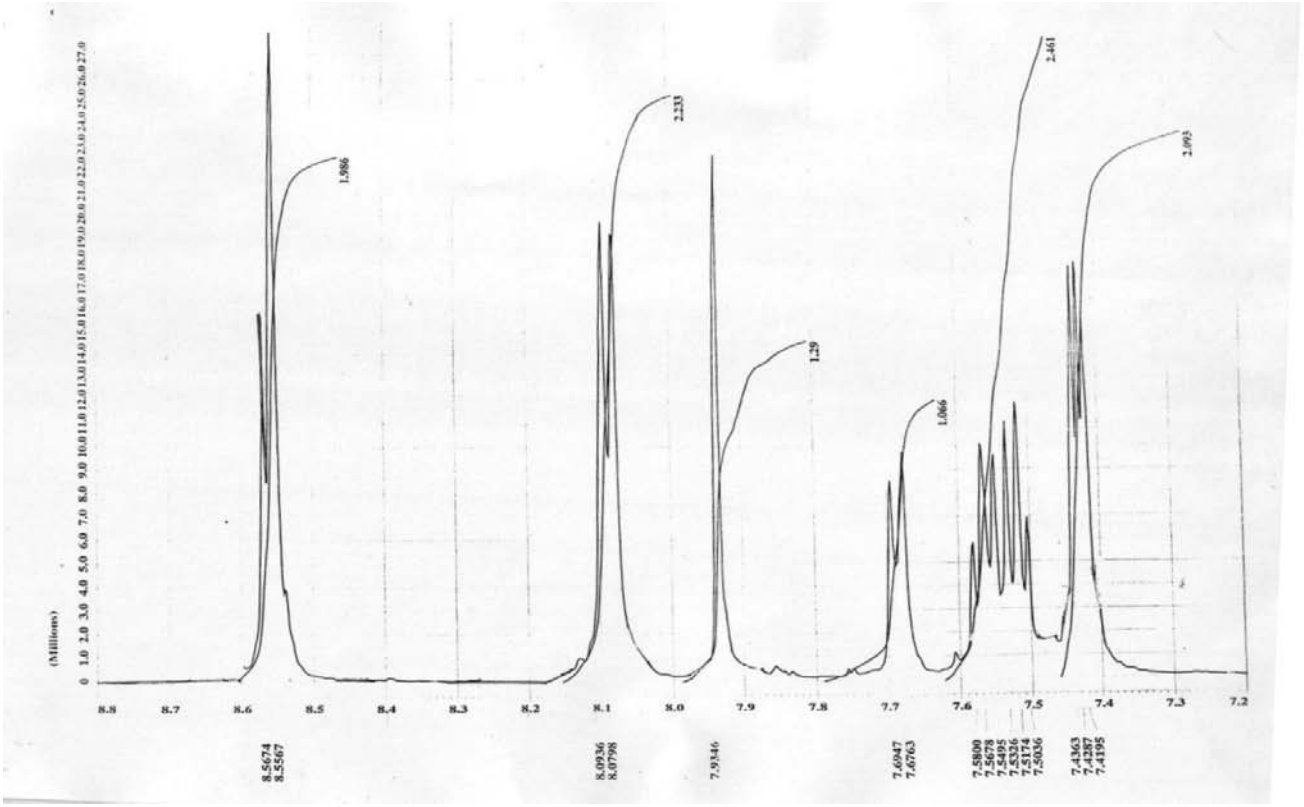

Figure S31. [1]H NMR spectrum of compound **11**.

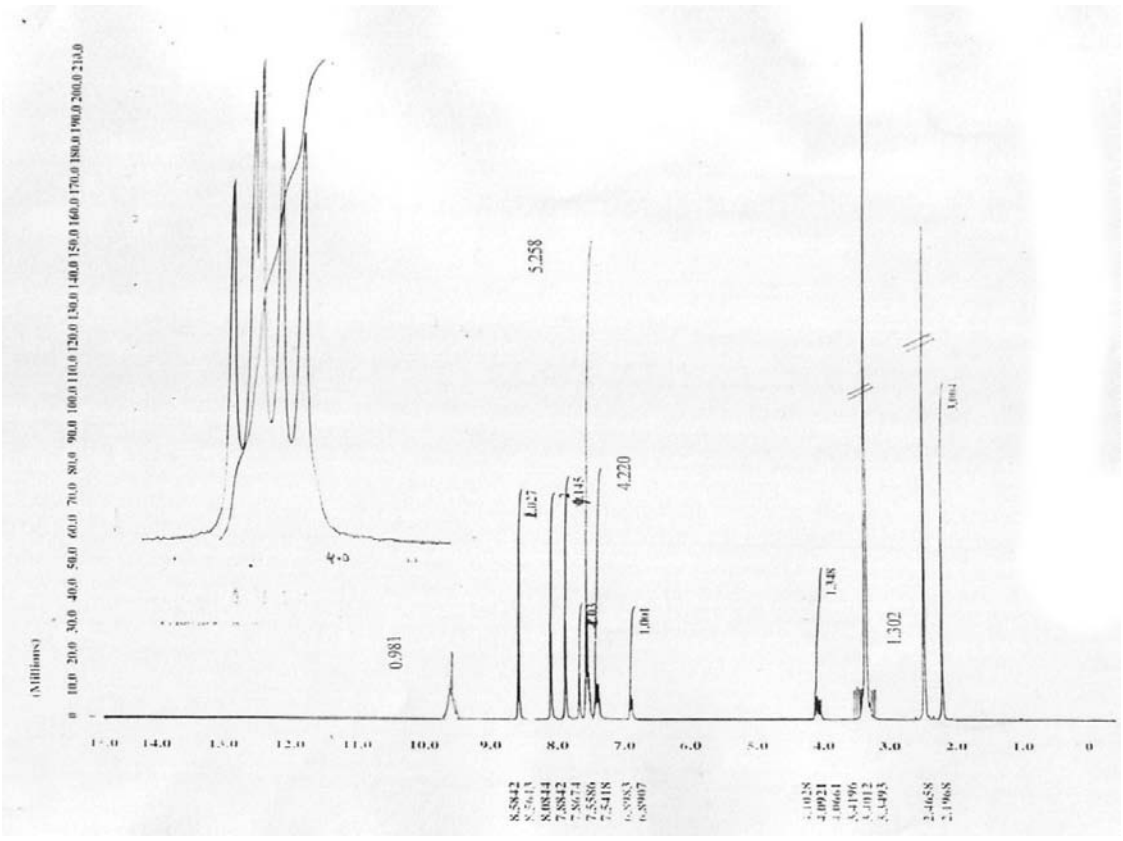

Figure S32. [1]H NMR spectrum of compound **14**.

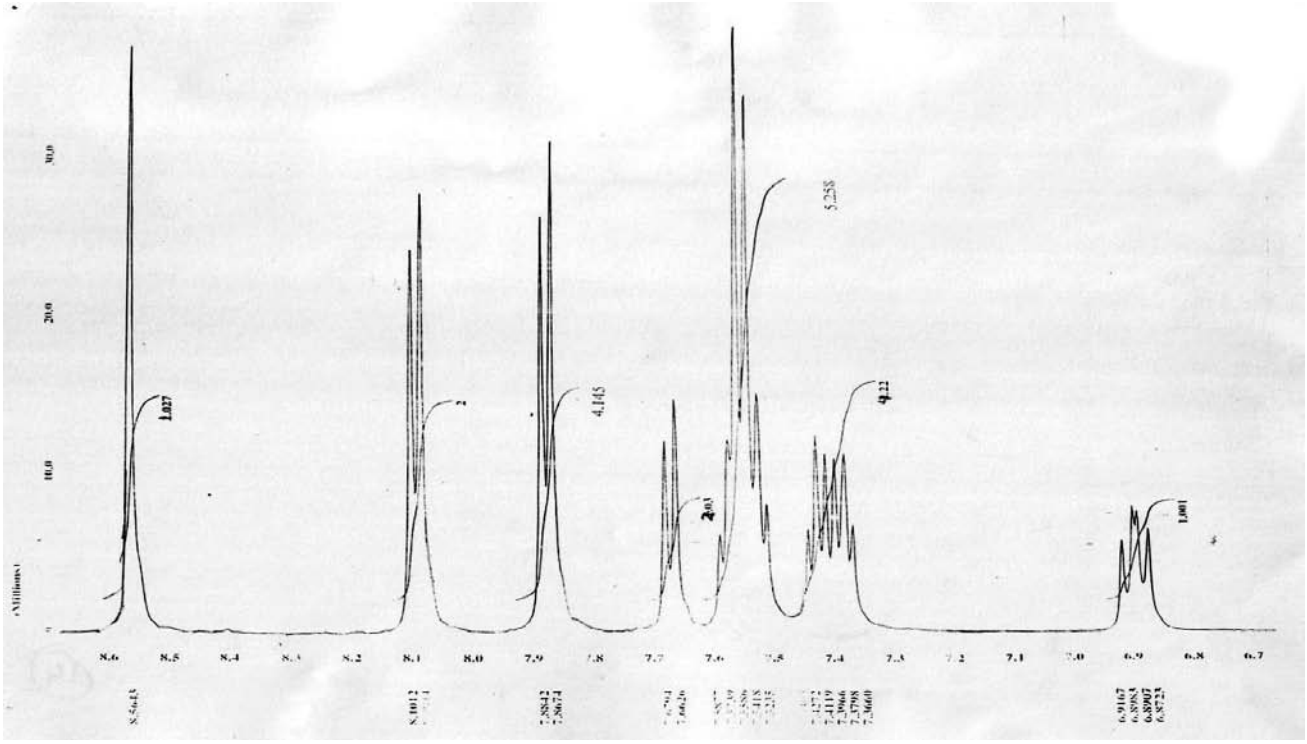

Figure S33. [1]H NMR spectrum of compound **14**.

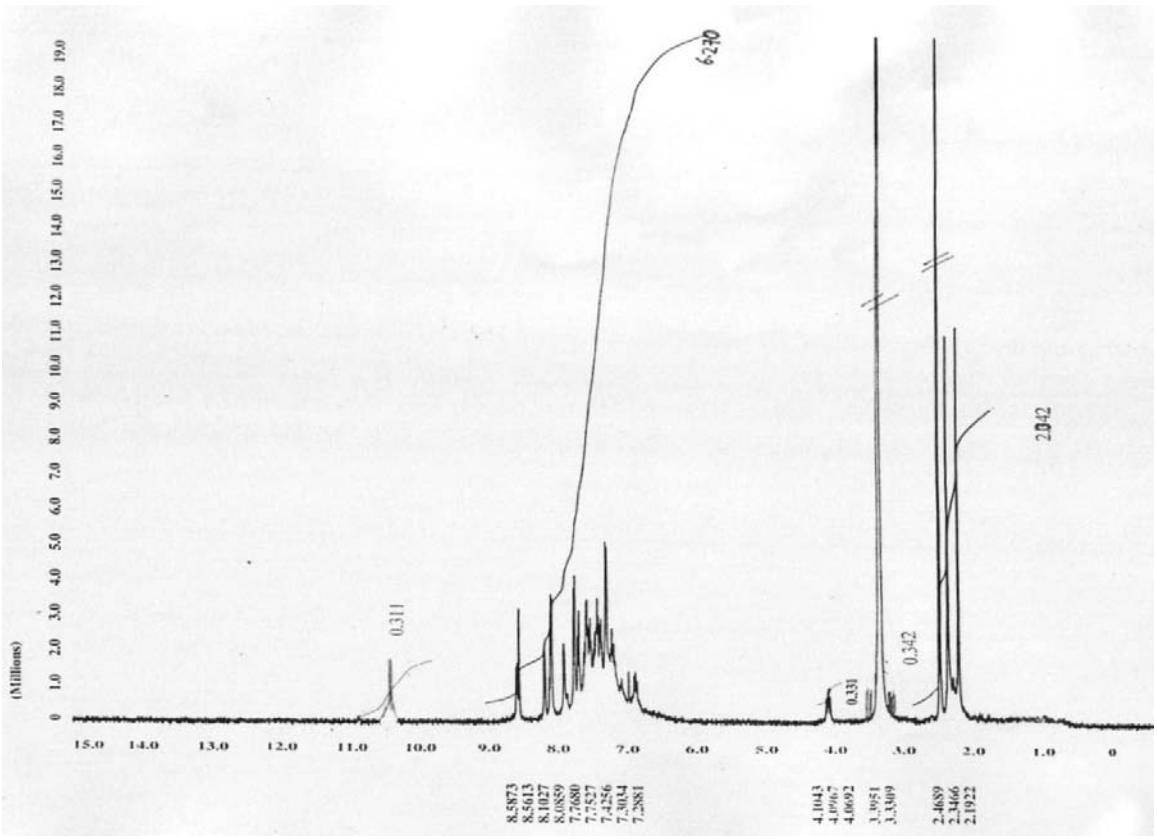

Figure S34. [1]H NMR spectrum of compound **15**.

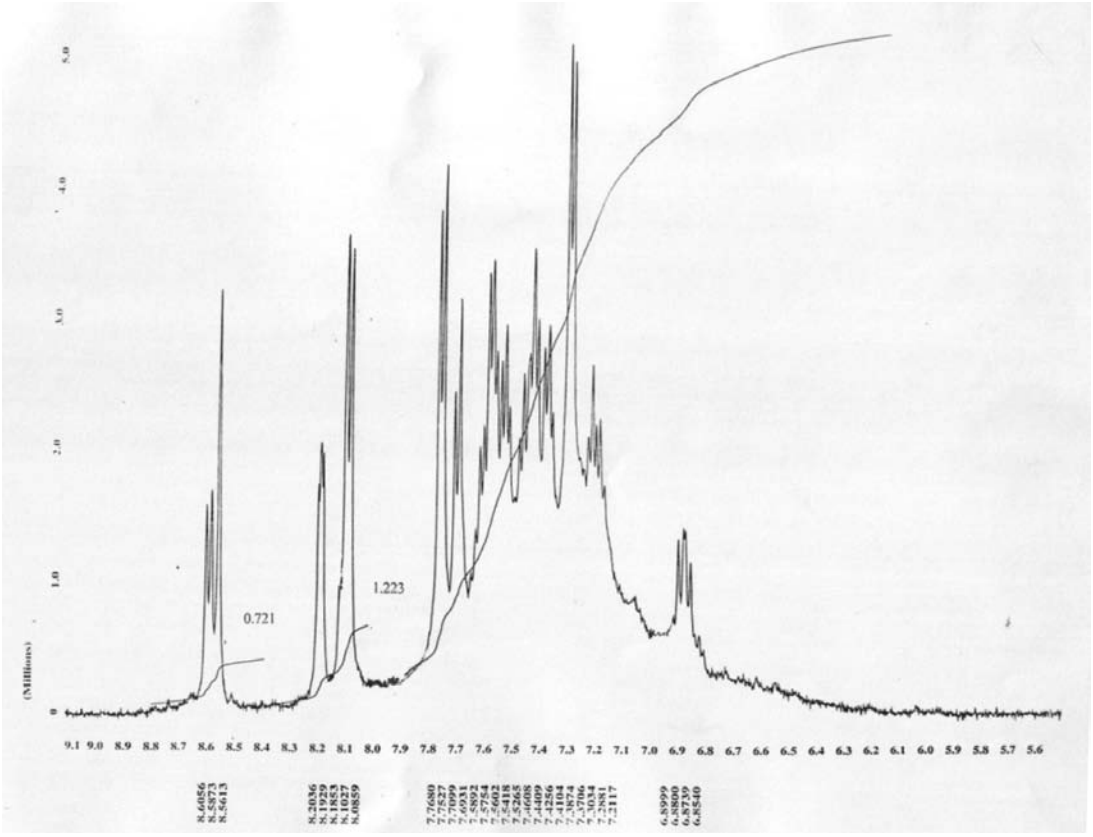

Figure S35. [1]H NMR spectrum of compound **15**.

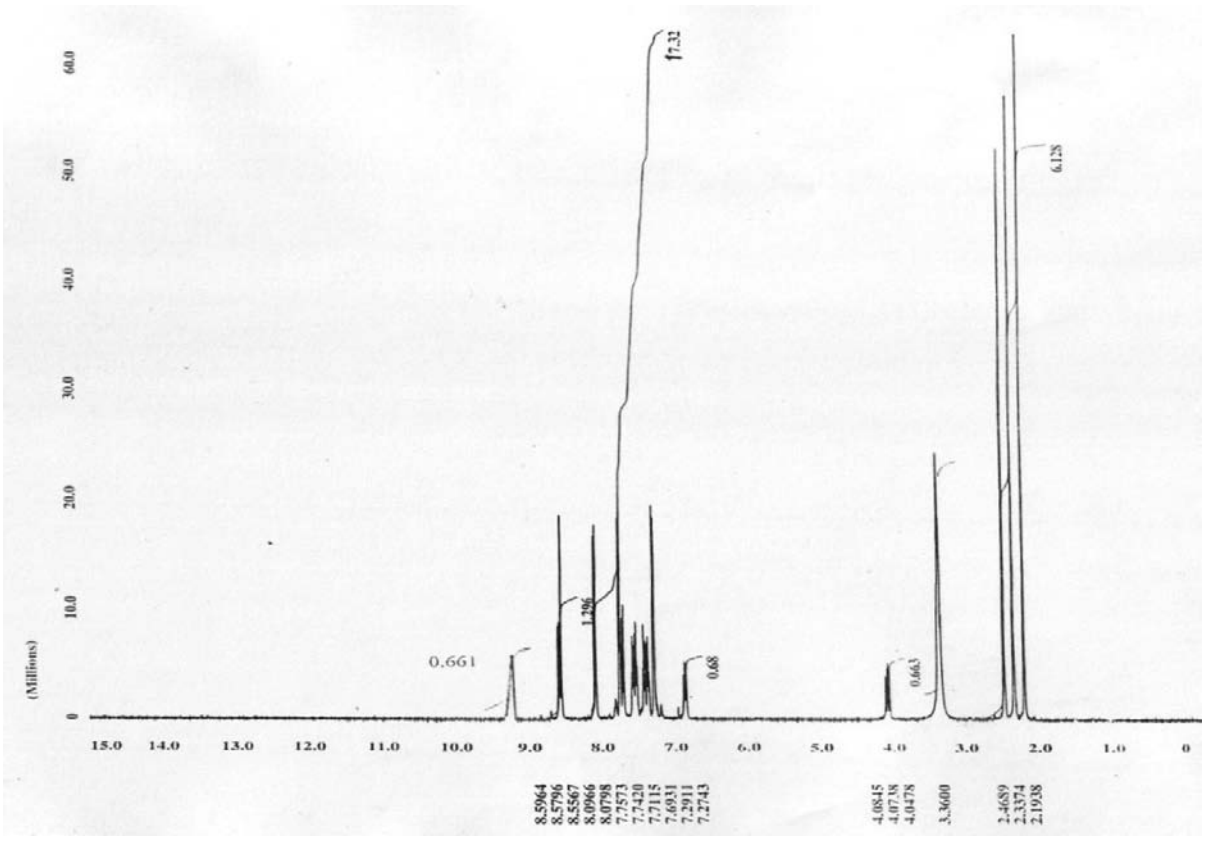

Figure S36. [1]H NMR spectrum of compound **17**.

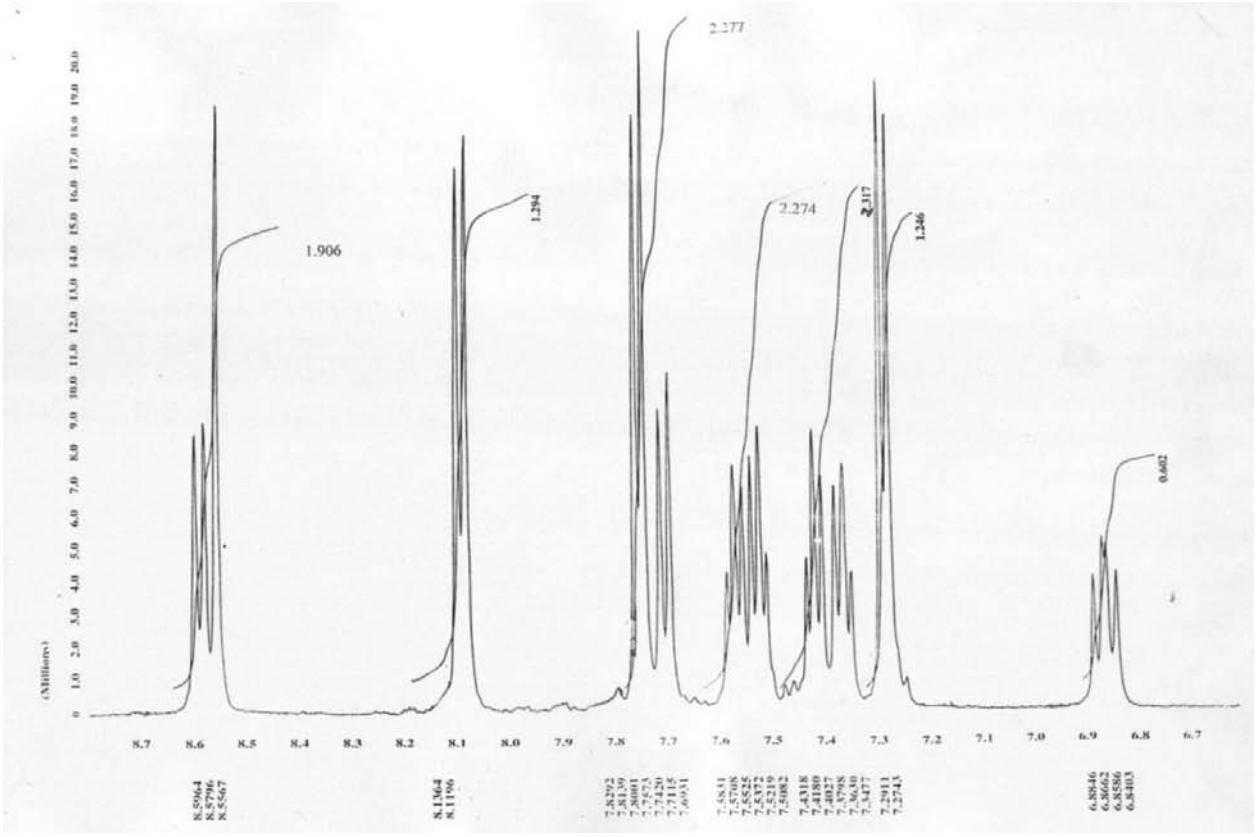

Figure S37. [1]H NMR spectrum of compound **17**.

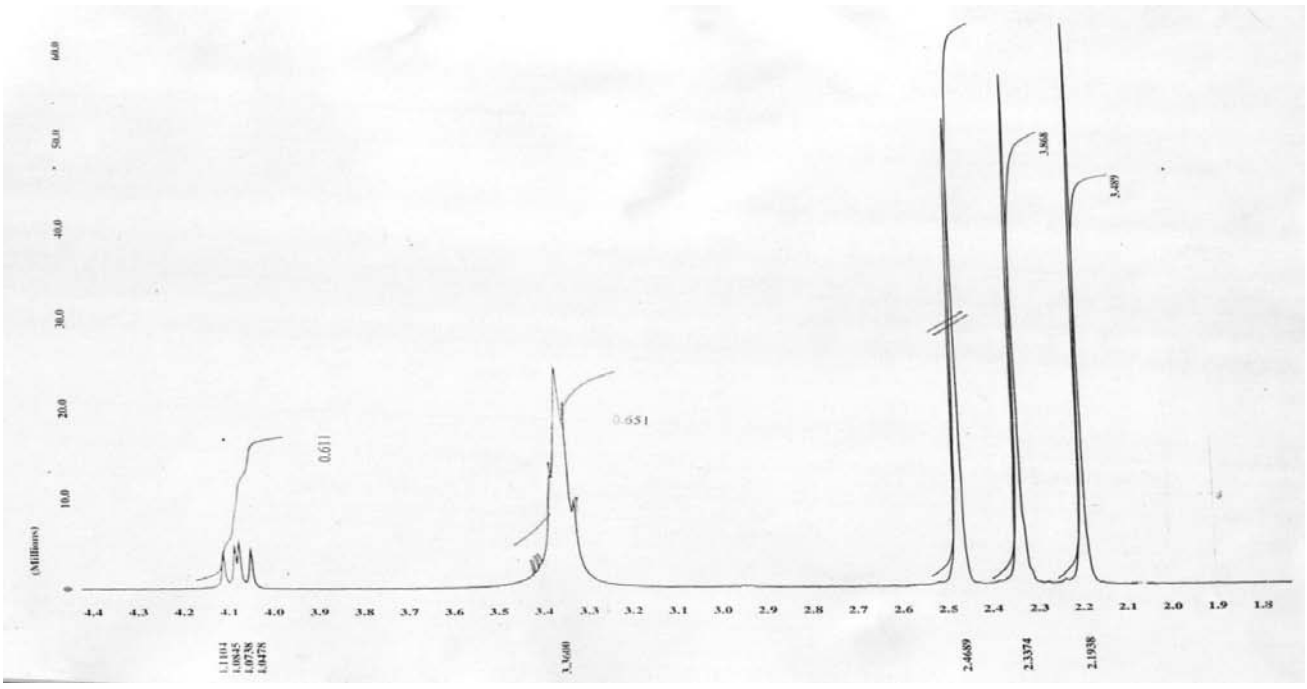

Figure S38. ^{1}H NMR spectrum of compound **17**.

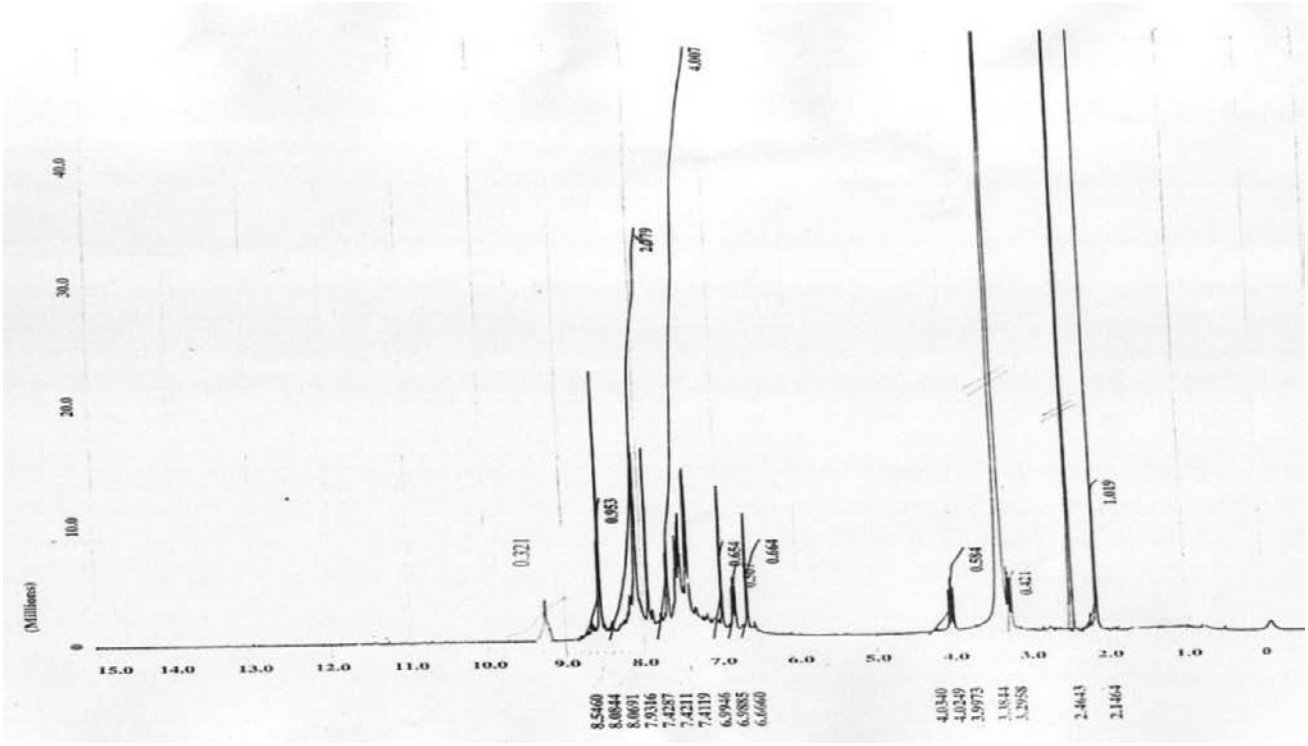

Figure S39. ^{1}H NMR spectrum of compound **18**.

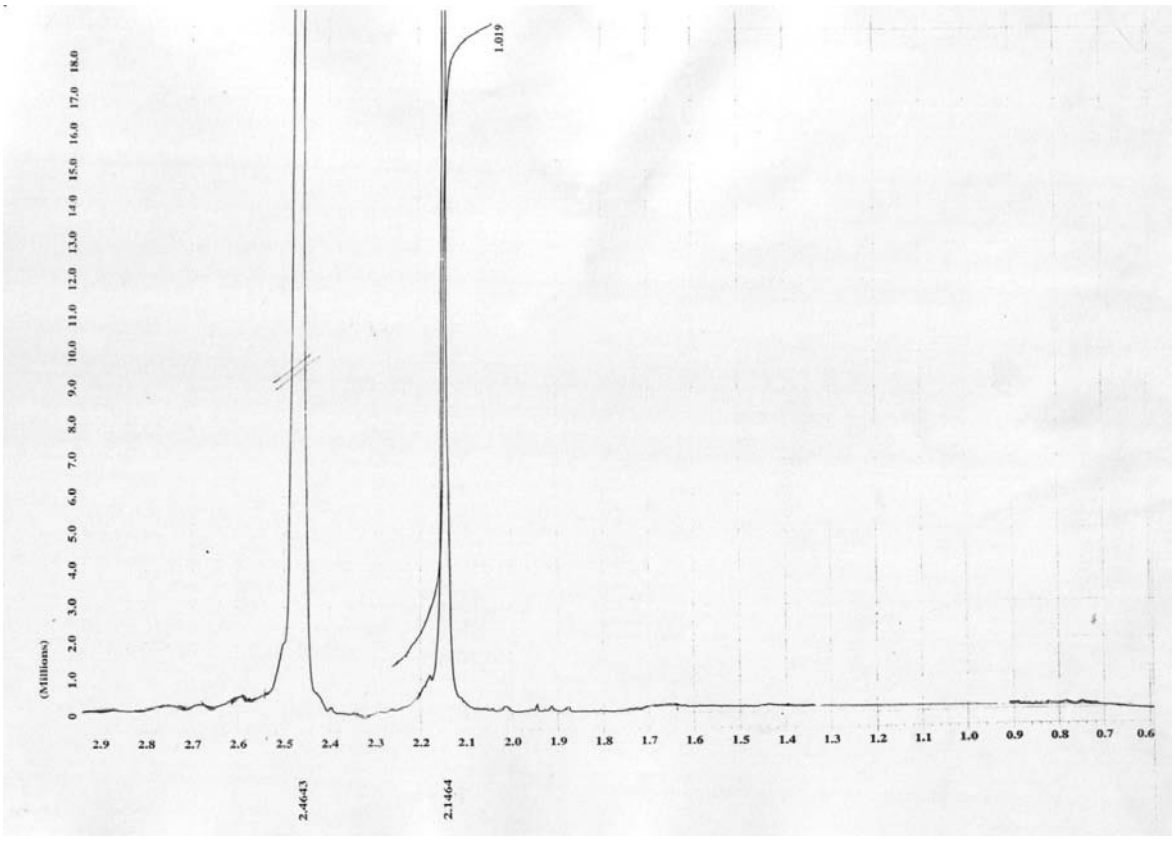

Figure S40. [1]H NMR spectrum of compound **18**.

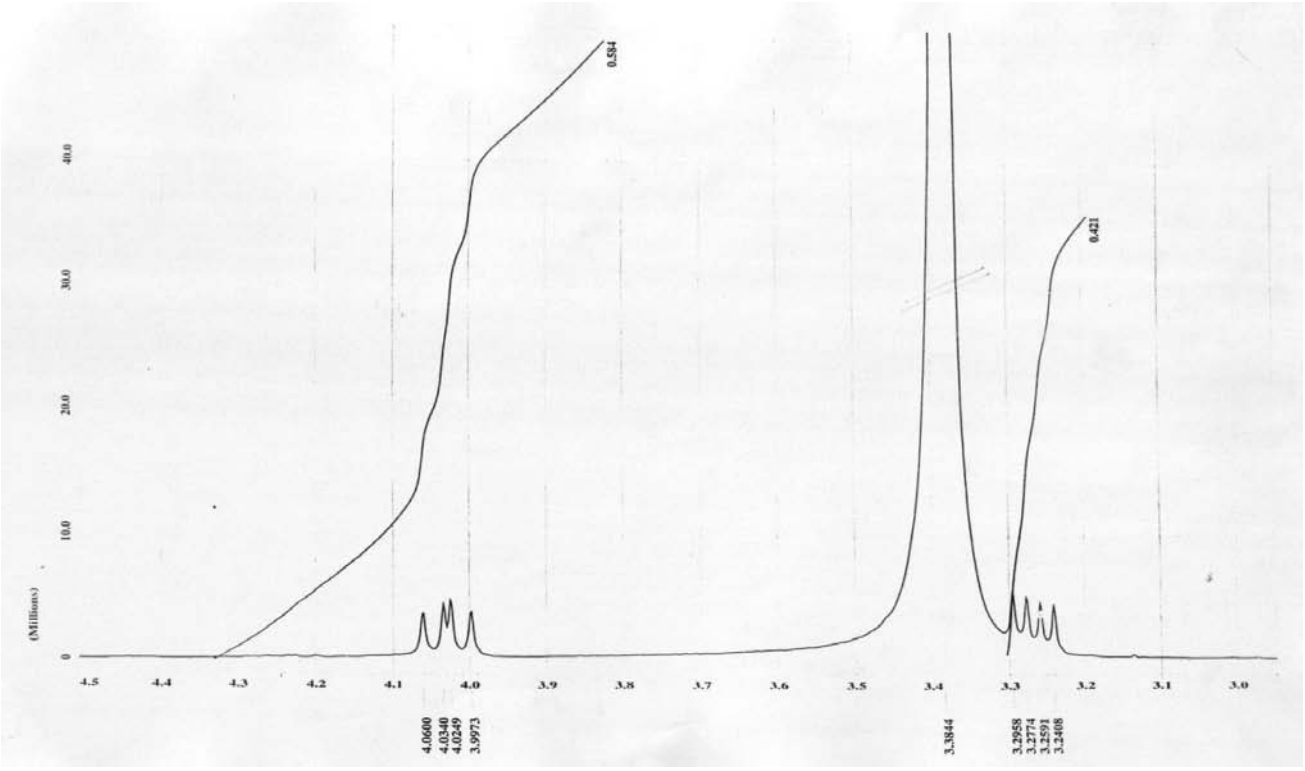

Figure S41. [1]H NMR spectrum of compound **18**.

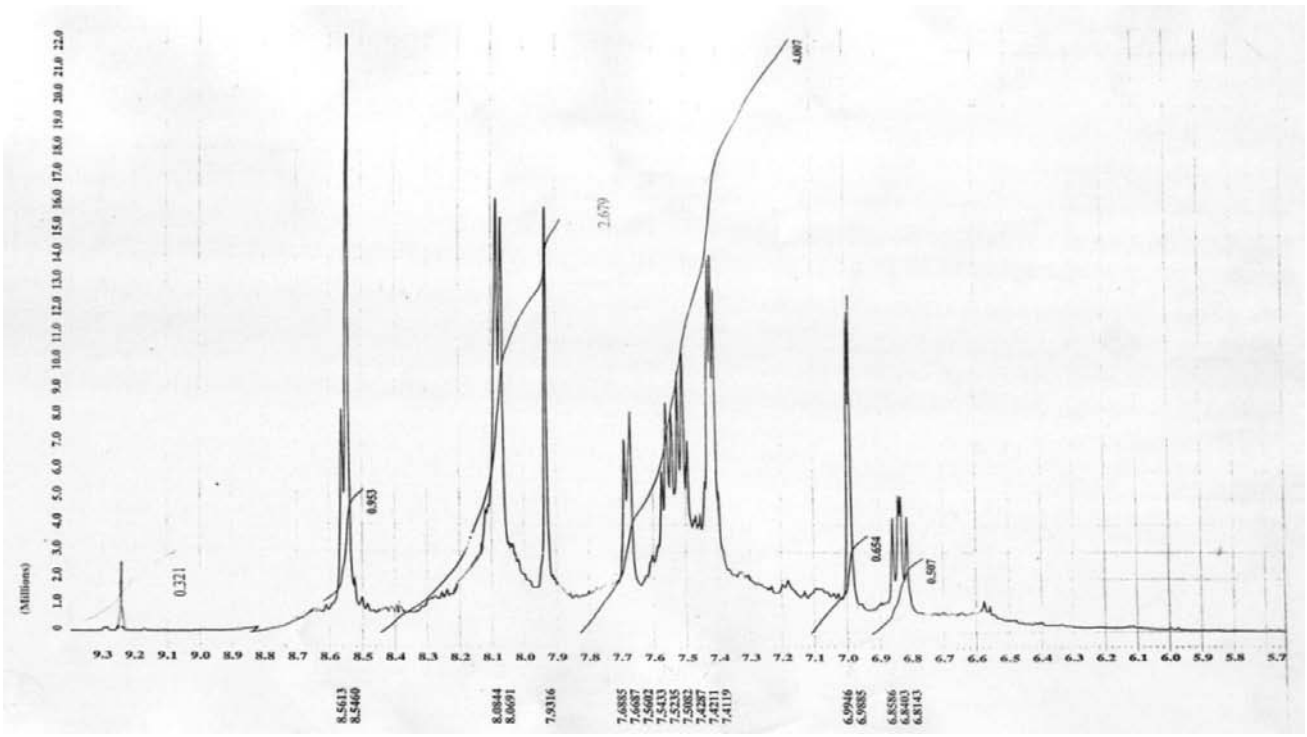

Figure S42. [1]H NMR spectrum of compound **18**.

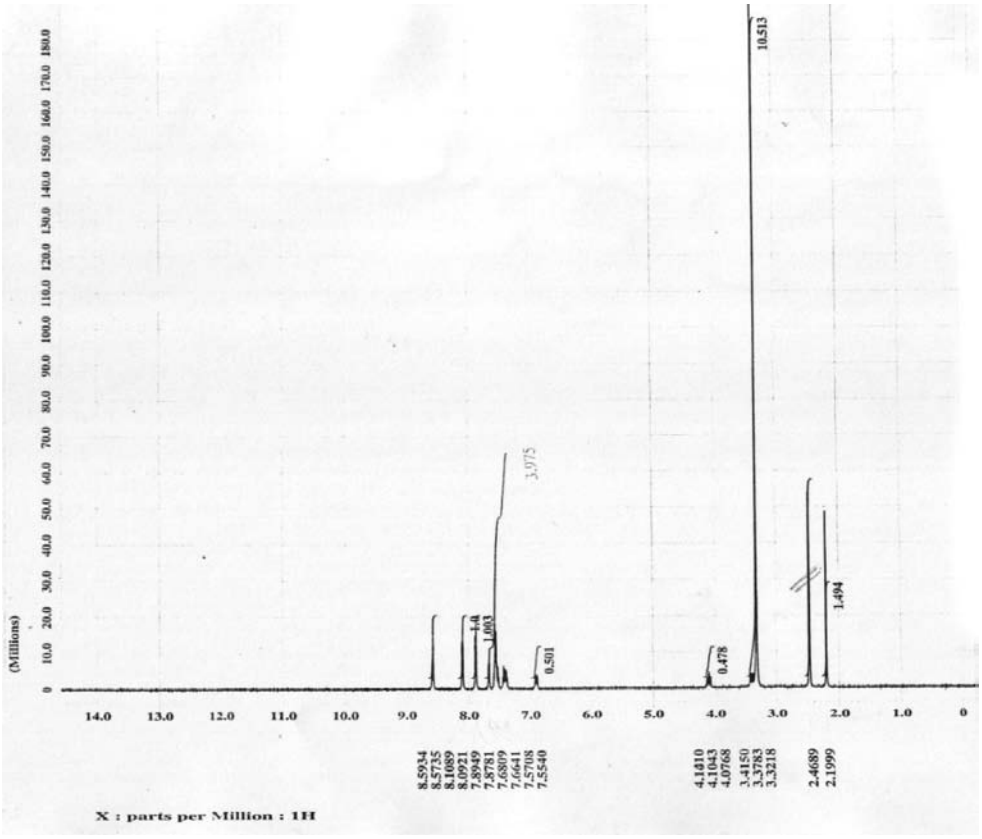

Figure S43. [1]H NMR spectrum of compound **19**.

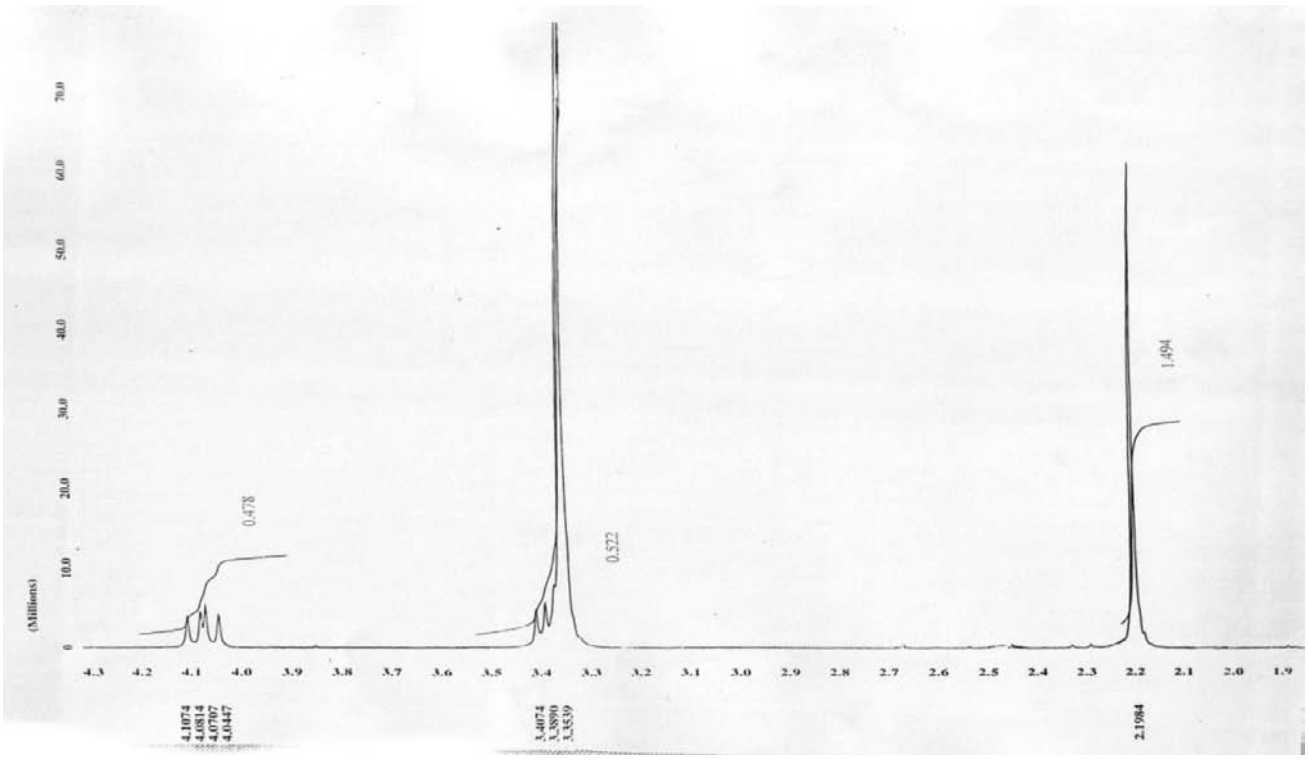

Figure S44. [1]H NMR spectrum of compound **19**.

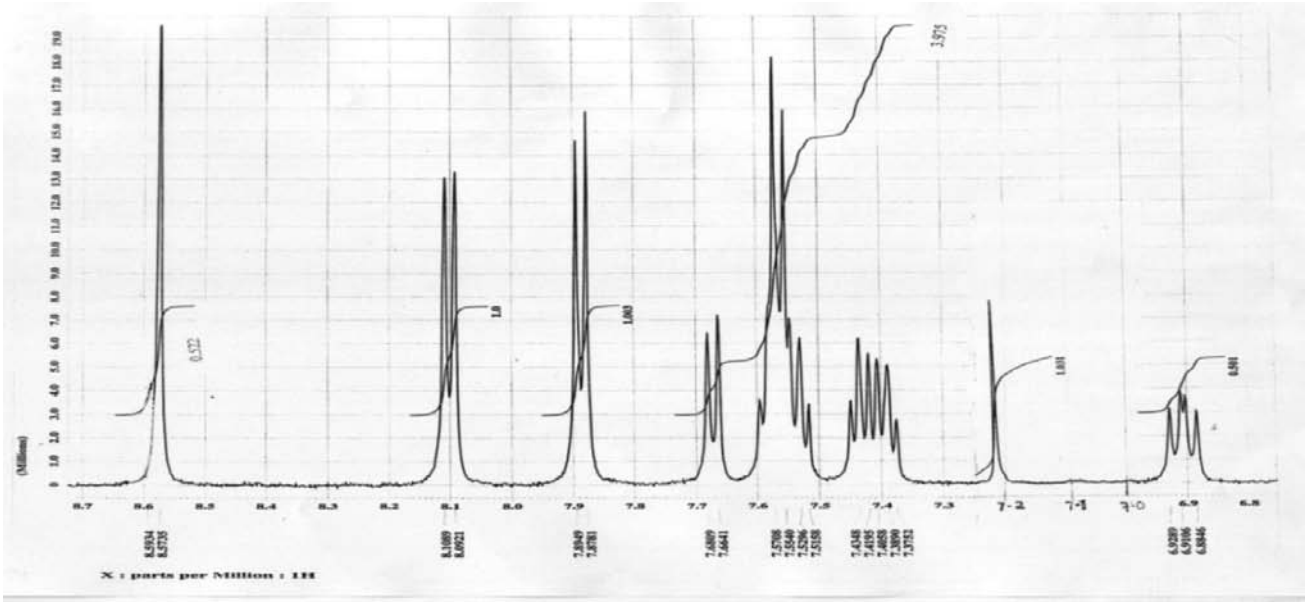

Figure S45. [1]H NMR spectrum of compound **19**.

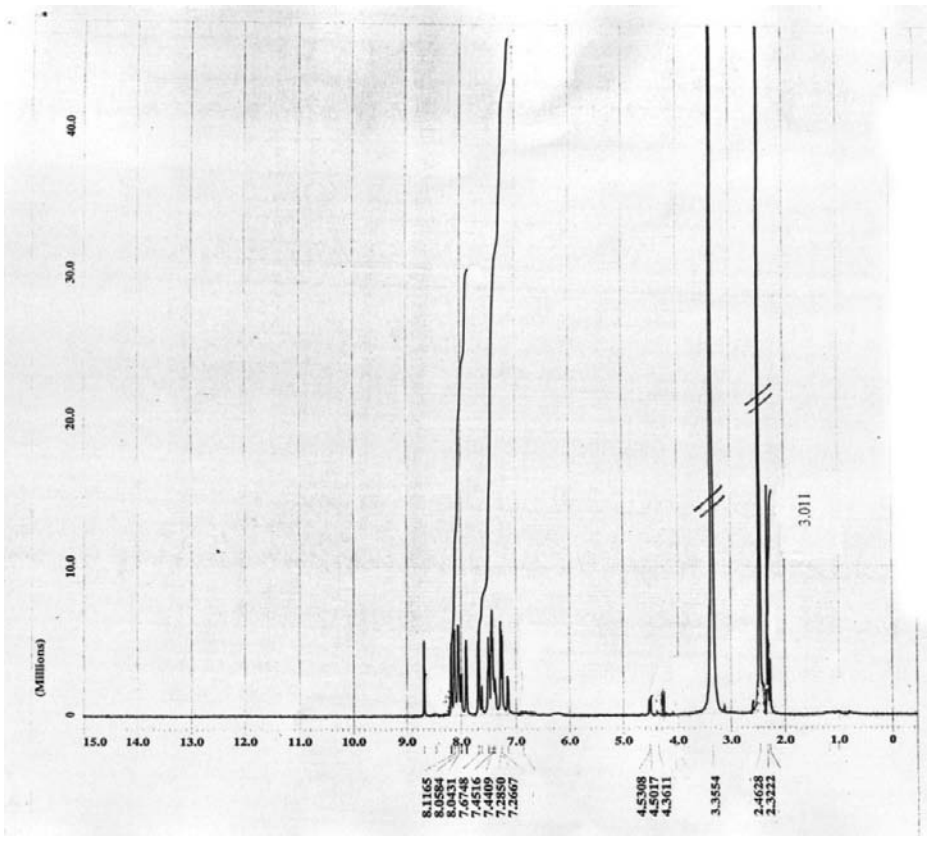

Figure S46. [1]H NMR spectrum of compound **20**.

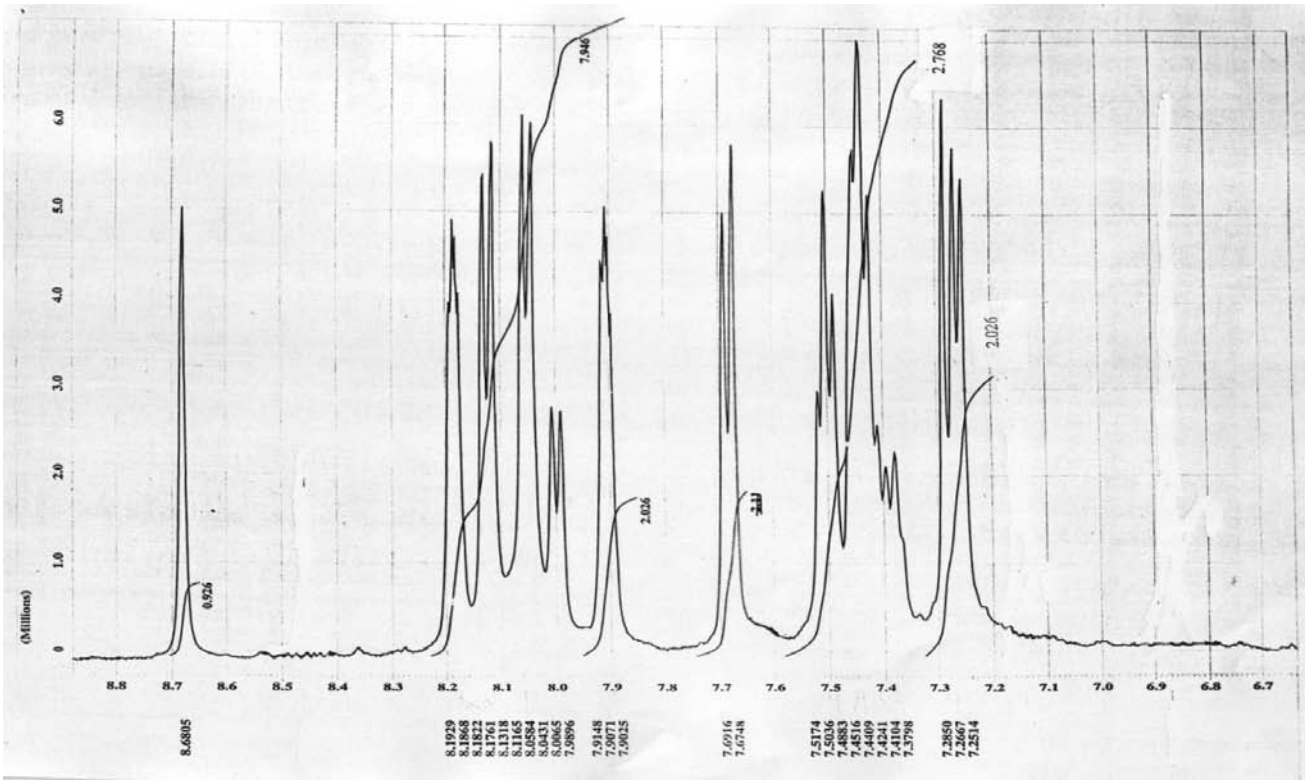

Figure S47. [1]H NMR spectrum of compound **20**.

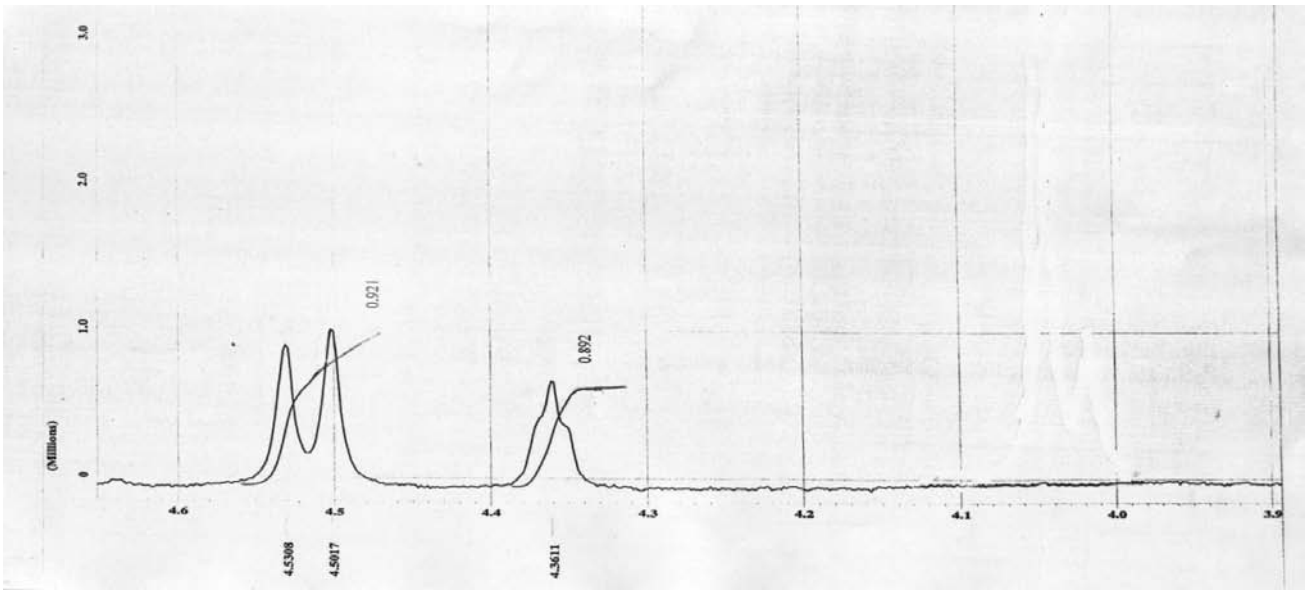

Figure S48. [1]H NMR spectrum of compound **20**

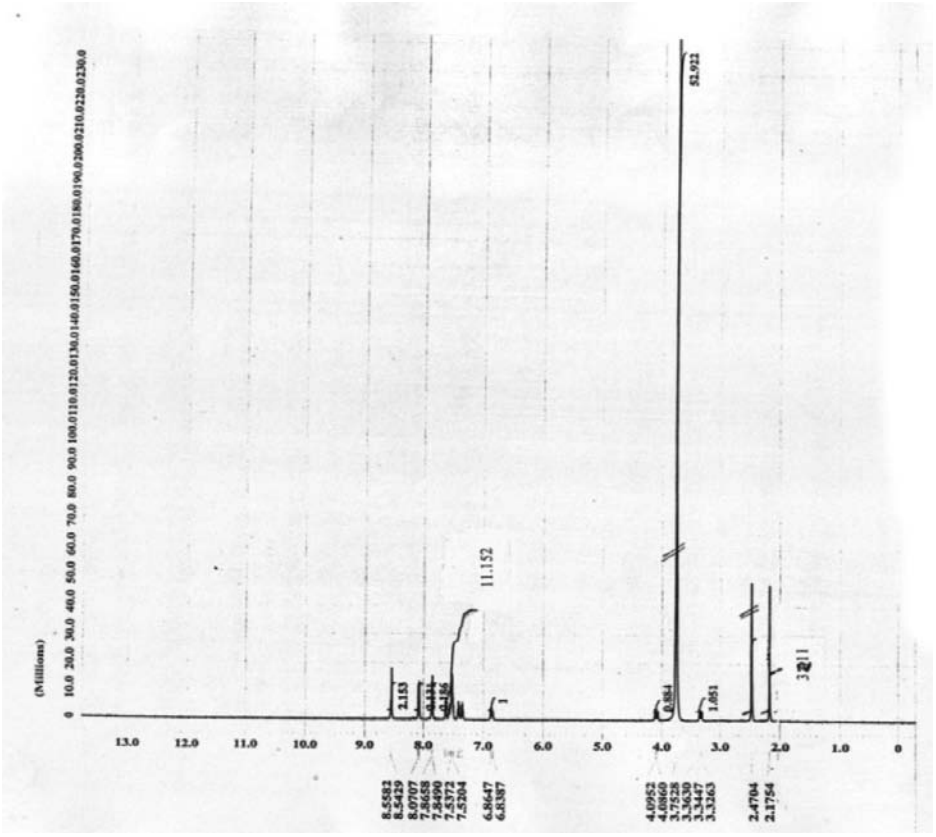

Figure S49. [1]H NMR spectrum of compound **22**.

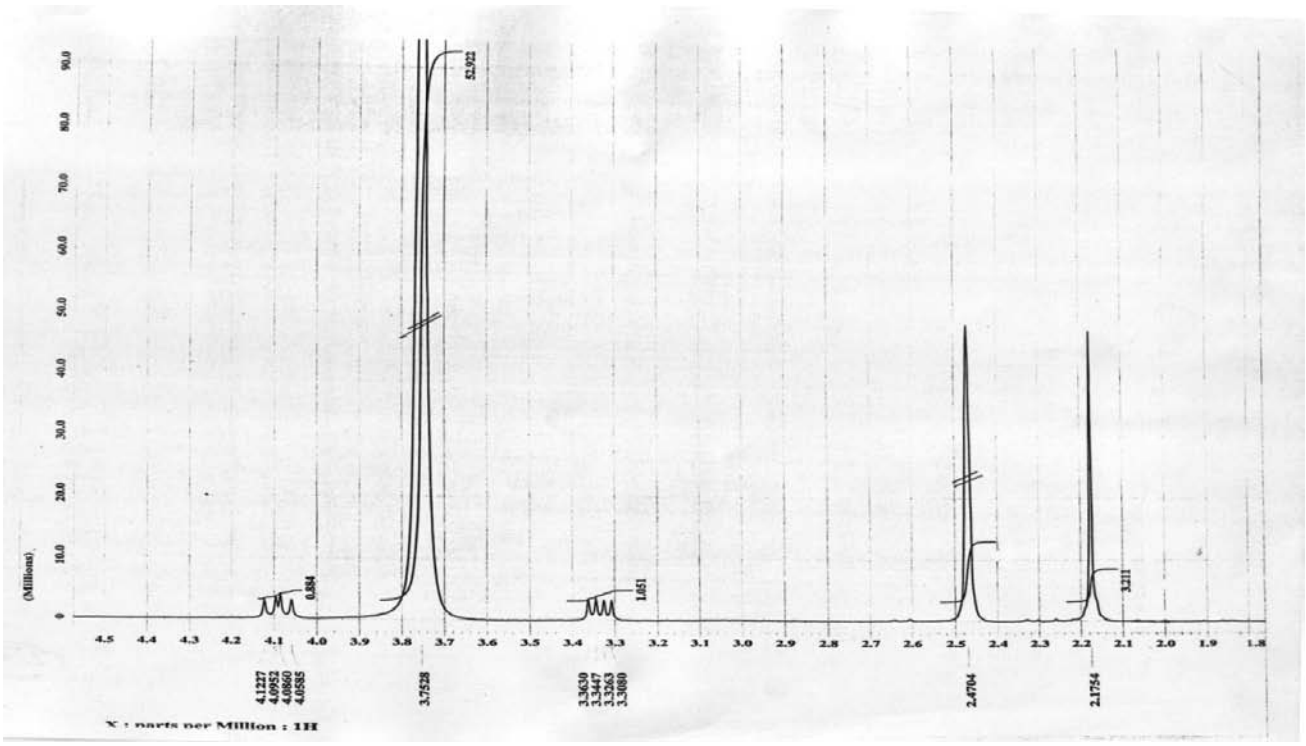

Figure S50. [1]H NMR spectrum of compound **22**.

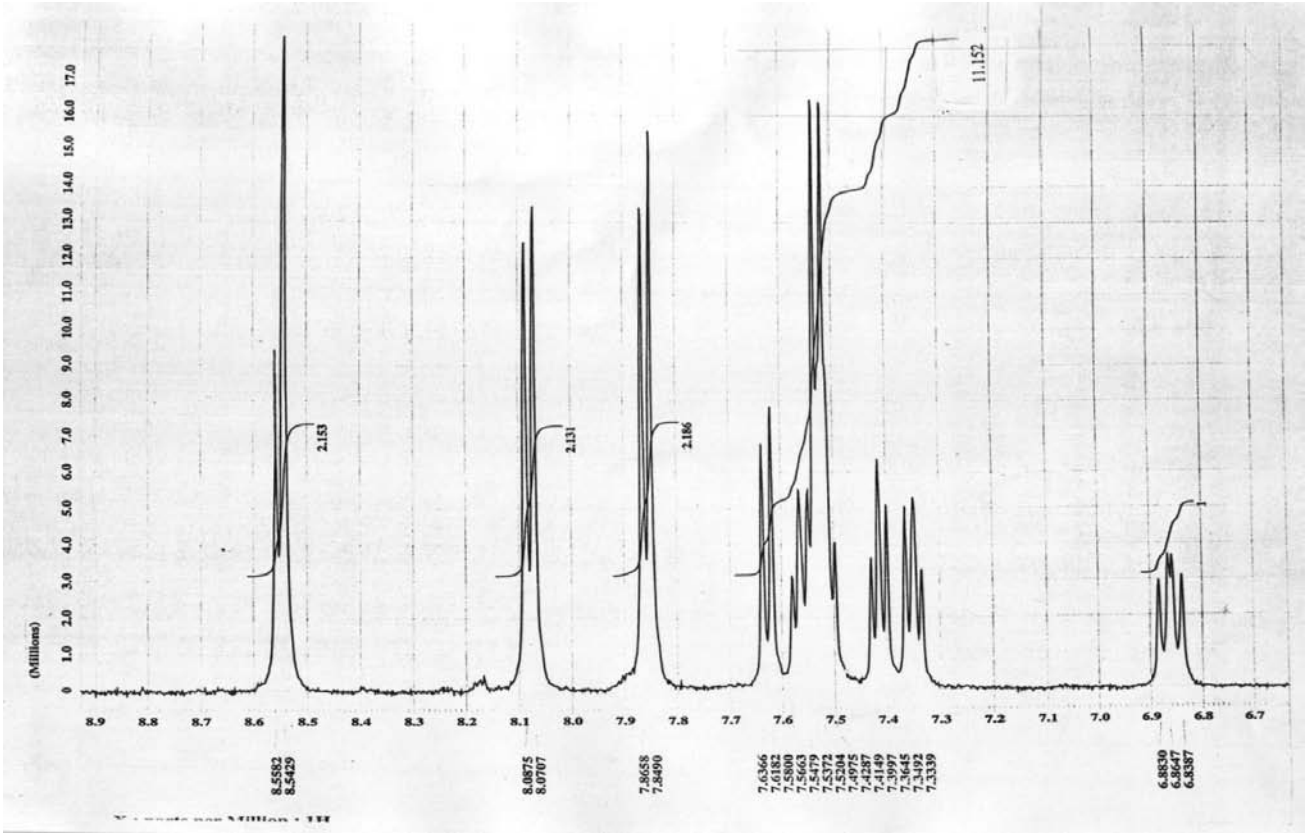

Figure S51. [1]H NMR spectrum of compound **22**.

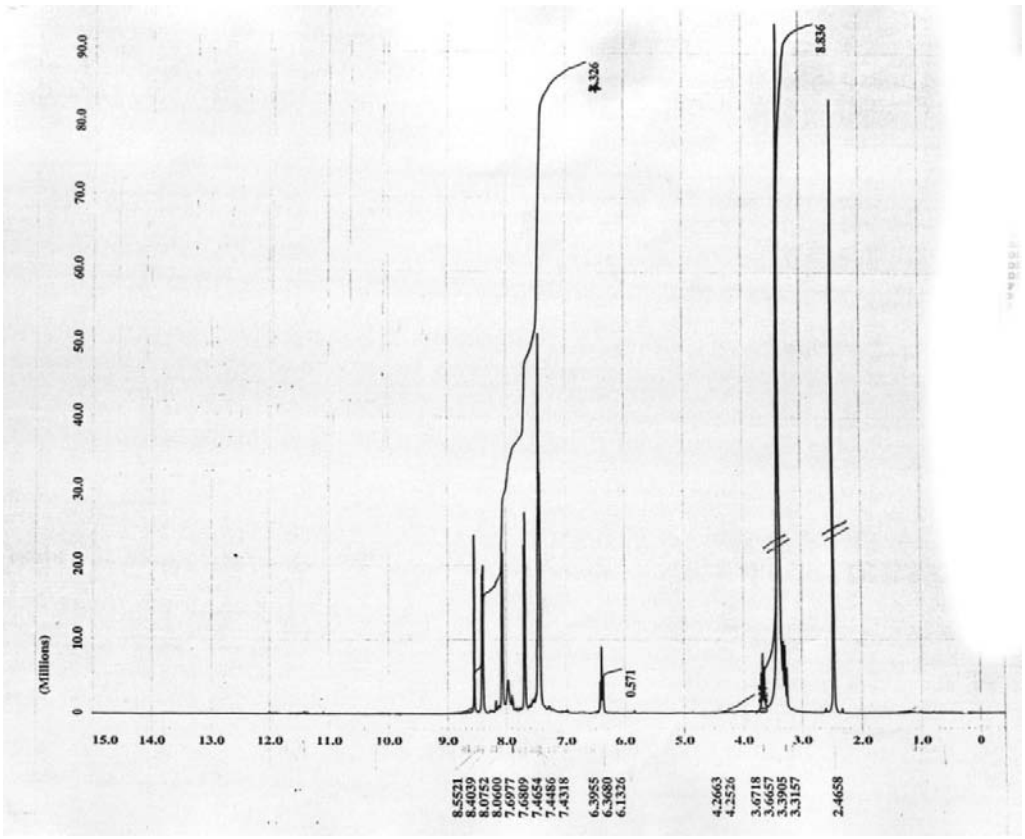

Figure S52. [1]H NMR spectrum of compound **26**.

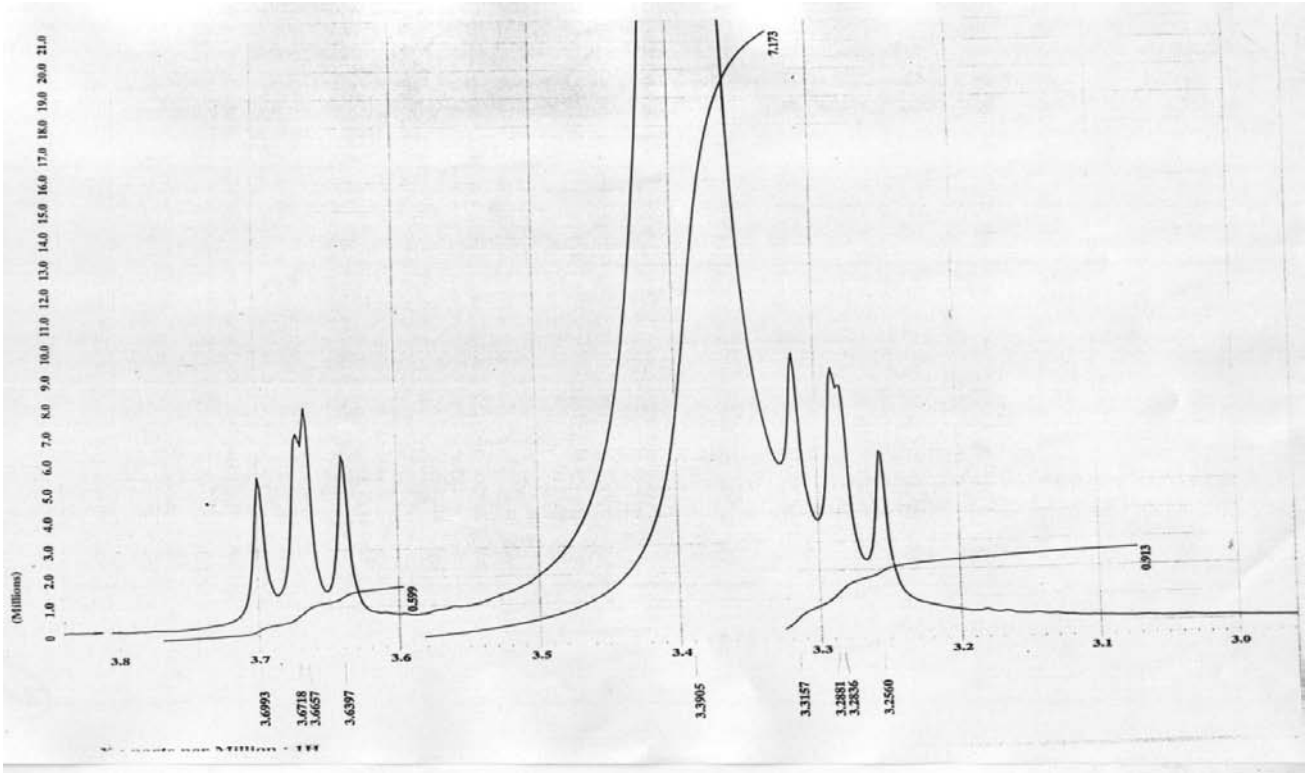

Figure S53. [1]H NMR spectrum of compound **26**.

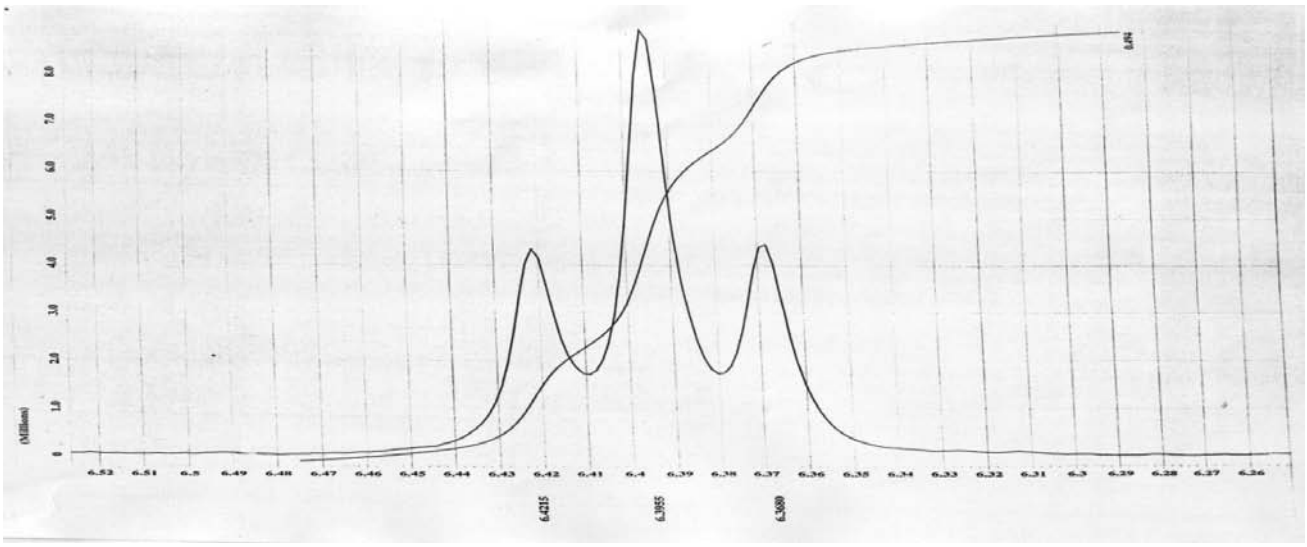

Figure S54. ^{1}H NMR spectrum of compound **26**.

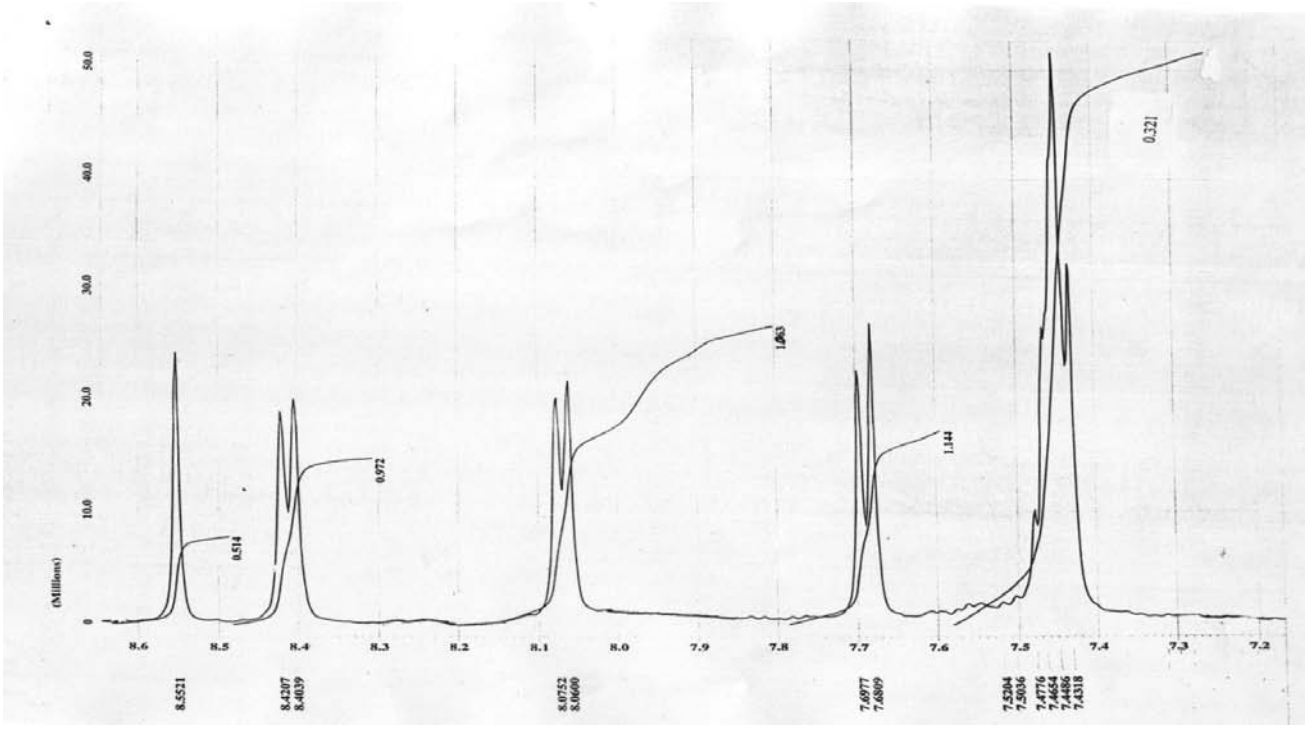

Figure S55. ^{1}H NMR spectrum of compound **26**.

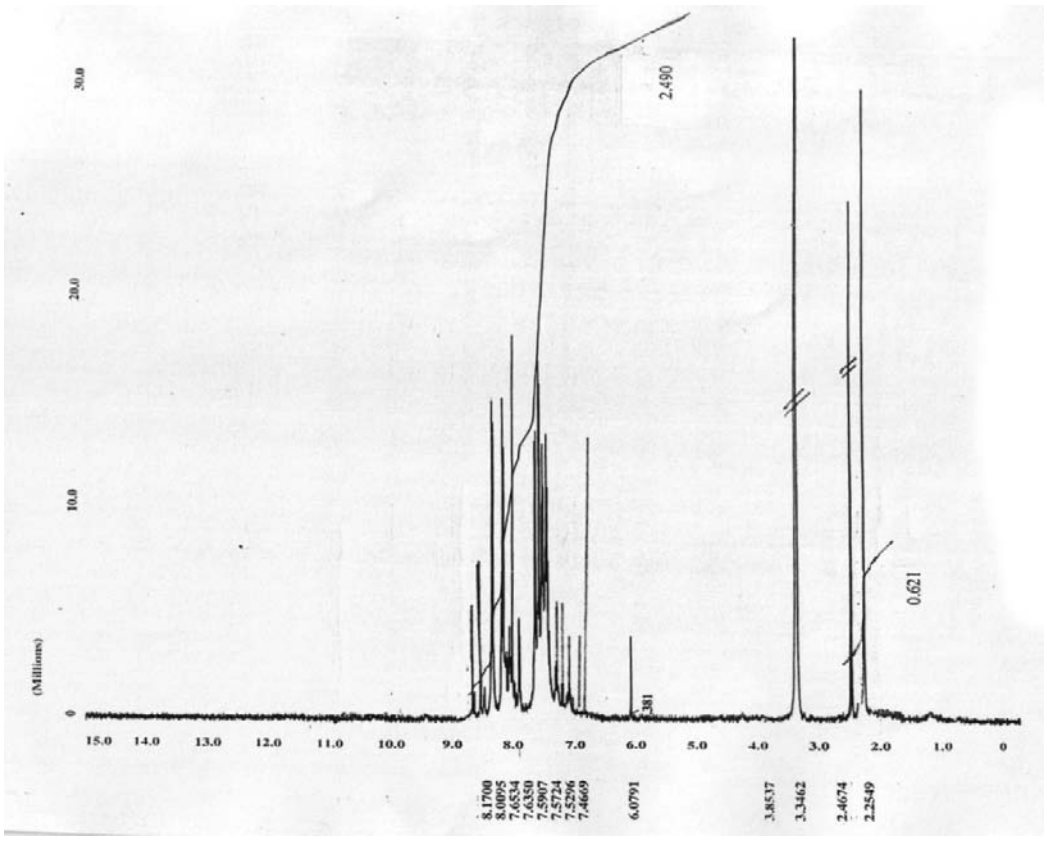

Figure S56. [1]H NMR spectrum of compound **33**.

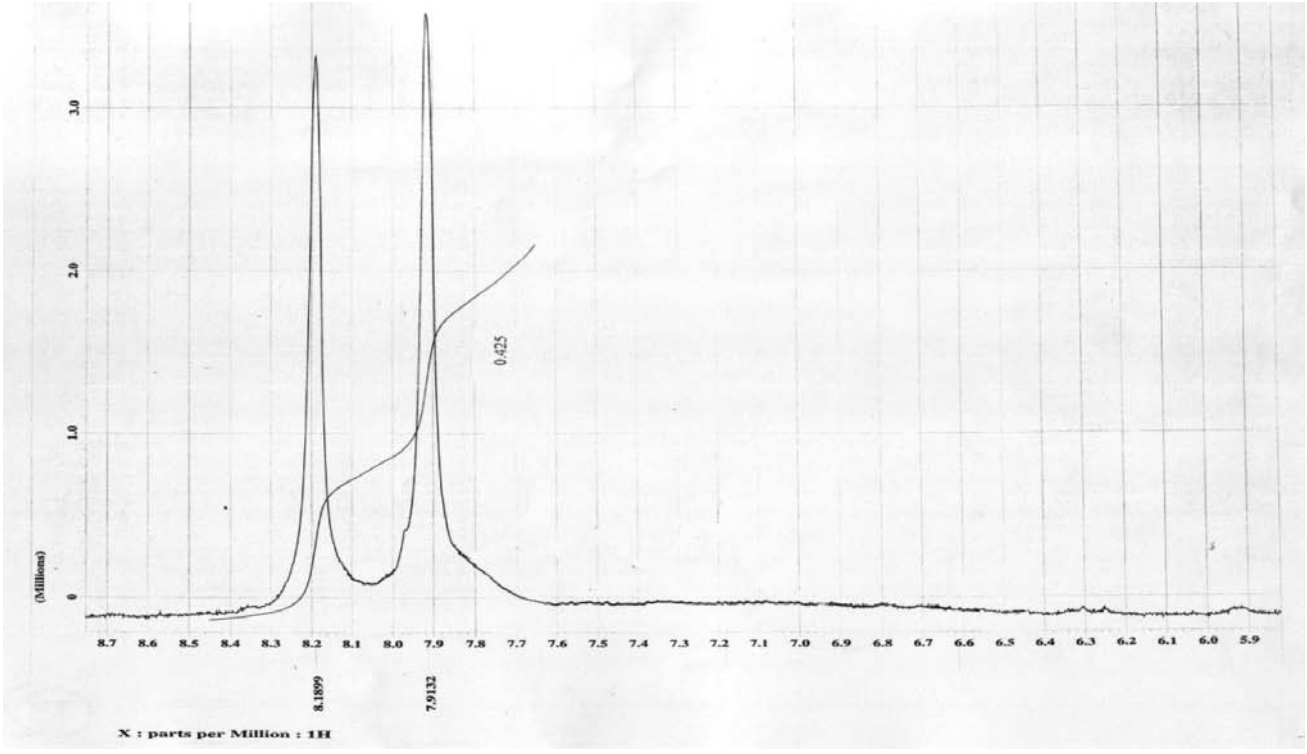

Figure S57. [1]H NMR spectrum of compound **33**.

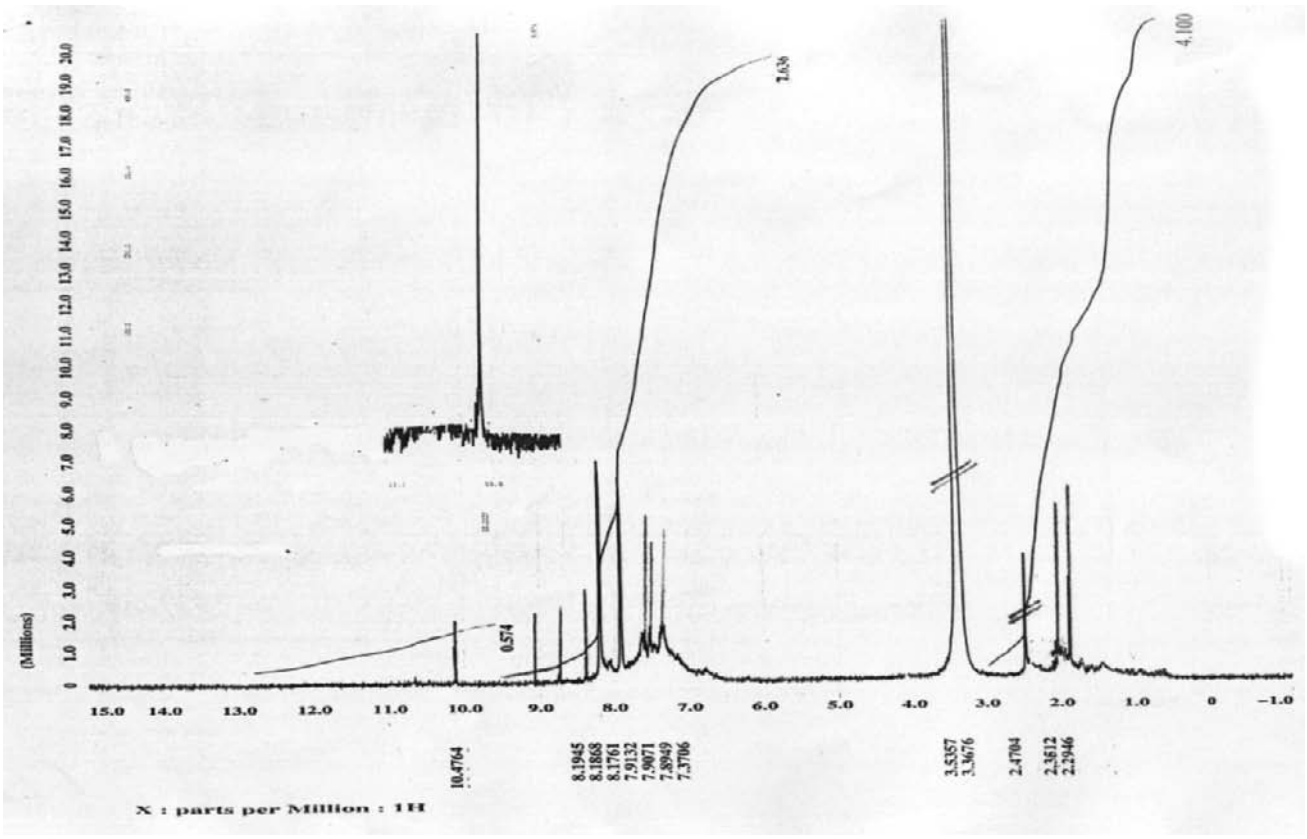

Figure S58. ^{1}H NMR spectrum of compound **36**.

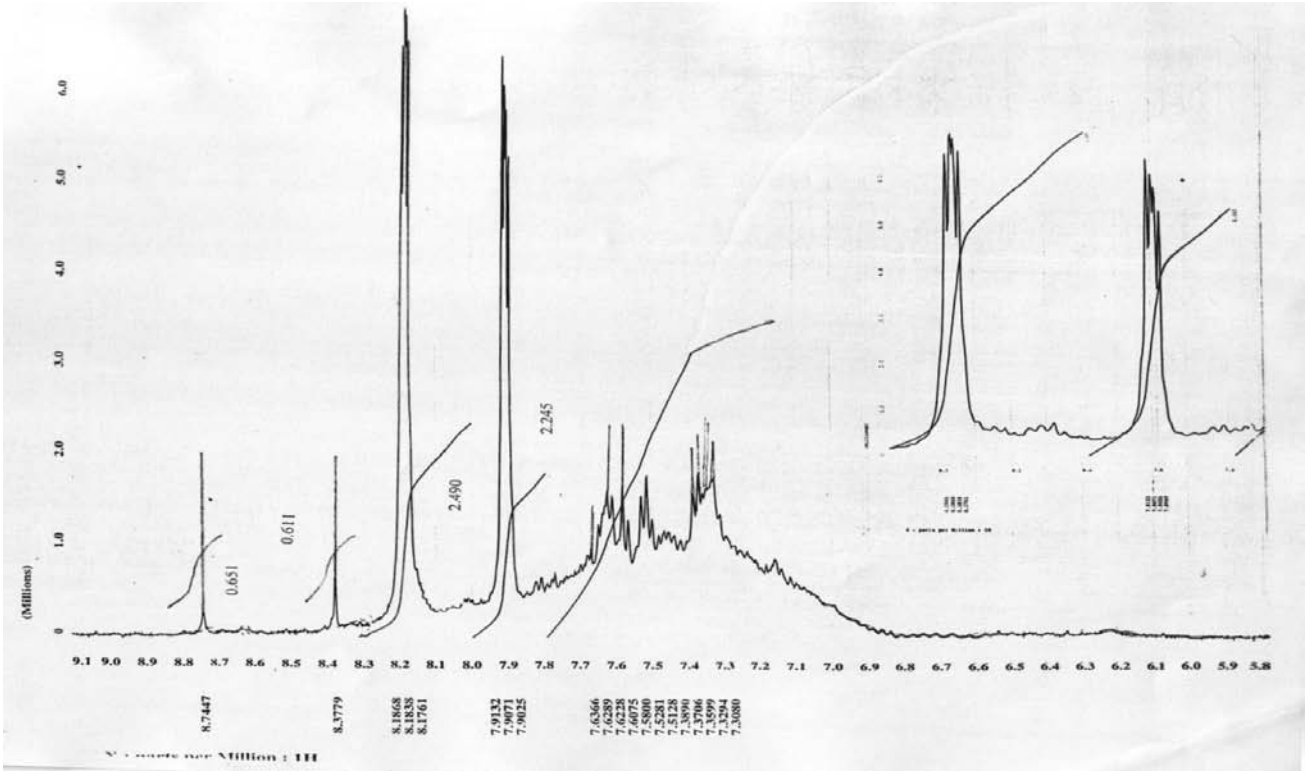

Figure S59. ^{1}H NMR spectrum of compound **36**.

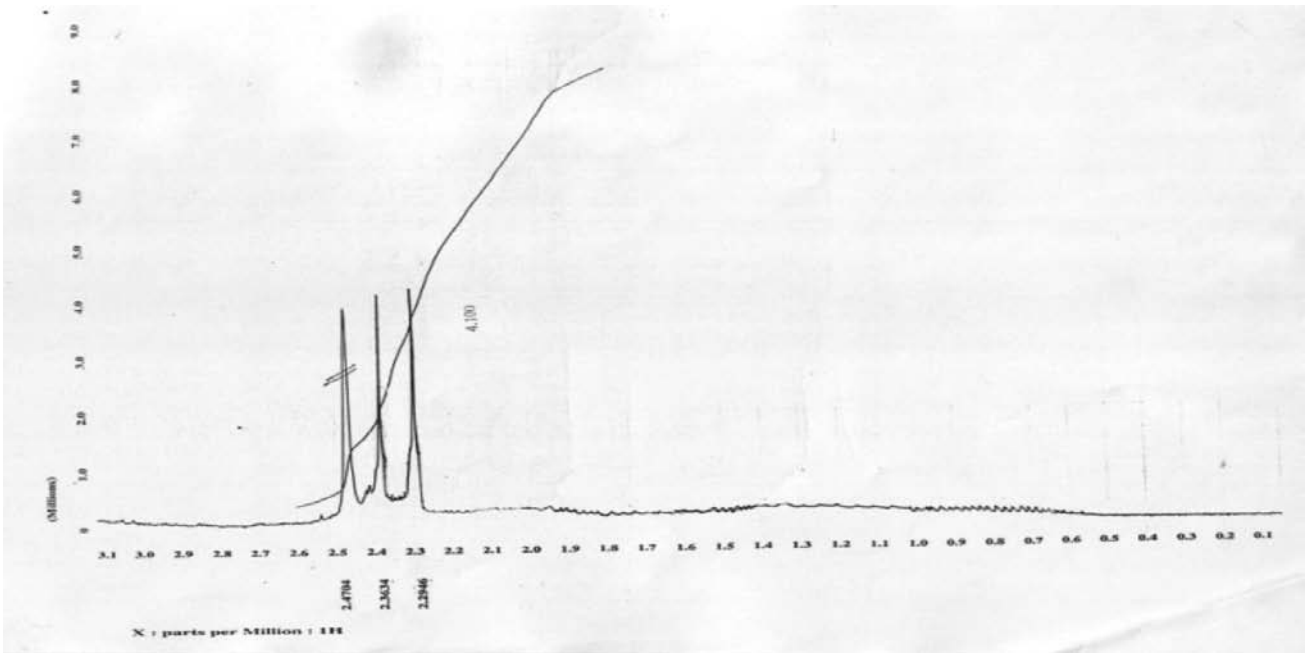

Figure S60. [1]H NMR spectrum of compound **36**.

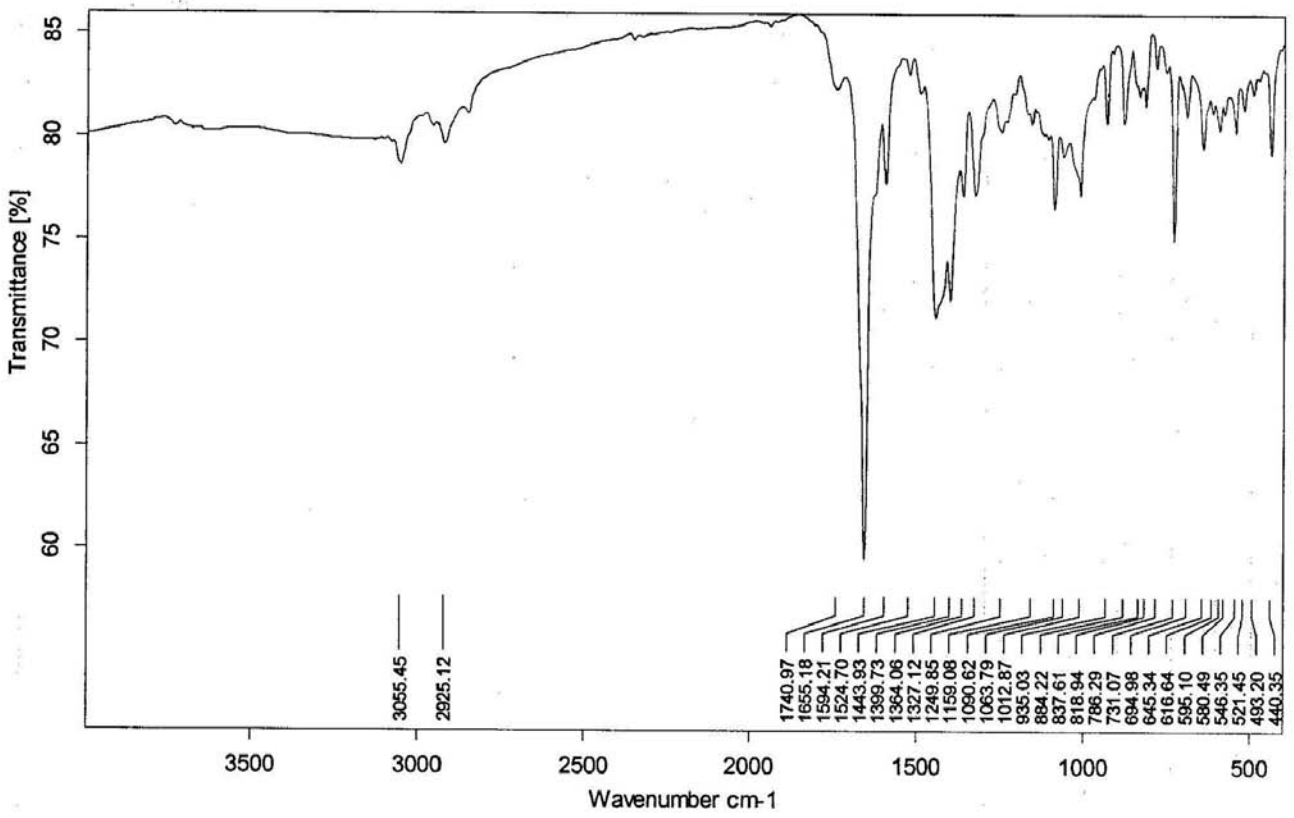

Figure S61. IR spectrum of compound **20**.

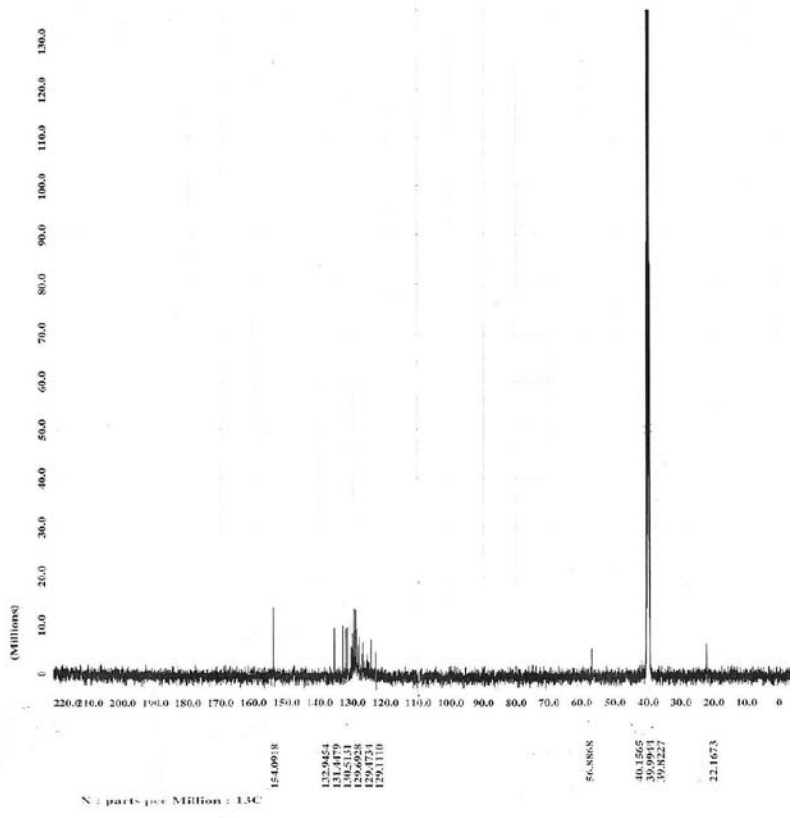

Figure S62. ^{13}C NMR spectrum of compound **20**.

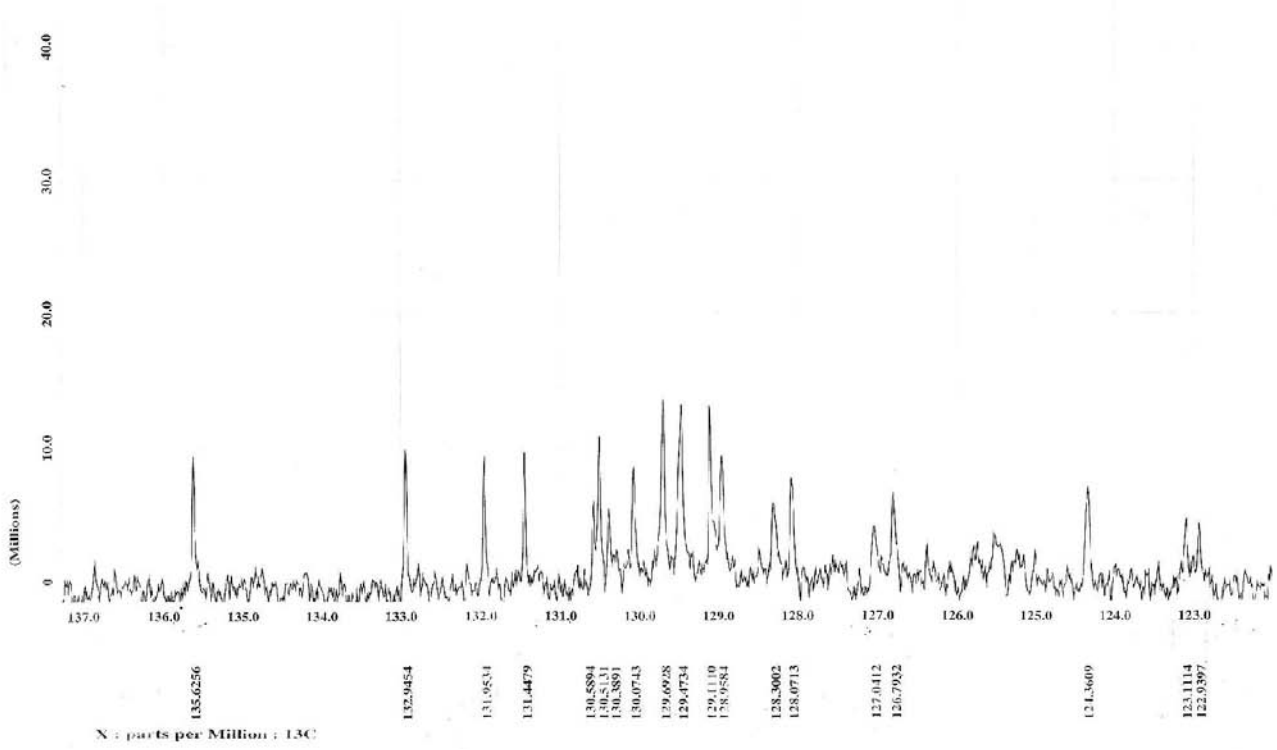

Figure S63. ^{13}C NMR spectrum of compound **20**.