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Synthesis of Some New Benzoxazepine Compounds Form Derivatives of Schiff Bases

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Abstract:

This study involved synthesize (1,3) oxazepine. The step 1 includes the preparation of compound (1), (5-Bromo-2-mercapto-6-(4-methoxyphenyl) pyrimidin-4(3H)-one), by the condensation of anisaldehyde and ethylbromoacetat and thiourea in EtOH. In the step2, chalcones (2-6) have been produced. The reaction of compound (1) with chalcones (2-6) that gives azo Michael adduct (7-11) is made in the third step. Schiff's bases (12-16) were prepared by the reaction ketones (7-11) with 2,4-dinitroaniline. Finally preparation of new benzo [1,3] oxazepine compounds (17-21) are prepared by the reaction of phthalic anhydride with Schiff's bases. The synthesized compounds are identified by physical (melting points, colour change) and spectral methods such as (IR, proton-nmr).

Keywords: β-amino ketones, Michael addition, Oxazepine

تحضير بعض مركبات البنزواوكسازبين الجديدة من مشتقات قواعد شيف

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الخلاصة

الدراسة تضمنت تحضير (3,1) اوكسازبين. في الخطوة الاولى تم تحضير المركب (1) 5- برومو-2-ميركابتو- 6-(4- ميثوكسي فنيل) بيرميدين- 4(3H) اون. بتكاثف الانيسالديهيد وايثايل برومو اسيتيت والثايوريا في الايثانول. الخطوة الثانية نتج عنها الجالكونات من (2- 6). وفي الخطوة الثالثة تم مفاعلة المركب 1 مع الجالكونات (2-6) لتعطي المركبات الكيتونية بيتا – امينو كيتون (7 -11). قواعد شيف (12-16) حضرت بمفاعلة مركبات (7-11) مع 4,2- ثنائي نايترو انيلين . في المرحلة الاخيرة تم تحضير المركبات الجديدة (3,1) بنزواوكسازبين (17- 21) التي حضرت من مفاعلة انهيدريد الفثاليك مع قواعد شيف. المركبات المحضرة شخصت بوساطة الخواص الفيزيائية (درجة الانصهار، اللون). الطرق الطيفية (الاشعة تحت الحمراء, الرنين النووي المغناطيسي)

الكلمات المفتاحية: بيتا- امينو كيتون, اضافة مايكل، اوكسازبين

Introduction

The Michael's addition includes the addition of nucleophile, also called a Michael donor that is added to an activated electrophilic olefin[1].The adducts of Michael reaction which are β-Amino ketones are important intermediates for the synthesis of a wide variety of compounds. The applications of this process of 1,4-addtion is the synthesis of β-amino Ketones; it can be done prepared throw the classical Mannich reaction, Therefor, a variety of methods appeared in the literature[2]. For synthesis of β-amino ketones, the Michael addition of nucleophilic compound to α, β-unsaturated carbonyl compounds is convenient rote for the construction of C-C and C-N[3,4,5] bands. These compounds were used as starting materials for the synthesis of different heterocycles[6]. Schiff's bases, (R-CH=N-R1) where R and R1 are alkyl, aryl, cyclo alkyl or heterocyclic group) are products of primary amines with carbonyl compound like β-amino carbonyl compounds[7]. They show biological activities including antibacterial, antifungal[8,9], anticancer[10] and herbicidal active[11]. Oxazpine is nonhomologous seven membered ring that contains two heteroatoms (oxygen and nitrogen)[12]. Schiff's bases react with phthalic anhydride to give 1,3-Benzooxazpine[13].

Experimental

All reagents and chemicals are from BDH and Fluka, used without purification. Melting points that measured using: Electro thermal IA 9100 melting points apparatus type (not corrected). Shimadzu FT- IR-8400 used to get the ir spectra. Proton nmr were recorded on Bruker 400MHz spectrometer using acetone-d^6 and $CDCl_3$ as solvent in UK, Leister University.

Sythesis of (5-Bromo-2-mercapto-6-(4-methoxyphenyl) pyrimidin-4(3H)-one)

Equimolar (0.001 mol) of anisaldehyde, ethylbromoacetate and thiourea were dissolved in abs. EtOH. Potassium carbonate (0.003 mol) is added to this reaction mixture and refluxed for 2h; the solvent was concentrated then poured in to ice cold water with stirring, neutralizion with glacial acetic acid[14].The solid produce filtered and washed with water as well as recrystallized from methanol. Table (1) involves physical properties.

Synthesis of Chalcones (2-6)

The mixture of substitute acetophenone and substitute benzaldehyde (0.01 mol) is dissolved in (30 ml) ethanol, then added (2 ml) to sodium hydroxide solution 40%, stirring the mixture for (2-4) hours[15,16]. The ppt obtained was filtered, washed with water and recrystallized from ethanol, Table (1) involves physical properties.

Synthesis of β-amino ketones compound (7-11)

To (0.01 mol) of compound (1), (0.01 mol) of various chalcone, and (2 ml) NaOH 30% were added to (30 ml) of ethanol, stirred for 4h on ice cold condition[17]. The solid formed is filtered and recrystallized from abs. EtOH Table (1) involves physical properties.

Synthesis of Schiff's bases (12-16)

A mixture of β-amino keton compounds (7-11) (0.01 mol) added to 2,4-dinitroaniline (0.01 mol) in abs. EtOH (25 ml) containing a few amount of glacial acetic acid is stirring for 4h[18] . The solvent was evaporated under vacuum. The solid yield is crystallized from methanol. Table (1) involves physical properties.

Synthesis of benzo[1,3] oxazepine derivatives (17-21)

A mixture of Schiff's bases (12-16) (0.0004 mol) added to (0.0006 mol) of phthalic anhydride in (20 ml) of abs. EtOH was refluxed for 6h[19]. The ppt was filtered,washed with water and recrystallized from ethanol. Table (1) involves physical properties.

Table(1) Some physical characteristic For comp. (1-21)

Comp. No	Moleculer Formula &M.Wt	m.p. ^{o}C &Color	Yield %
1	$C_{11}H_9BrN_2O_2S$ 313	268-270 Yellow	93
2	$C_{15}H_{11}NO_3$ 253 253	132-134 Yellow	**70**
3	$C_{15}H_{11}NO_3$ 253	129-131 Yellow	61
4	$C_{15}H_{12}O$ 208	124-126 Yellow	85
5	$C_{17}H_{16}O_2$ 252	180-182 Light Green	71
6	$C_{15}H_{11}NO_3$ 253	84-86 Brown	75
7	$C_{26}H_{20}BrN_3O_5S$ 566	248-250 Yellow	66
8	$C_{26}H_{20}BrN_3O_5S$ 566	260-262 Yellow	65
9	$C_{26}H_{21}BrN_2O_3S$ 521	234-236 Orange	75
10	$C_{28}H_{25}BrN_2O_4S$ 565	240-242 Orange	80
11	$C_{26}H_{20}BrN_3O_5S$ 566	213-215 Orange	75
12	$C_{32}H_{23}BrN_6O_7S$ 731	215-217 Orange	65
13	$C_{32}H_{23}BrN_6O_7S$ 731	218-220 Yellow	51
14	$C_{32}H_{24}BrN_5O_6S$ 686	207-209 Yellow	55
15	$C_{34}H_{28}BrN_5O_7S$ 730	120-122 Yellow	69
16	$C_{32}H_{23}BrN_6O_8S$ 731	239-240 Orange	71
17	$C_{40}H_{27}BrN_6O_{11}S$ 879	208-210 Yellow	63
18	$C_{40}H_{27}BrN_6O_{11}S$ 879	244-246 Yellow	62
19	$C_{40}H_{28}BrN_5O_9S$ 834	189-191 Yellow	60
20	$C_{42}H_{32}BrN_5O_{10}S$ 878	147-149 Orange	55
21	$C_{40}H_{27}BrN_6O_{11}S$ 879	267-278 Yellow	70

Results and Discussions.

Formation of new β-amino Ketones compound (7-11)[20] Were obtained from the reaction of compound (1) and chalcones (2-6), which is shown in the following mechanism. Then Schiff bases (12-16) are prepared by the reaction of compounds (7-11) with 2,4-dinitro aniline in abs. EtOH, using glacial acetic acid as catalyst. When Schiff bases reacted with phthalic anhydride presence abs. EtOH, as a solvent, produces seven membered heterocyclic rings (cyclic addition reaction)[21]. All the spectrum data were involved in table (2).

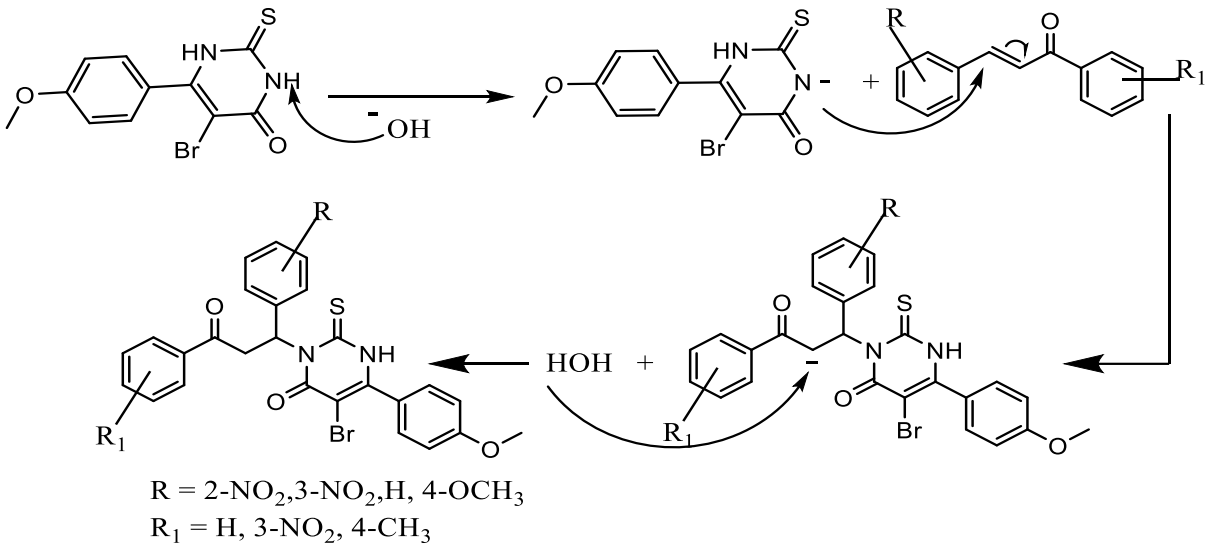


Figure1: Mechanism of syntheses β-amino ketones compound (7-11)

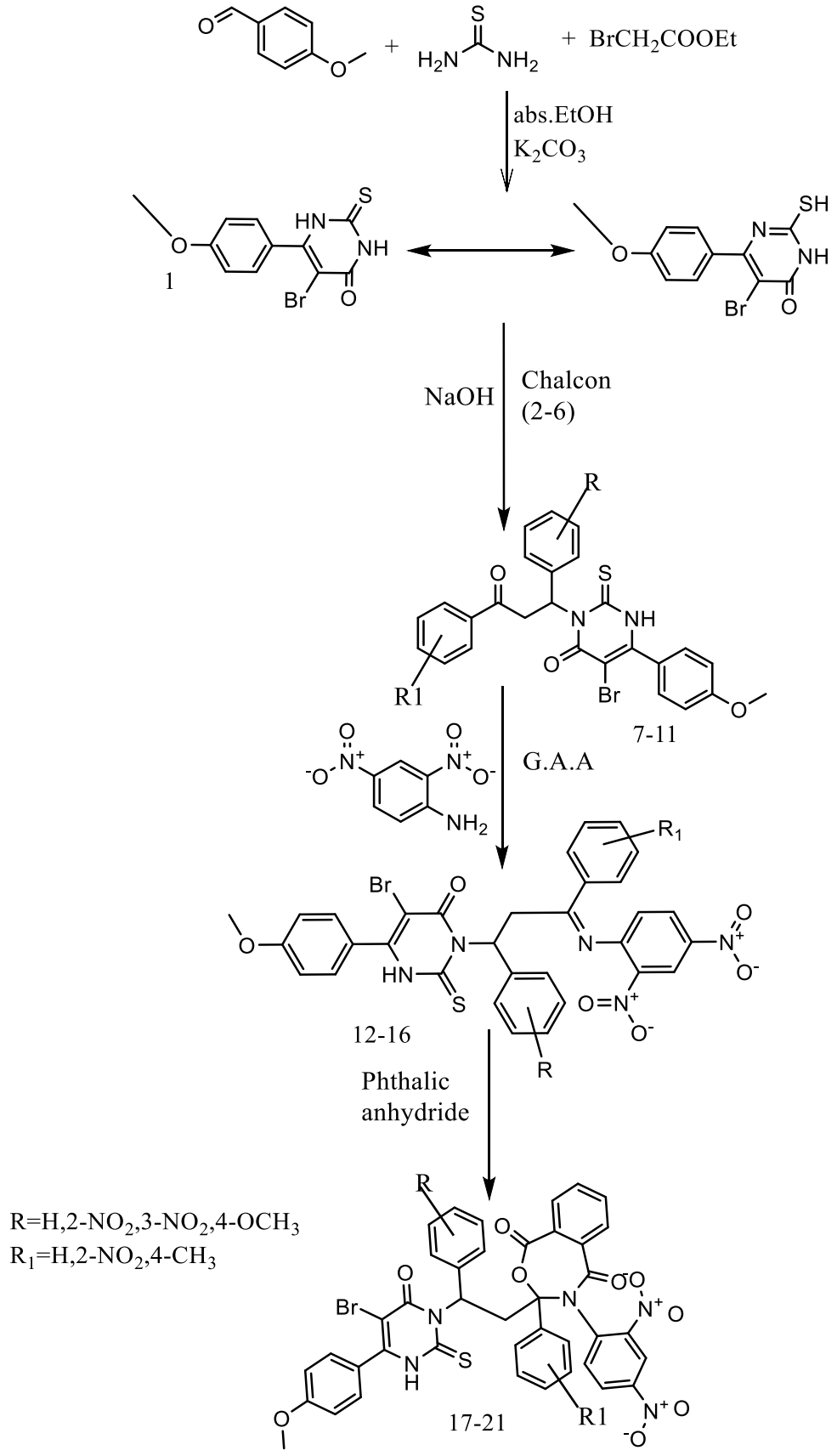
Table (2) Some spectral data for compounds (1-10)

Comp. No	1HNMR	IR ν cm $^{-1}$				
		N-H	Aro	Alp	C=O amide	Other
1*	δ: 3.82(s,3H,OCH_3),7.09-7.55(d,4H,ph), 9.03(s, 1H,NH),,9.34(s,1H,NH)	3195	3058	2981	1662	Ar-C=C (1600-1444) C=S (1251) (Asy, C-O-C) (1145) (Sym,C-O-C) (1076) C-Br (746)
2	……..	……	3040	……	1662 keton	C=C (1606) Ar-C=C (1483) (Asy, NO_2) (1571) (Sym, NO_2) (1348)
3	……..	……	3033	……	1662 keton	C=C (1604) Ar-C=C (1442) (Asy, NO_2) (1525) (Sym, NO_2) (1340)
4	……..	……	3061	……	1663 Keton	C=C (1595) Ar-C=C (1415)
5	……..	……	3001	2972	1654 Keton	Ar-C=C (1454) C=C (1602) (Asy, C-O-C) (1168) (Sym,C-O-C) (1029)
6	……..	……	……	2873	1650 Keton	Ar-C=C (1422) (Asy,NO_2) (1562) (Sym,NO_2) (1342)
7	……..	3390	3105	2848	1665	(C=O, Ketones) (1708) (Asy,NO_2) (1539) (Sym,NO_2) (1345) (C=S) (1195) (Asy, C-O-C) (1103) (Sym,C-O-C) (1004) (C-Br) (736)
8*	δ: 3.33(s-distroted,3H,$CHCH_2$), 3.811(s,3H,OCH_3), 7.10-8.23(m,13H,Ar-H),8.79(s,NH)	3209	3080	2962	1666	(C=O, Ketones) (1691) (Asy,NO_2) (1527,1508) (Sym,NO_2) (1348) (C=S) (1249) (Asy, C-O-C) (1031) (Sym,C-O-C) (1008) (C-Br) (684)
9**	δ: 2.60(s-distroted,3H,$CHCH_2$), 3.88(s,3H,OCH_3), 6.98-7.93(m,14H,Ar), 9.879(s,1H,NH)	3199	3010	2937	1662	(C=O, Ketones) (1729) (C=S) (1251) (Asy, C-O-C) (1103) (Sym,C-O-C) (1006) (C-Br) (702)
10*	δ: 2.61(s,3H,CH_3), 3.45(s-distroted,3H,$CHCH_2$), 3.91(s,3H,OCH_3),7.02-8,06(m,12H,Ar-H), 9.33(s,1H,NH)	3210	3001	2972	1656	(C=O, Ketones) (1690) (C=S) (1253) (Asy, C-O-C) (1170) (Sym,C-O-C) (1033) (C-Br) (676)

Table (2) Some spectral data for compounds (11-21)

11**	δ: 1.53(br,2H,CH_2),2.1(s,2H,CH_2), 3.82(s,3H,OCH_3), 6.88-8.18(m,13H,Ar), 9.07(d,1H,NH)	3211	3005	2995	1668	(C=O, Ketones) (1705) (Asy,NO_2) (1508) (Sym,NO_2) (1373) (C=S) (1209) (Asy, C-O-C) (1029) (Sym,C-O-C) (1004) (C-Br) (721)
12*	δ: 3.33(s,1H,CH), 3.81(s,OCH_3), 5.80(s,CH_2),6.94-8.21(M,8H,Ar-H), 9.09(s,1H,NH)	3193	3006	2985	1666	(C=N) (1602)
13	……	3202	3030	2945	1666	(C=N) (1602)
14	……..	3197	3001	2960	1670	(C=N) (1629)
15	……	3336	3052	2933	1654	(C=N) (1630)
16	……..	3205	……..	2997	1668	(C=N) (1631)
17*	δ: 3.34(s-distroted,3H,$CHCH_2$), 3.81(s,3H,OCH_3), 7.08-8.17(m,20H,Ar), 9.09(s,1H,NH)	3194	3001	2961	1663	(C=O, lacton) (1715)
18	……	3193	3010	2951	1663	(C=O, lacton) (1705)
19***	δ: 2.87(br,3H,$CHCH_2$), 3.82(s,3H,OCH_3), 7.22-8.18(m,21H,Ar), 8.92(s,1H,NH)	3195	3043	2952	1663	(C=O, lacton) (1702)
20	……	3205	3008	2924	1639	(C=O, lacton) (1700)
21*	δ: 3.33(br,3H,$CHCH_2$), 3.81(s,3H,OCH_3), 7.08-8.83(m,20H,Ar), 9.09(s,1H,NH)	3184	3002	2941	1662	(C=O, lacton) (1716s)

*(solvent, DMSO), **(solvent, $CDCL_3$), ***(solvent, Aceton-d_6)



Scheme (1) illustrates the prepared compounds (1-21)

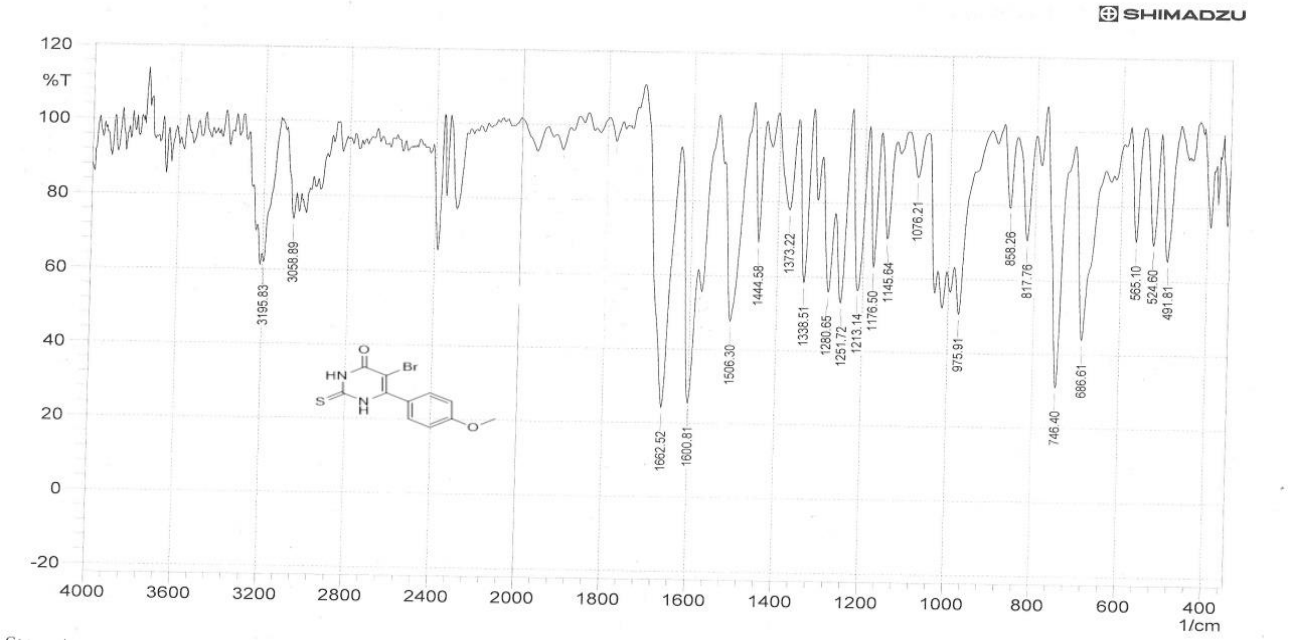


Figure2: FT-IR For- comp: (1)

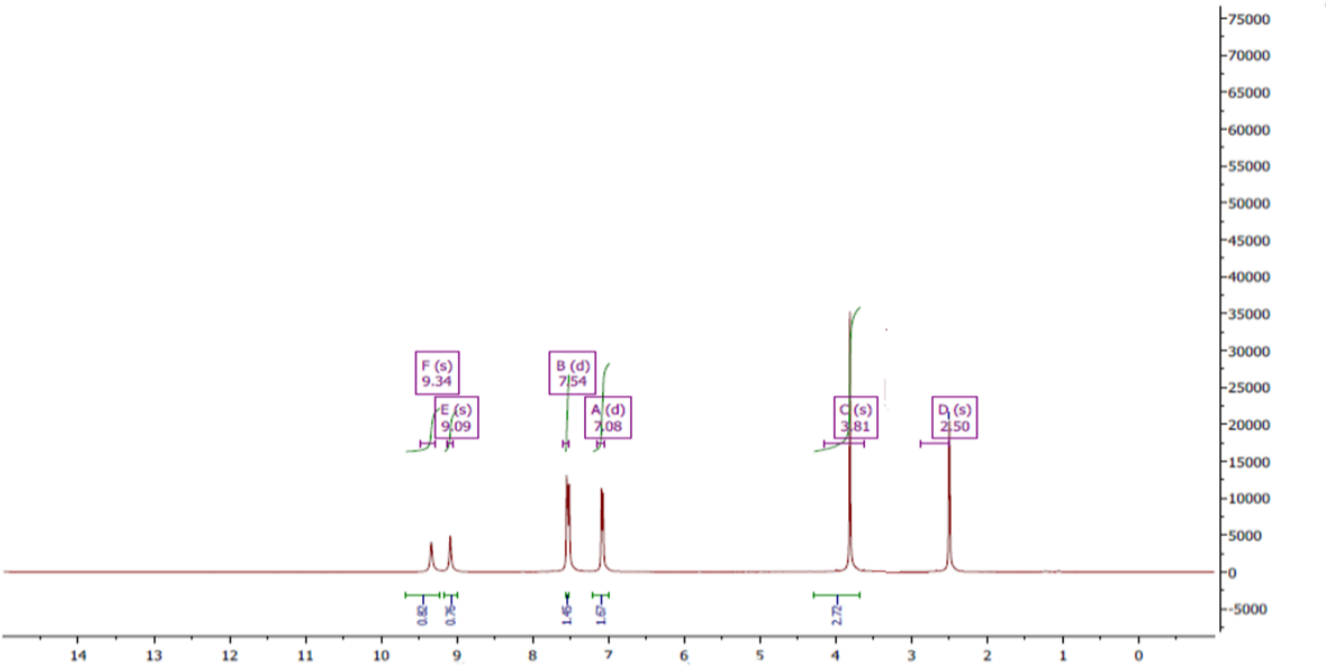


Figure3: 1HNMR For- comp: (1)

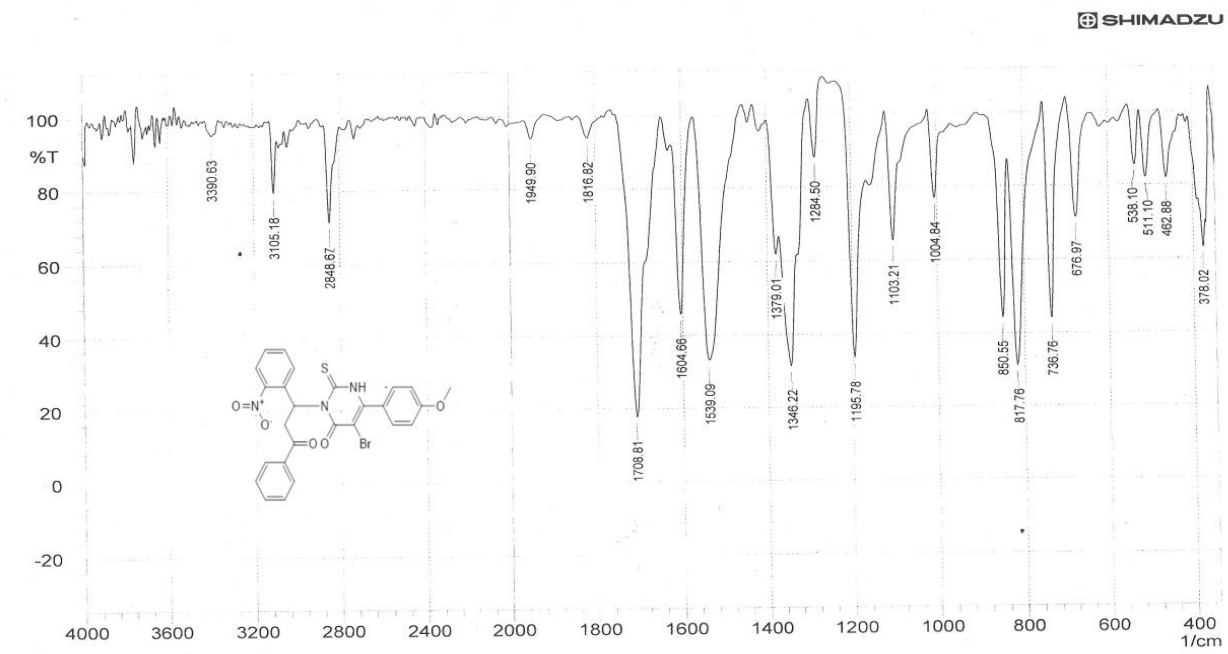


Figure4: FT-IR For- comp: (7)

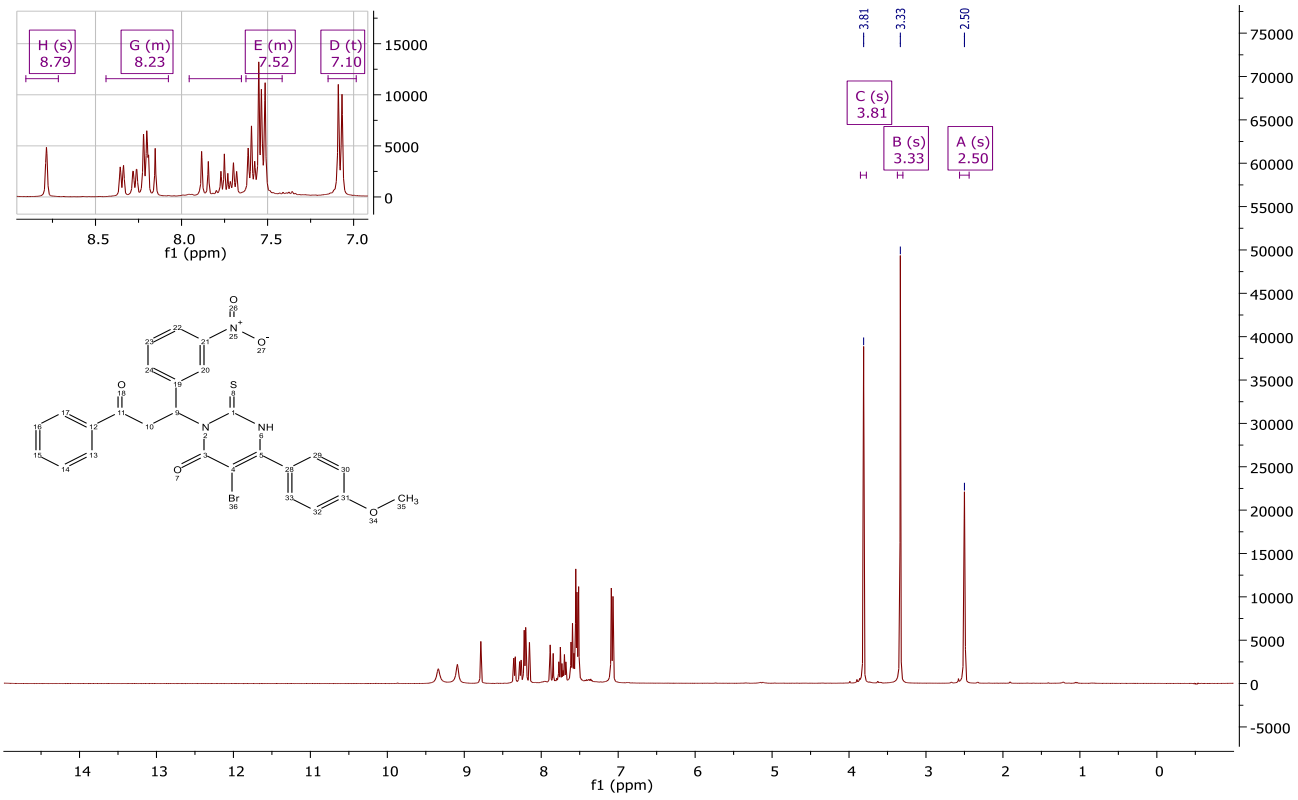


Figure5: 1HNMR For- comp: (8)

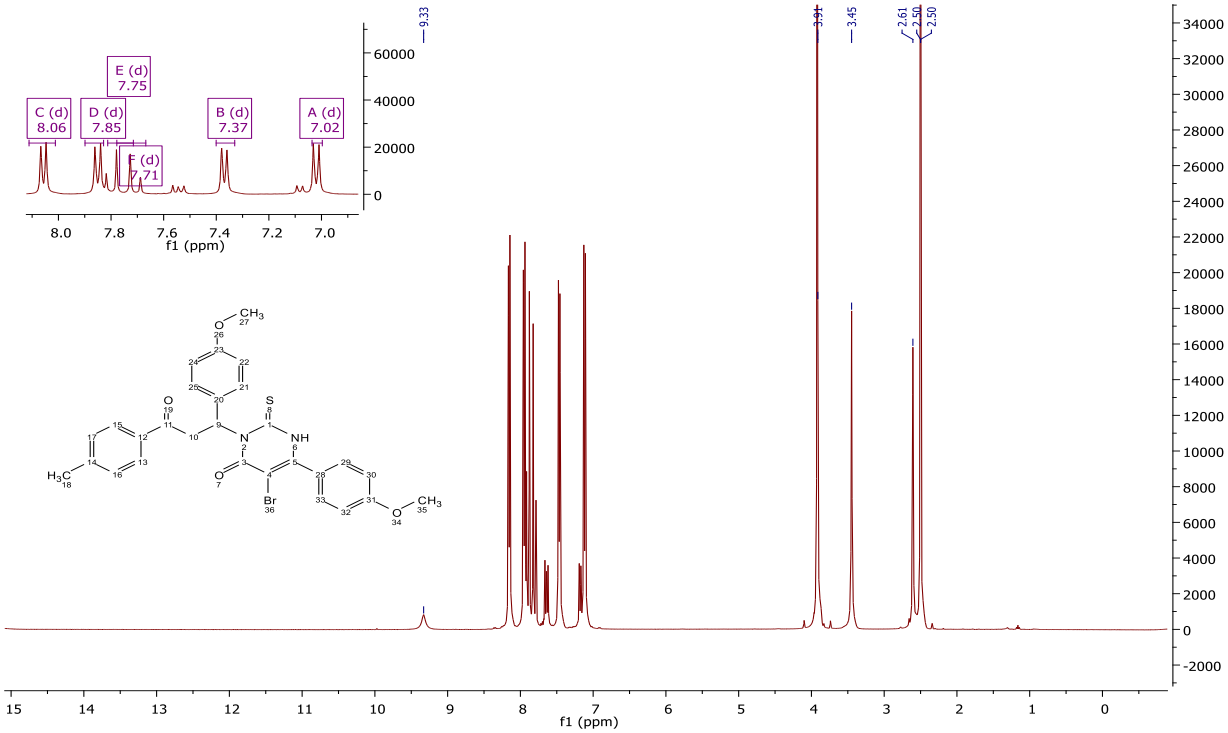


Figure6: 1HNMR For- comp: (10)

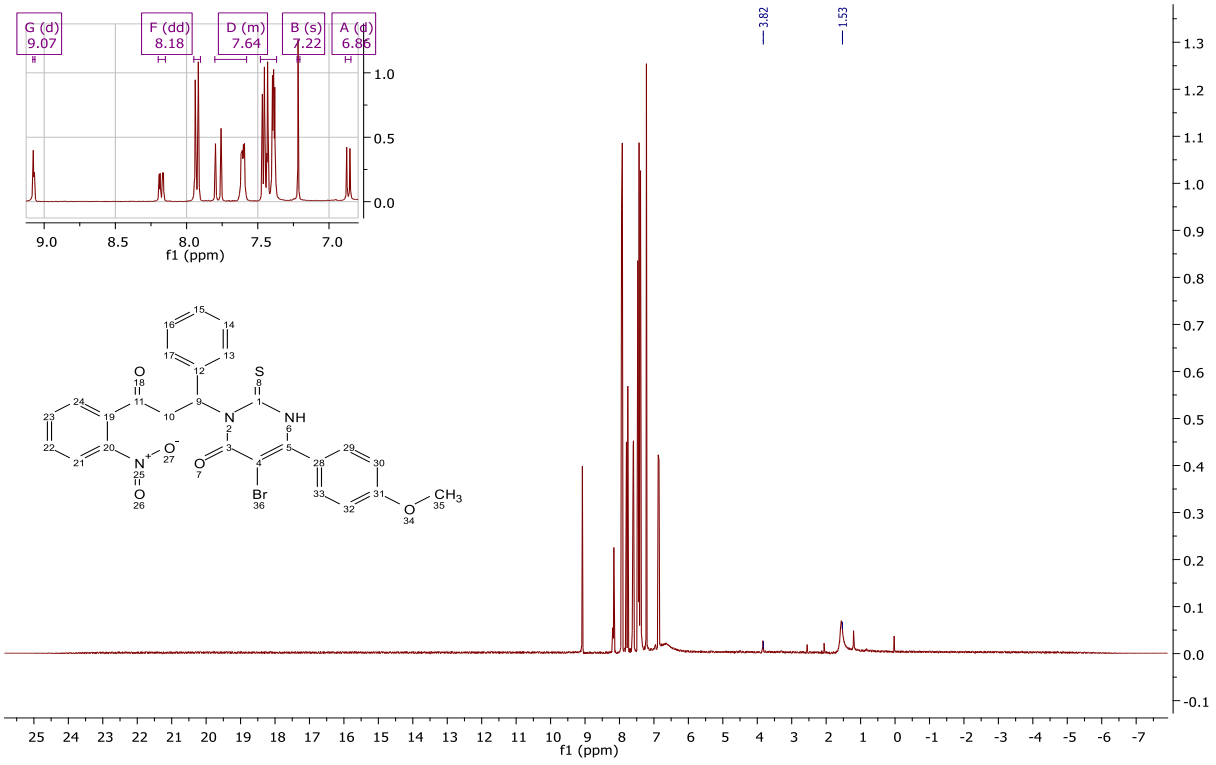


Figure7: 1HNMR For- comp: (11)

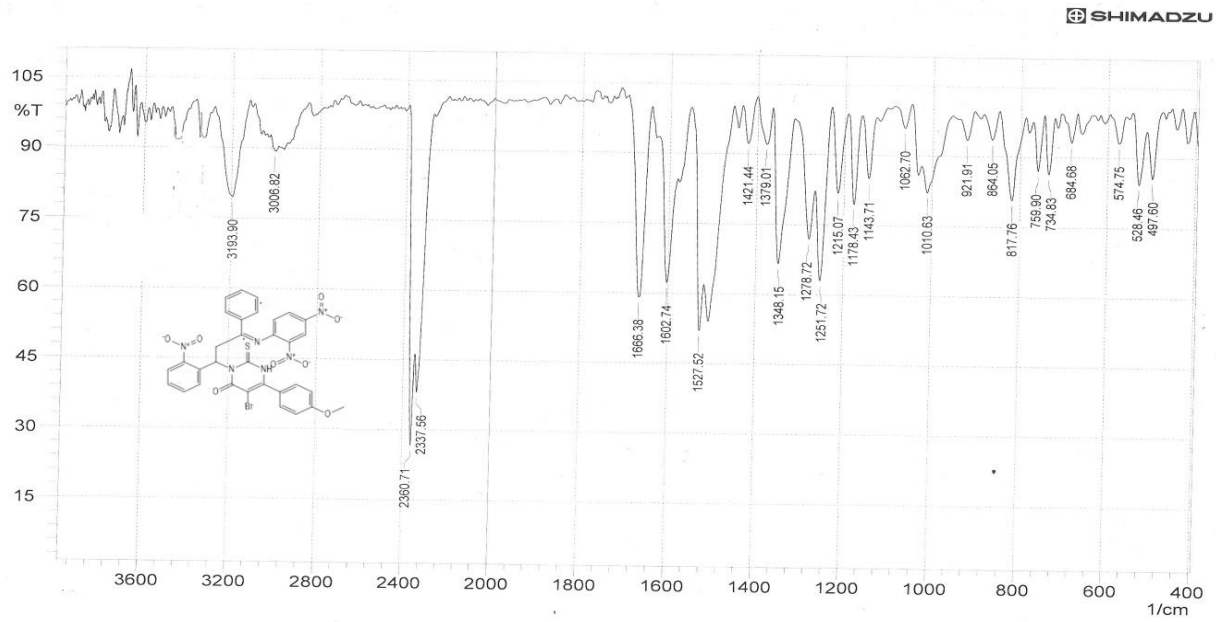


Figure8: FT-IR For- comp: (12)

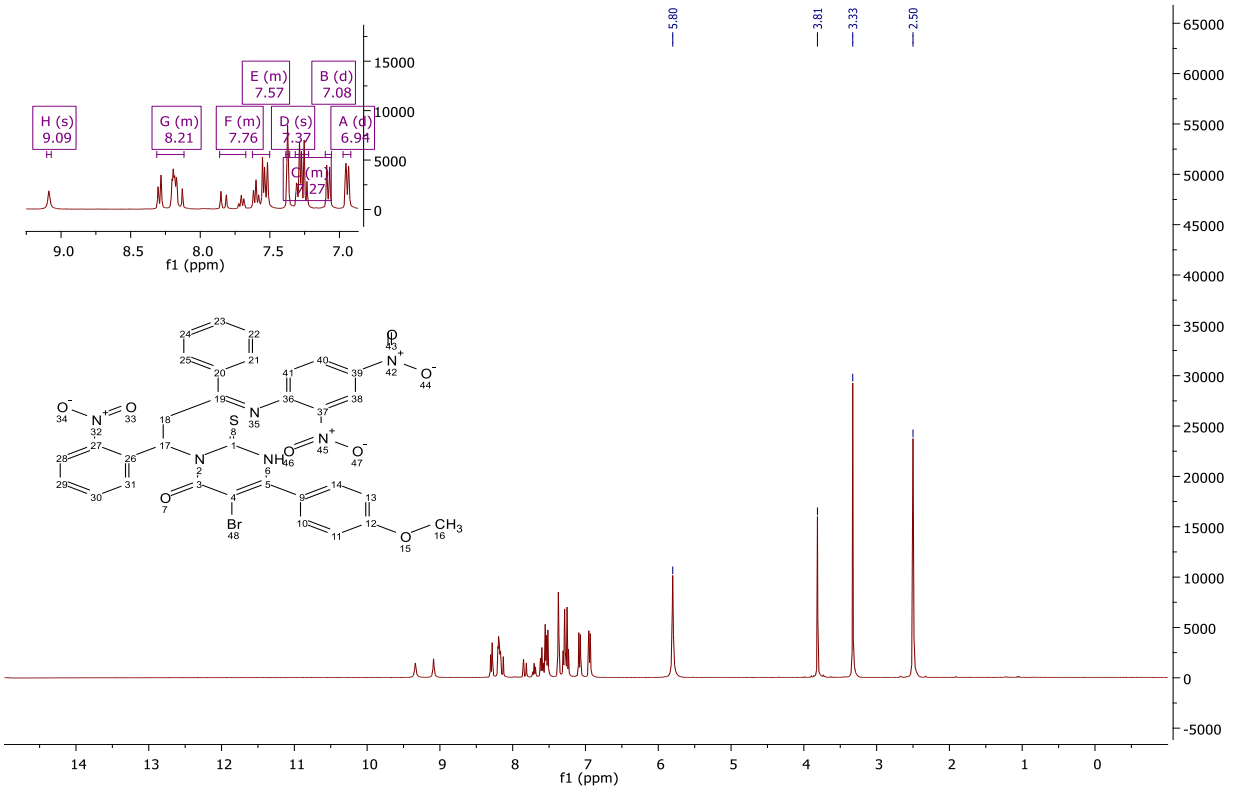


Figure9: 1HNMR For- comp: (12)

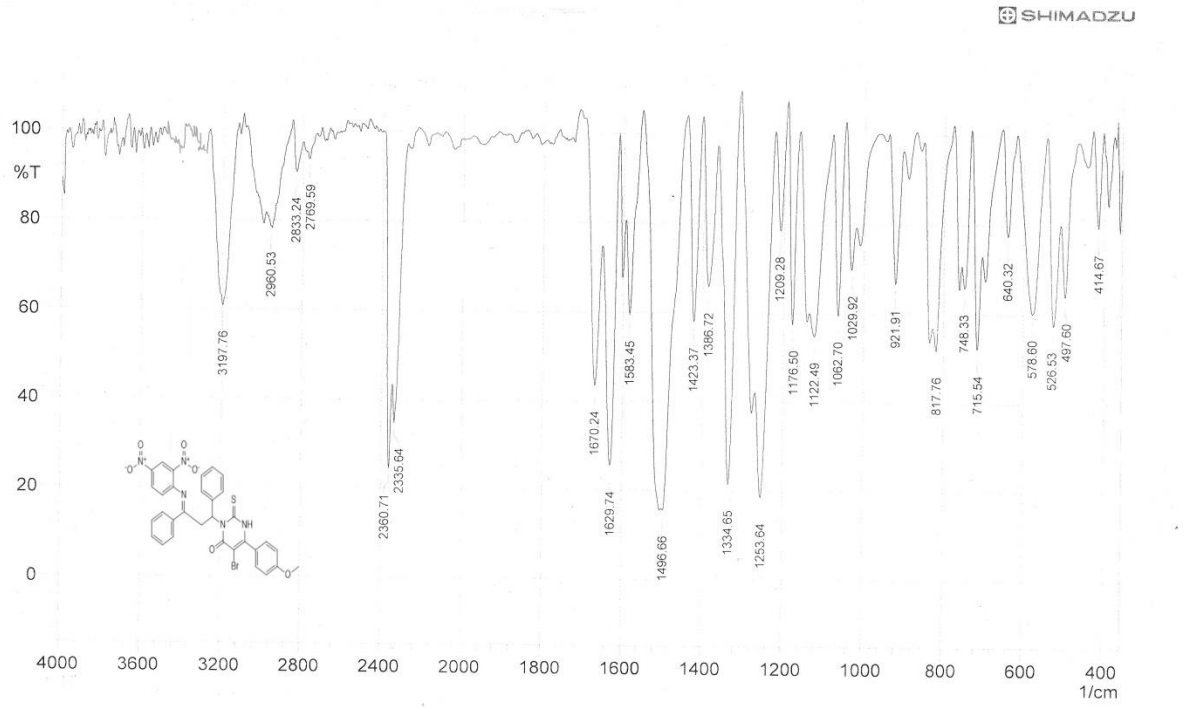


Figure10: FT-IR for comp. (14)

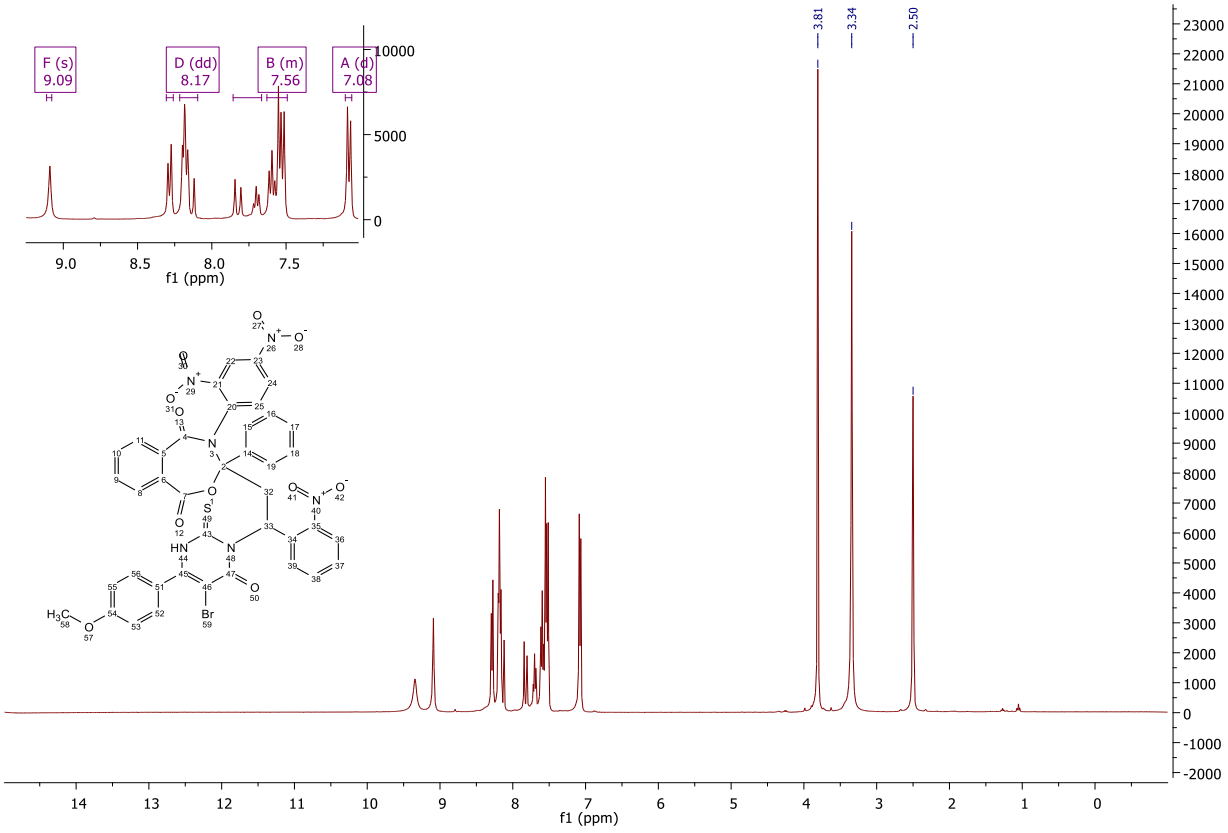


Figure11: 1HNMR For- comp: (17)

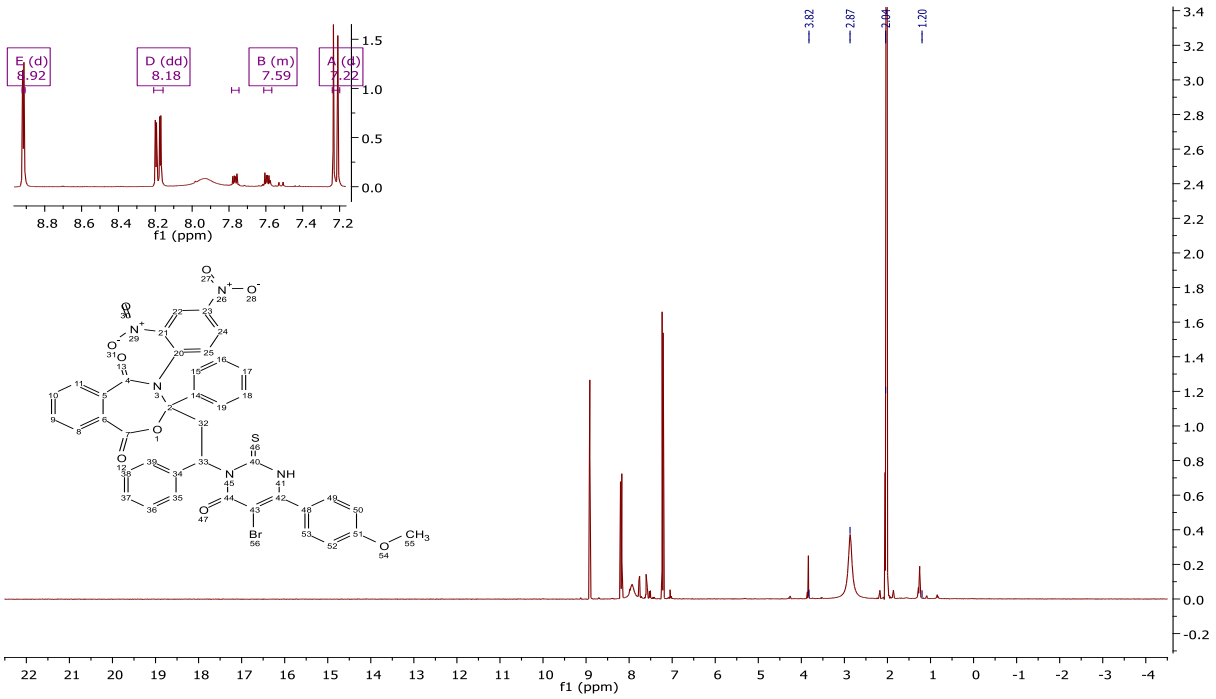


Figure12: 1HNMR For- comp: (19)

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Reference

1. Sasai T., Arai. T., Satow. Y., Houk. K. N., Shibasaki. M. J. Am., Chem. Soc., 117, 6194-6191, (1995).

2. Shibasaki M., Sasai. H & Arai. T., Angew., Chem. Ed. Engl.,36, (1997).

3. Fernandez I., Araujoc. S., Romero. J., Alcudia. F., Khiar. N., Tetrahedron, 56,3749-3753, (2000).

4- Lee P. H. Ahn, H., Lee, K., Sung, S., Kim, S., Tetrahedron Lett., 42,37-39, (2001).

5- Shaikh N. S., Deshpande. V. H., BedeKar. A. V., Tetrahedron, 57, 9045, (2001).

6- Cheng S., Cromer. D. D., Tetrahedron Lett., 43,1179-1181, (2001).

7- Aralmurugan S. K., Venkatraman. H. P., Rasayan. P. R., J. Chem.,3, 385, (2010).

8- Wadeher J. S., Puranik. P. M., Karande. A. N., Yeole. G. P., I. J. of Pharm. Tech. Research, pp.22-33., 1. (2009).

9- Desai S. B., Desai. P. B., Hetrocycl Common, pp. 83-90., 7(1). (2001).

10- Pathak P., Jolly. V. S., Sharma. K., Oriental J. Chem., pp.161-162, 16(1), (2000).

11- Samadhiya S., Halva. A., Oriental J. Chem., pp.119-122, 17(1),(2001).

12-Wilson O. C., Givold. O., "Text book of organic medicinal and pharmaceutical Chemistry", 5th. Ed, (1966).

13- Yass A. I., Kerbala J. of pharmaceutical science, p.49-58, (2010).

14- Mohammed J.M., Ahmad. Kh. A., Abachi. T. F., Tikrit J. of Pharmaceutical Sciences.12(1),76-89. (2017).

15- Furniss S. B., Hannaford. J. A., Smith. C. W. P., and Tatchell. R. A., Vogel's Text book of Practical Organic Chemistry, Fifth edition. 1023-1036. (1989).

16- Himaja M., Rout. K . P., Karigar. A. A., Daspoppy. D. Munirajsekhar, Universal, J.of Pharmacy, 1(1), 72-77, (2012).

17- Mohmed Z. Waffa. B., Bouchaib. B. Ahmed. R., Said. S., Arkivoc, 150-161, (2005).

18- Al-Rawi S. M., Ph.D. Thesis. Department of Chem., College of Education Ibn-AlHaitham, University of Baghdad. Baghdad, Iraq, (2011), (In Arbic)

19- Hallinan A. E., Hagen. J. T., Tsymbalov. S., Husa. K. R., Stapelfeld. C. A., Savage. A. ,M., J. Med. Chem. 39(2), 609-613, (1996).

20- Al-Jaber A.N., Bougasim. A. A., Karah. S. M., . J. of Saudi Chemical Society. 16,

45-53. 16, (2012).

21- Level A., Comm., Reg. Issue 42. 75s(9). 2187-2192, (2008).