SYNTHESIS AND CHARACTERIZATION OF HETEROAROMATIC CHALCONES

A DISSERTATION

Submitted in partial fulfillment of the requirements for the award of the degree of

MASTER OF TECHNOLOGY

in

ADVANCED CHEMICAL ANALYSIS

By

ANJU YADAV

DEPARTMENT OF CHEMISTRY
INDIAN INSTITUTE OF TECHNOLOGY ROORKEE
ROORKEE-247 667 (INDIA)

JUNE, 2012

INDIAN INSTITUTE OF TECHNOLOGY, ROORKEE
DEPARTMENT OF CHEMISTRY
ROORKEE-247667, UTTRAKHAND, INDIA
Tel: + 91-1332-285745(Off) 285010(Res)
E-mail: nasemfcy@iitr.ernet.in

Dr. Naseem Ahmed
Assistant Professor

CERTIFICATE

This is to certify that the thesis entitled "***Synthesis and characterization of heteroaromatic chalcones***" submitted by Anju Yadav, who has registered as M.Tech student in Advanced Chemical Analysis in chemistry department, Indian Institute of Technology Roorkee since July 2011. This work is done by him under my supervision and neither this thesis nor any part of it has been submitted for any degree / diploma or any other academic award any where before.

Date: 15.6.2012

(Dr. Naseem Ahmed)
Signature of Supervisor
with official seal

INDIAN INSTITUTE OF TECHNOLOGY ROORKEE
ROORKEE

CANDIDATE'S DECLARATION

I hereby certify that the progress report presented in the dissertation in the entitled ***"synthesis and characterization of heteroaromatic chalcones"*** for the award of the degree of Master of Technology submitted to the Indian institute of Technology Roorkee is an authentic record of my won work carried out by me during the period from July 2011 to June 2012 under the supervision of Dr. Naseem Ahmed, Assistant Professor, Department of Chemistry, Indian Institute of Technology Roorkee, Roorkee.

The matter presented in this thesis has not been submitted by me for the award of any other degree of this or any other Institute.

Place: Roorkee Anju Yadav **(Anju Yadav)**

Date: 15-6-2012

This is to certify that the above statement made by the candidate is correct to the best of our knowledge.

Date: 15-6-2012

Dr. NASEEM AHMED
Assistant Professor
Department of Chemistry
IIT, Roorkee.

Abstract

Chalcones are well known naturally occurring pigments which serve as valuable intermediate in organic synthesis of flavonoid compounds. It has found significant role in pharmaceutical effects including antioncogenic, antiinflammatory, antiulcerative, analgesic, antiviral, antimalarial and antibacterial activities. Chloroquinoline and indole compounds are known to exhibit variety of antimicrobial activity. Also, it has been reported that chalcone having quinoline moiety is an intermediate for the synthesis of chloroquinoline cyanopyridines and cyanopyrans derivatives. Here an efficient method for quinoline and indole based chalcones synthesis described. 2-chloroquinoline aldehyde synthesized by using acylation of aniline followed by cyclization in presence of DMF/$POCl_3$ obtained quinoline aldehyde (**2a**) in 65% yield. Indole aldehyde synthesized accordingly "Vilsmayer reaction" by reacting indole with DMF/$POCl_3$ obtained Indole aldehyde (**1b**) 90 % yield. Indole based chalcones were synthesized accordingly Claisan-Shmidt condensation of indole aldehyde with various aromatic acetophenones by using piperidine as a base in ethanol obtained indole based chlacones (**2b-7b**) in 60-80% yield. Quinoline based chlacones also prepared accordingly Claisan-Shmidt condensation of 2-chloroquinoline aldehyde with various aromatic acetophenones by using 40 % aq NaOH as a base in ethanol obtained quinoline based chlacones (**3a-8a**) in 70-76 % yield.

Acknowledgement

As I reflect upon the years gone by, I deeply feel the need to acknowledge my gratitude to many wonderful people who have helped me reach this day.

In the first place, I would like to express my deep and sincere gratitude to my supervisors, Dr. Naseem Ahmed for their supervision, advice and guidance from the very early stage of this research as well as giving me extraordinary experiences throughout the work. Above all and the most needed, they provided me unflinching encouragement and support in various ways. Their scientific intuitions have made them as a constant oasis of ideas and passions in science, which inspired and enriched my growth as a student, a researcher and to become a scientist. I am indebted to them for their valuable guidance.

I would like to express my heartiest thankful to Dr. V.K.Gupta, Professor and Head, Department of Chemistry, Indian Institute of Technology, Roorkee for extending various facilities during the course of this work.

I am especially indebted Dr. R. K. Dutta (Coordinator of M.Tech Programme), Assistant Professor, all the faculty members and staff of Department of Chemistry, IIT Roorkee, for their support during the entire period of M.Tech programme.

I wish to express my thanks to my lab mats B. Venkata Babu , Naveen kumar, Praveen, Shaily, friends, the staff of Institute Instrumentation Centre, Central Library and Computer Centre, who are the part to the completion of my work.

Where would I be without my family? I am indebted to my father, Mr.kailash chand yadav, for his care and love. I cannot ask for more from my mother, Mrs. Savtri Devi, as she is simply perfect. I have no suitable word that can fully describe them everlasting love to me and I remember, most of all for her delicious dishes.

Last but not least, thanks to God for granting me the faith and will to obtain this academic achievement that has culminated in this thesis.

Place: Roorkee

Date- 15-6-2012

Anju Yadav

Anju Yadav

M.Tech (A.C.A.)

Department of Chemistry, IIT Roorkee

CONTENTS

Chapter - 1

Introduction

CHAPTER 1

INTRODUCTION

1.1 Introduction:

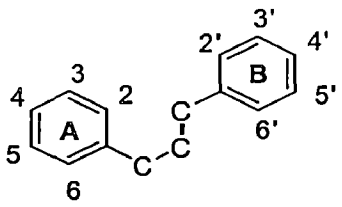
There is no exaggeration in the statement that plants have sustained and are sustaining human life on this planet. The plant chemistry (also known as natural products chemistry) is a wide and distinct field, which concerned with enormous variety of organic substances accumulated by plants, for example alkaloids amino acids, flavonoids, terpenes, fatty acids steroids etc. The flavonoids are one of the most fascinating areas of the plant chemistry. Flavonoids (also known bioflavonoid) secondary metabolites in almost all vascular plants and are widely distributed in leaves, stem, root, fruits, seeds. More than 5000 chemically unique flavonoids have been identified in different plant species, which are responsible for the vibrant colors of leaves, flowers and fruits. These polyphenolic organic compounds have no direct involvement with the growth or development of plants. However they play an important role in protecting the plants form microbe and insect attacks[1].

Among the natural compound with high antioxidant activity, flavonoids, widely distributed class of phytochemicals have a central role[2]. The key stage in biosynthesis of all flavonoids is reached via the formation of chalcone, which is distributed in different plant tissues. Along the Aurones, chalcone are best known yellow to orange colored flowering pigment .Chalcones are well known natural or synthetic compounds also well known intermediate for synthesizing various heterocyclic compounds bearing the 1, 3- diphenylprop-2-en-1-one framework that have displayed a wide biological activities such as antimicrobial , anti-inflammatory, analgesic , antiplatelet , antiulcerative , antimalarial , anticancer , antiviral , antileishmanial ,antioxidant , antitubercular , antihyperglycemic ,immunomodulatory , inhibition of chemical mediators release inhibition of leukotriene B_4 , inhibition of tyrosinase and inhabition of aldose reductase activities[2-6]. Many studies of chalcone related to cancer have demonstrated. The presence of a reactive α, β-unsaturated keto function in the chalcone is found to be responsible for their microbial activity. The chalcone are acyclic polyphenolic compounds possessing 15 carbon atoms (Figure 1) two benzene rings joined by a linear three carbon chain[7]. They constitute one of the most characteristic classes of compounds in higher plants.

Chalcones are well known natural compounds and in synthetic chemistry a well known intermediates for synthesizing various heterocyclic compounds bearing the 1, 3- diphenylprop-2-en-1-one framework that have displayed a wide biological activities such as antimicrobial, anti-inflammatory, analgesic, antiplatelet, antiulcerative, antimalarial, anticancer, antiviral, antileishmanial , antioxidant , antitubercular, antihyperglycemic, immunomodulatory inhibition of chemical mediators, release inhibition of leukotriene B_4, inhibition of tyrosinase and inhabition of aldose reductase activities[25-29].

The majority of the naturally occurring chalcones contain either hydroxyl (OH) or methoxy (OCH_3) substituents on the two aromatic rings[30]. However, the number of different chalcones that are theoretically possible in nature is extremely high since each of the groups can be substituted by one or more sugars, which in turn can be acylated with different phenolic of aliphatic moieties. Synthetic and naturally occurring hydroxychalcones and methoxychalcones are of particular interest as they display a wide range of biological properties and exert diverse pharmacological activities. In fact, because of their chemical structures, these compounds can promote both antioxidant and pro-oxidant effects and, as a consequence, have been shown to be effective chemopreventive agents as well as to exert bactericidal, antifungal, anticarcinogenic, and anti-inflammatory actions[31,32]. The mechanism(s) responsible for this pleiotropism remain to be fully understood, but it is becoming evident that more than one specific cellular target is implicated in the pharmacological actions mediated by chalcones. For instance, the anti-inflammatory properties of 4-dimethylamino-3′,4′-dimethoxychalcone and 2′,5′-dihydroxy-4-chloro-dihydrochalcone in murine macrophages were initially reported to involve a direct scavenging effect on superoxide anion production and inhibition of inducible nitric oxide synthase (iNOS) expression[33,34].

Many studies of chalcone related to cancer have demonstrated. The presence of a reactive α,β-unsaturated keto function in the chalcone is found to be responsible for their microbial activity. The chalcone are acyclic polyphenolic compounds possessing 15carbon atoms (Figure 1) two benzene rings joined by a linear three carbon chain[35]. They constitute one of the most characteristic classes of compounds in higher plants.



The skeleton above, can be represented as the

$C_6 - C_3 - C_6$ system.

Flavonoids are also present as aglycones, glycosides and methylated derivatives. In plants, flavonoids aglycones (i.e., flavonoids without attached sugar) occur in a variety of structural forms[10-12]. The different way to close this ring associated with the different oxidation degrees of ring A provide the various classes of flavonoids.

Figure 1

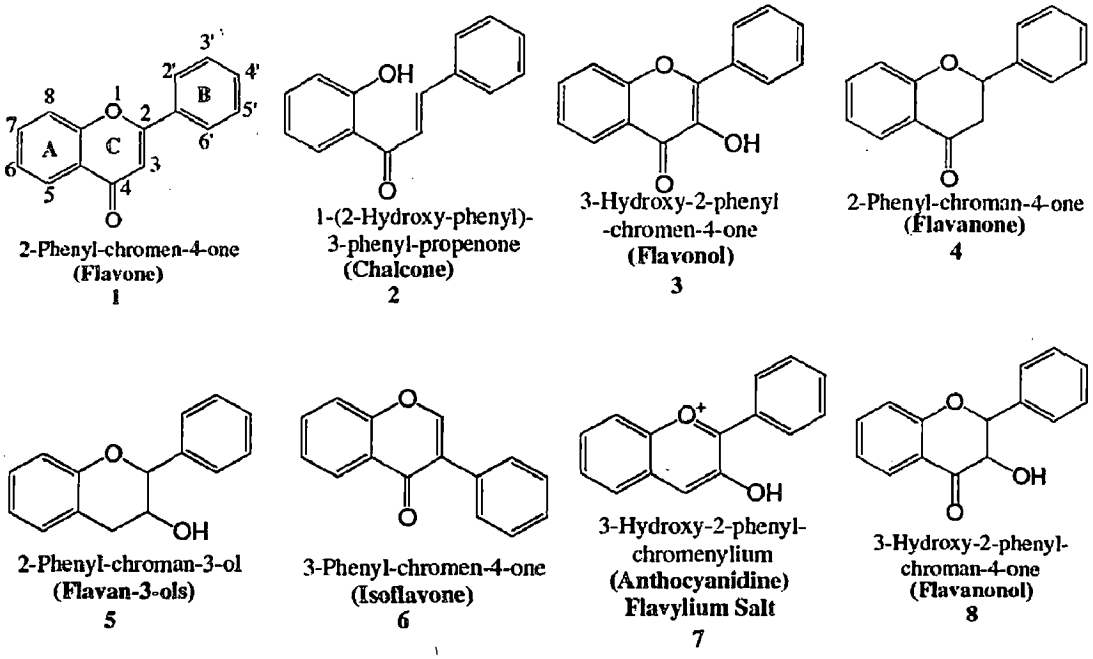


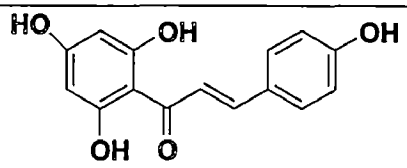
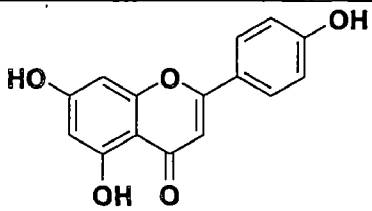
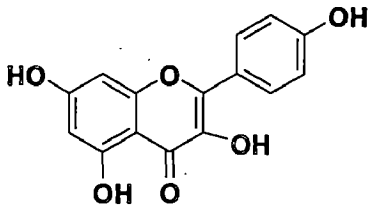
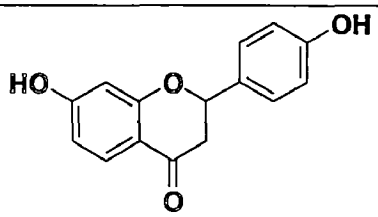
Figure1 Chemical structure of some representative flavonoids

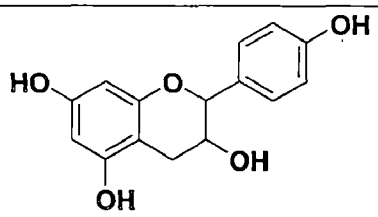
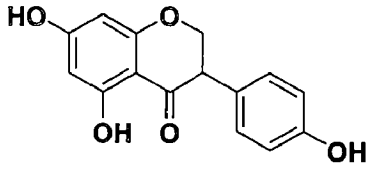
The six- membered ring condensed with the benzene ring is either a γ-pyrone flavanones (4) or flavan-3-*ols* (5)).The position of the benzenoid substituent divides the flavonoids into two classes: flavonoids (1) (2 -position) and isoflavonids (6) (3- position) [13-15].

1.2 Classifications of flavonoids:

Flavonoids are divided into six groups; chalcone, flavonols, flavones, flavanones, flavan-3-ols and anthocyanins. Most flavonoids occur in plants as glycoside, meaning that they are bound to sugar molecules[16-19]. Some well know flavonols are Quercetin and Kaempferol. Flavanones are mainly found in citrus fruits. The US-FDA (United State Food and Drug Administration) has on the website comprehensive table of flavonoids, flavonols, flavones, flavanones, flavan-3-ols, anthocyanins and isoflaviones of many foods. The mean intake of flavonoids was 17 mg and the mean intake of isoflaviones 47 mg. The following phytochemical were determined in the food: genistein, daidzien, myrcetin, fisetin, quercetin, Kaempferol and liteolin. Quercetin was the most important flavonoids followed by kaempferol.[20-25]

Table 1: Sub-groups of flavonoids

S.No	Flavonoids subgroup	Structure
1.	Chalcones	
2.	Flavones (generally in herbaceous families, e.g.Labiatae, Umbelliferae, Compositae) Apigenin, Luteolin	
3.	Flavonol (generally in wood angiosperms), Quercitol, Kaempferol, Myricetin	
4.	Flavanone	

5.	Anthocynin	
6.	Isoflavanone	

1.3 Properties of flavonoids:

1.3.1 Antioxidant:

The flavones and catechins seem to be the most powerful flavonoids for protecting the body against reactive oxygen species (ROS). Body cell and tissues are continuously threatened by the damage caused by free radicals and ROS which are produced during normal oxygen metabolism or are induced by exogenous damage. Quercetin, kaempferol, morin, Myricetin by acting as antioxidant, exhibited beneficial effect such as anti-inflammatory, antiallergic, antiviral, anticancer activity as well as play a protective role in liver diseases, cataracts, and cardiovascular diseases. Quercetin and silybin, acting as free radical scavengers, to exert a protective effect in liver reperfusion ischemic tissue damage. The scavengering activity of flavonoids reported to be in the order: Myrcetin >Quercetin > Rhamnetin > Diosmetin > Naringenin > Apigenin > Catechin >5,7-dihydroxy-3',4',5',- trimethoxy-flavone > Robinin > Kaempferol > Flavones[24-26].

1.3.2 Antimicrobial, antibacterial, antifungal activity:

Flavonoids and esters of phenolic acids have also been investigated for theirs antimicrobial, antifungal and antiviral activities. Quercetin has been reported to completely inhibit the growth of *staphylococcus* aureus. Most of the flavonones having no sugar moiety showed antimicrobial activities. A number of flavonoids isolated for fungi static activity. Chlorflavonin was the first chlorine- containing flavonoids which used antifungal antibiotic. Now synthetic modifications of natural compounds to improve antiviral activity. Quercetin,

morin, rutin, taxifolin, apigenin, catechin, and have been reported to possess antiviral activity against some of the 11 types of viruses. Recently, world wide spread of HIV since the 1980s, the antiviral activity of flavonoids has mainly focused. A natural plant flavonoids polymer of molecular weight 2,100 daltons was found to have antiviral activity against two strain of **type 1, type 2** Herpes simplex viruses[26-27].

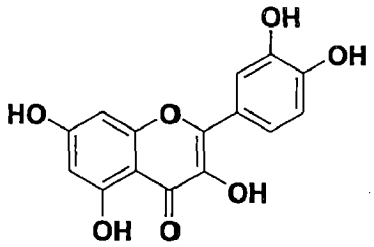


Figure 4: Quercetin molecule

1.3.3 Anti-inflammatory and antiulcer activity:

Flavones / flavonols glycosides as well as flavonoids/flavonols kaempferol, quercetin, myricetin, fisetin were reported to possess LO and COX inhibitory activities Hesperidin, a citrus flavonoids, possesses significant anti-inflammatory and analgesic effects. Recently apigenin, luteolin and quercetin have been reported to exhibit anti-inflammatory activity. Some recent studies have indicated that flavonoids glycosides of *Ocimum basilicum* decreased ulcer index[26, 27].

1.3.4 Cardio protective and central nervous system effects:

The consumption of flavonoids can prevent a number of cardiovascular diseases including hypertension and atherosclerosis by enhancing the vasorelaxant process leading to a reduction of arterial pressure. Flavonoids are polyphenolic compound have higher propensity to transfer electrons, to chelate ferrous ions, due to this properties, flavonoids have been considered as potential protectors against chronic cardio toxicity caused by the cytostatic drug doxorubicin[28-32].

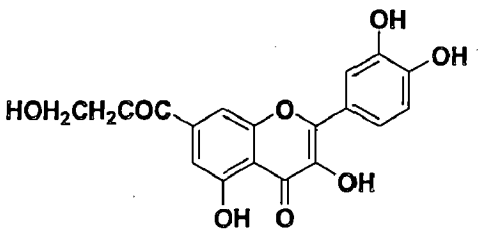


Figure 5: Structure of doxorubicin (7-monohydroxyethylrutoside)

Synthetic flavonoids, such as 6-Bromoflavone and 6-bromo-3'-nitroflavones, possess antioxidant- like properties similar or superior to that of diazepam. There widespread occurrence, broad spectrum diversity and natural origin make them appropriate chemical scaffolds for novel therapeutic agents over other therapeutic agent for the following reasons:

1) Many diets are rich in these phenolics and are daily consumed.

2) They really have any side effects.

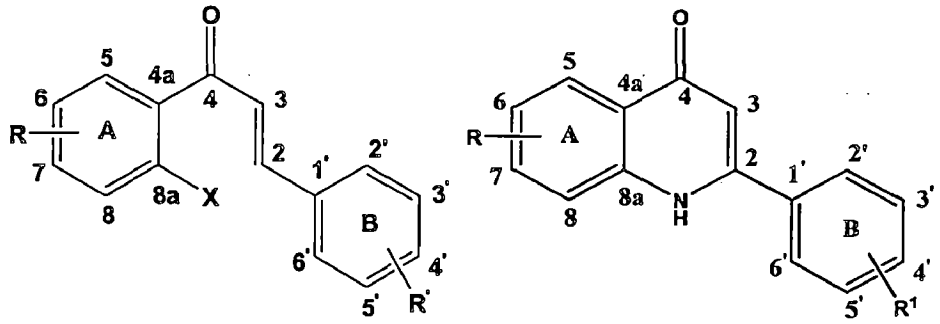
3) They have relatively long half-life; also can be easily absorbed in the intestine after ingestion.

Therefore, we think that natural and synthetic flavonoids will become effective future drugs against the most common degenerative diseases such as cancer, diabetes and cardiovascular complication.

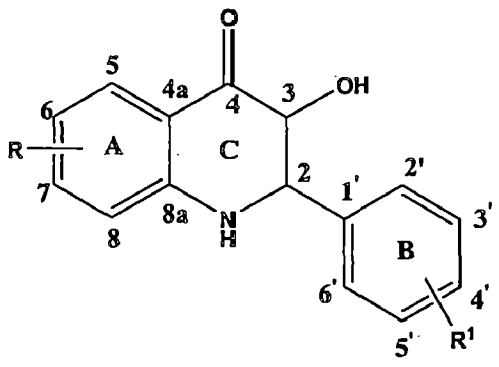
1.4 Aza-Flavanone:

2-Aryl-2, 3-dihydro-4-quinolones (also known aza flavanones) are the central intermediate in the biogenesis of naturally occurring flavonoid-type derivatives and a useful material in the laboratory syntheses. They are isomeric with the corresponding 2'-aminochalcones, and the two species undergo interconversion in the presence of acid and/or base. Derivatives like 2-aryl-4-quinolones and 2-aryl-3-hydroxy-2,3-dihydro-4-quinolones were displayed many interesting biological properties, such as cytotoxicity against human tumor cell lines,[2a] anticancer activity in the xenograft ovarian OVCAR-3 model, treated mice demonstrated 13% increase in life span, inhibit tubulin polymerization and colchicines binding to tubulin, hepatoprotective agents and a potential use as scintillator dyes in photo oxidative stability. Quinolones are analogues of flavanones and thiaflavanones which are characterized by a fused benzo ring A and phenyl substituent B at position 2 of the heterocyclic ring C as shown by the generalized (Figure 6). Flavanones have an ether linkage (X=O) whereas the Quinolone have an aza linkage ($X=NH_2$; R=H) and thiaflavanones have a thioether linkage (X=S) . Quinolones and flavanones are widely distributed in plants and can also be synthesized in the laboratory using various methods. On the other hand, thiaflavanones are only accessible in the laboratory by the

reaction of cinnamic and thiophenol to afford the 3-(phenylmercapto) propanoic acid which when converted to acid chloride undergoes Friedel-Crafts cyclization to afford thiaflavanones.[38]



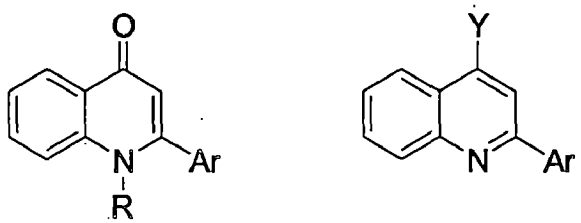
(1) (2)



(3)

Figure 6: (1) R=R[1]=H, X= H (chalcone), NH_2 (2-Aminochalcone)

The C ring of quinolone 3 contain several reactive sites (position 1, 3 and 4) and can also allow different degree of unsaturation in the heterocyclic ring as, observed in quinolin-4(1H)-ones 4 and the fully aromatic quinolone derivatives 5. The A ring of structure 1 (R= Cl, Br) can also be modified by Nucleophilic at either 6 or 8.



4 5

Figure 7: R= H, alkyl, acetyl or sulfonyl Y= Alkoxy, amino

References:

1. Wilkerson, W. W.; Galbraith, W.; Gans-Brangs K.; M. Grubb, Hewes, W. E.; Jaffee, B.; Kenney, J. P.; Kerr, J.; Wong, N. *J. Med. Chem.* **1994**, *37*, 988–998.
2. Wilkerson, W. W.; Copeland, R. A.; Trzaskos, J. M. *J. Med. Chem.* **1995**, *38*, 389–391.
3. Khanna, I. K.; Weier, R. M.; Yu, Y.; Collins P. W.; Miyashiro, J. M.; Koboldt, C. M.; Veenhuizen, A. W. *J. Med. Chem.*, **1997**, *40*, 1619–1633.
4. Khanna, I. K.; Weier, R. M.; Yu, Y.; Xu, X. D.; Koszyk, F. J.; Collins, P. W.; Koboldt, C. M. Masferrer, J. L.; . Isakson, P. C. *J. Med. Chem.* **1997**, *40*, 1634–1647.
5. Tsuji, K.; Nakamura, K.; Konishi, N.; Tojo, T.; Ochi, T.; Senoh, H.; Matsuo, M. *Chem. Pharm. Bull.* **1997**, *45*, 987–995.
6. Tsuji, K.; Konishi, N.; Spears, G. W.; Ogino, T.; Nakamura, K.; Tojo, T.; Ochi, T.; Shimojo, F;. Senoh, H.; Matsuo, M. *Chem. Pharm. Bull.* **1997**, *45*, 1475–1481.
7. Bansal, E.; Srivastava, V. K.; Kumar, A. Eur. *J. Med. Chem.* **2001**, *36*, 81–92.
8. Mana, F.; Chimenti, F.; Bolasco, A.; Cenicola, M. L.; Parrillo, M. D. C.; Rossi,E. Marmo F. *Eur. J. Med. Chem.* **1992**, *27*, 633–639.
9. Milano, J.; Oliveira, S. M.; Rossato, M. F.; Sauzem, P. D.; Machado, P.; Beck, P.; Zanatta, N.; Bonacorso, H. G. *Eur. J. Pharmacol.* **2008**, *54*, 86–96.
10. Tabarelli, Z.; Rubin, M. A.; Berlese, D. B.; Sauzem, P. D.; Missio, T. P.; Teixeira, M. V. A.; Sinhorin, P.; Martins, M. A. P. *J. Med. Biol. Res.* **2004**, *37*, 1531–1540.
11. Godoy, M. C.; Fighera, M. R.; Souza, F. R.; Rubin, M. A.; Oliveira, M. R.; Zanatta, N.; Martins, M. A.; Bonacorso, H. G.; Mello, C .F. *Eur. J. Pharmacol.* **2004**, *96*, 93–97.
12. (a) Toja, E.; Omodei-Sale, A.; Cattaneo, C.; *Eur. J. Med. Chem.* **1982**, *17*, 223–227; (b) Johnson, A. L.; Sweetser, P.B. DE **1972**, 2219702; (c) Beyer E. M.; Johnson, A.;

Sweetser, L. *P. B. Plant Physiol.* **1976**, *57*, 839–841; (d) Katekar, G. F.; Geissler, A. E.; *Plant Physiol.* **1980**, *66*,1190–1195; (e) Katekar, G. F. *E.Plant Physiol.* **1981**, *68*, 1460–1464.

13. (a) Katritzky, A. R.; Pozharskii, A. F. *Handbook of Heterocyclic Chemistry:* **2000**, 233-235; (b) Noga, E. J.; Barthalmus, G. T.; Mitchell, M. K. *Cell Biology Int. Rep.* **1986**, *10*, 239-242 (c) Kodama, T.; Tamura, M.; Oda, T.; Yamazaki Y. M. U.S. *Patent* 983928, **2003**.

14. Elguero, J. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R. Ed.; Pergamon Press: New York, **1984**, *5*, 291-297.

15. Sperandeo, N. R.; . Brun, R. *ChemBioChem;* **2003**, *4*, 69-72

16. Nargund, R. P.; Vander Ploeg, L. H. T.; Fong, T. M.; MacNeil, D. J.; Chen, H. Y.; Marsh, D. J.; Warmke, J. U. S. *Pat. Appl. Publ.*, **2004**, *43*, 225-227.

17. (a) Elguero, J. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R.; Rees, C. W.; Scriven, E. F. V., Eds.; Pergamon-Elsevier Science: Oxford, UK, **1996**, *6*, 1-75. (b) Sutharchanadevi, M.; Murugan, R. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, Eds.; Pergamon-Elsevier Science: Oxford, UK, **1996**, *6*, 221- 260. (c) Diana, P.; Carbone, A.; Barraja, P.; Martorana, A.; Gia, O.; Dallavia, L.; Cirrincione, G. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 6134-6137 (d) M. Patel and R. Desai,; *RKIVOC* **2004**, 123-129.

18. (a) Dominguez, J. N.; Leon, C.; Rodrigues, J.; de Dominguez, N. G.; Gut, J.; Rosenthal, P. J. *J. Med. Chem.* **2005**, *48*, 3654-3657; (b) Xue, C. X.; Cui, Y. S.; Liu, C.; Hu, Z. D.; Fan, B. T. *Eur. J. Med. Chem.* **2004**, *39*, 745-747; (c) M. Liu; P. Wilarat; M. L. Go.; *J. Med. Chem.*, **2001**, *44*, 44-46.

19. (a) Liu, M.; Wilairat, P.; Croft, S. L.; Tan, A. L.; Go, M. *Bioorg. Med. Chem.* **2003**, 11, 27-29; (b) Kayser, O.; Kiderlen, A. F. *Phytother. Res.* **2001**, *15*, 148-150.

20. Meng, C. Q.; Zheng, X. S.; Simpson, J. E.; Worsencroft, K. J.; Hotema, M. R. *J. Med. Chem.* **2002**, *45*, 54-57.

21. Skudlarek, J. W.; Gilmore, J. M.; Hoong, L. K.; Hill, R. R.; Marino, E. M.; Suen, K. L.; Kunsch, C. *Bioorg. Med. Chem. Lett.* **2004** ,*14*, 15-13; (b) Zwaagstra, M. E.; Timmerman, H.; Tamura, M.; Tohma, T.; Wada, Y.; Onogi, K.; Zhang M. Q. *J. Med. Chem.* **1997**, *40*, 1075-1077.

22. Yayli, N.; Aydin, F. E.; Gçk, Y.; Baltasi, A. C.; Yildirim, N.; *J. Photochem. Photobiol.*, **2005**, *169*, 229-231.

23. Williams, C. A.; Grayer, R. J. Anthocyanins and other flavonoids. *Nat. Prod. Rep.* **2004**, *21*, 539–573.

24. Go, M. L., Wu, X.; Liu, X. L. Chalcones: an update on cytotoxic and chemoprotective properties. *Curr. Med. Chem.* **2005**, *12*, 481–499.

25. Nowakowska, Z. A review of anti-infective and anti-inflammatory chalcones. *Eur. J. Med. Chem.* **2007**, *42*, 125–137.

26. Herencia, F.; Ferrandiz, M. L.; Ubeda, A.; Guillen, I.; Dominguez, J. N.; Charris, J. E.; Lobo, G. M. *Free Radical Biol. Med.* **2001**, *30*, 43–50.

27. Huang, Y. C.; Guh, J. H.; Cheng, Z. J.; Chang, Y. L.; Hwang, T. L.; Lin, C. N.; Teng, C. M. *Life Sci.* **2001**, *68*, 2435–2447.

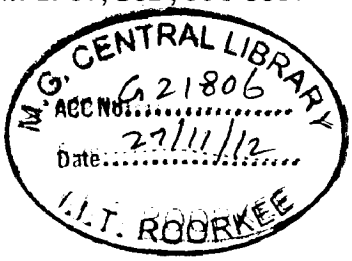
28. Elguero, J.; Bulton McKillop (editors), Comprehensive Heterocyclic Chemistry, Pergamon Press, **1984**, *5*, 293-295.

29. Dambal, D. B.; Pattanashetti, P. P.; Tikare, R. K.; Badami, B. V.; Puranik, G. S. *Indian J. Chem.* 1984, *23B*, 186-187.

30. Kulkarni, S. E.; Man, R. A.; Ingle, D. B. *Indian J. Chem.* **1986**, *25B*, 452-454.

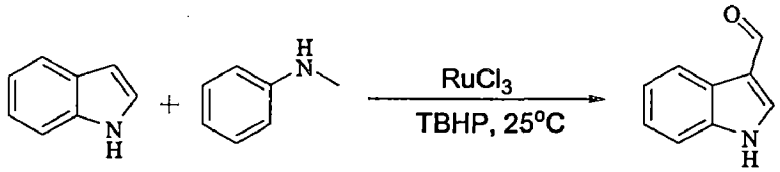
31. Cremlyn, R. J.; Swinbourne, F. J.; Mookerjee, E. *Indian J. Chem.* **1986**, *25B*, 562-564.

32. Gawande, N. G.; Shingare, M. S. *Indian J. Chem.* **1987**, *26B*, 351-353.

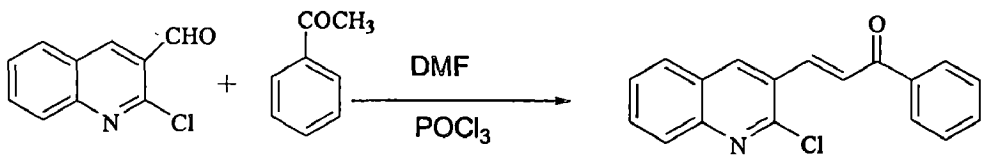


1.2 Literature survey:

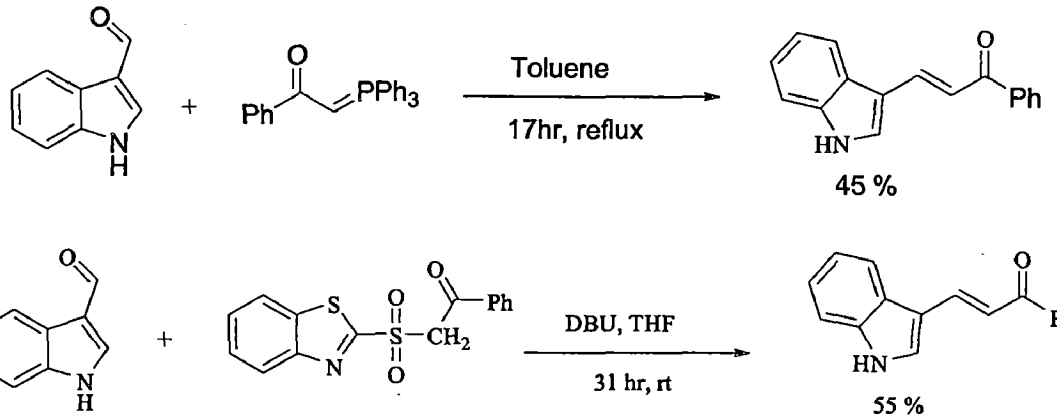
Chalcone was synthesized using Claisen-Schmidt reaction. In chalcone, more important moiety is α,β unsaturated ketone, which has more important for biological activity. The α,β-unsaturated ketones can play the role of versatile precursors in the syntheses of the various derivatives like flavones, pyrazoline, sulfone derivatives[1-6]. The synthesis and transformation of indoles has been and continues to be a focus of research efforts for synthetic organic chemists because the indole nucleus is found in countless biologically active molecules and medicinally relevant structures.[7] 3-Formylindoles are versatile starting materials for syntheses of a broad range of indole derivatives since their carbonyl groups can readily undergo a variety of transformations such as C-C and C-N coupling reactions and reductions.[8] Weiping Su *et. al* C3- selective formylation of free (N-H) indoles under mild conditions can be achieved by using Ru- catalyzed oxidative coupling of free (NH) indoles with anilines, respectively[9].



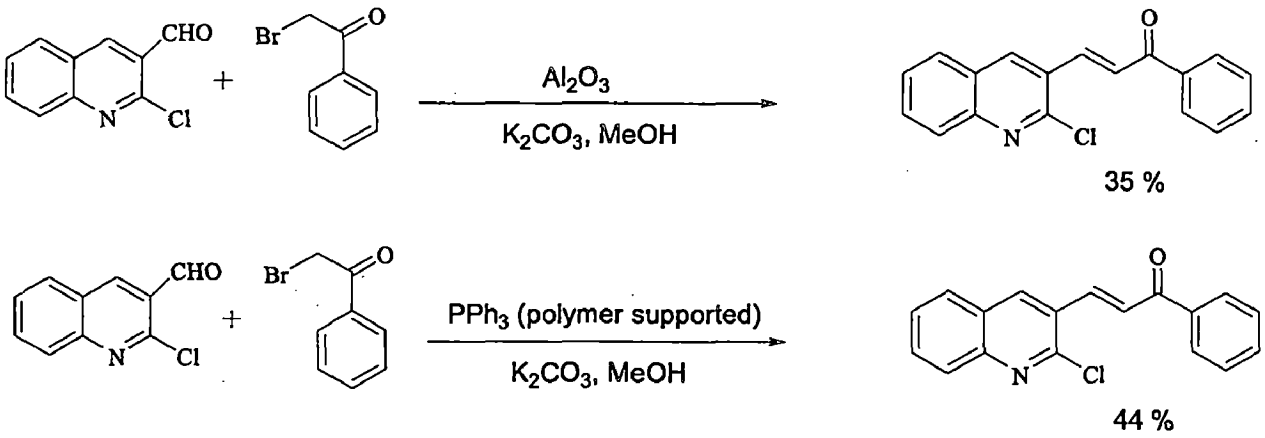
The importance of quinoline and its annelated derivatives is well recognized by synthetic and biological chemists.[10] Compounds possessing this ring system have wide applications as drugs and pharmaceuticals.[11] Pulak J. Bhuyan *et. al.* recently prepared 2-chloro quinoline aldehydes synthesized by reaction of N-acyl anilines with DMF/$POCl_3$[12].



Previously indole based chalcone are reported but they are used costly wittig reagents[13] or costly bases[14], harmful solvents and long reaction times. But here we have synthesized by using low cost chemicals, environment friendly solvents and good yield.



Previously 2-chloro quinoline based chalcone are reported but they are getting low yield. Tiwari, Vandana et al reportedsynthesis of 2-chloro quinoline based chalcone by using Al_2O_3 [15]but they got only 35% yield. And Westman et al. also used polymer supported PPh_3[16] but also very less increment of yield observed. But here we have done with 40% aq NaOH we got 76 % yield.

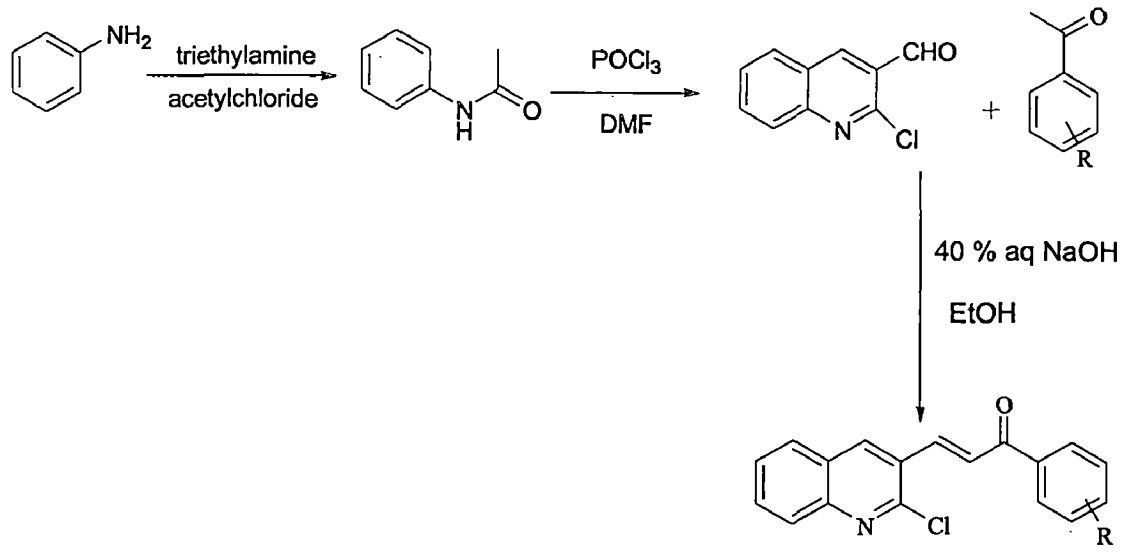


References:

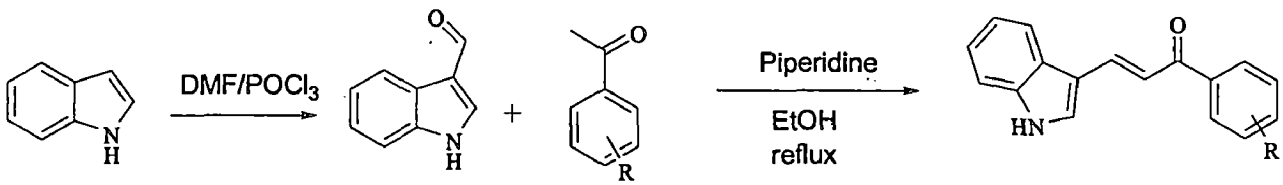
1. Mancuso, B.; Salerno, R.; Lupinacci, G.; Ruffolo, E.; Costa, G. M. *J. Org. Chem.* **2008**, *73*, 4971-4973
2. Dobson, I. C.; Fletcher, B. C.; Franklin, S. R. *Eur. J. Org. Chem.* **2007** , *16*, 2676-2678
3. Wu, W.; Su, W.; *J. Am. Chem. Soc.* **2011**, *133*, 11924 –11927.
4. Kalita, P. K.; Baruah, B.; Bhuyan, P. J. *Tetrahedron Lett.* **2006**, *47*, 7779–7782.
5. Lundy, B. J.; Popova S. J. J. A. *Org. Lett.*, **2011**, *13*, 4958–4961.
6. Kumar, A.; Sharma, S.; Tripathi, V. D.; Srivastava, S. *Tetrahedron* **2010**, 66, 9445-9449
7. Tiwari, V. *Green Chem. Lett. Rev.* **2011**, 4, 219-224.
8. Westman, J. *Org. Lett.* **2001**, *3*, 3745-3747.

Aim and scope of the present work

Chalcone is a very special α,β-unsaturated ketone system. The α,β-unsaturated ketones play the important role of versatile precursors in the synthesis of the many natural product and biological active compounds. Chalcone are convenient and versatile materials for the synthesis. of many chalcone derivatives. Some reagent including, sodium hydroxide, piperidine and some solvent ethanol, dimethyl formamide. The present study deals with the synthesis of chalcone from many aromatic compound indole-3-carbaldehyde, 2-chloro quinoline-3-carbaldehyde as representative of aldehyde reacts with different acetophenone. For the different chalcone, indole-3-carbaldehyde reacts with different acetophenone using piperidine base. For the different chalcone 2-chloroquinoline-3-carbaldehyde reacts with different-different acetophenone using NaOH base.



Scheme 1



Scheme 2

Chapter - 2

Synthesis and Characterization

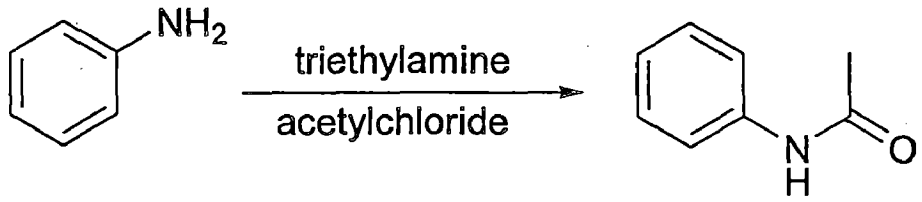
2A: SYNTHESIS AND CHARACTERIZATION OF 2-CHLORO QUINOLINE BASED CHALCONE DERIVATIVES

2A. 1 Instruments and Chemicals used

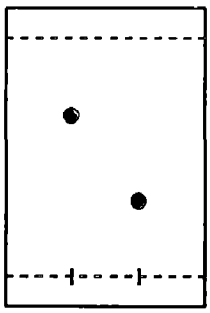
Flash chromatography was performed on silica gel (Rankem laboratory, 60-120 mesh). TLC was performed on aluminum-backed silica plates (contain -13% $CaSO_4$ ½ H_2O, SILICA Gel /UV_{254}), which were developed by using UV fluorescence. Melting points were determined on kofler apparatus melting point apparatus and are uncorrected. Elemental analysis was performed on a Vario EL CHNS analyzer. Infrared spectra were recorded on a Nexus Thermo Nicolet FT-IR spectrometer using KBr pellets .^{1}H NMR spectra were recorded at 500 MHz on Brucker ultra shield AC 300 and DPX 300 instruments, respectively; ^{13}C NMR spectra at 125.5 MHz's chemical shifts are given in parts per million (ppm) referenced to TMS. High resolution mass spectra (m/z) were recorded on a Perkin Elamer GC-MS spectrometer. All commercially available chemicals were used with further purification. Anhydrous solvents were distilled from appropriate drying agents prior to use.

2A. 2 Synthesis of acetanilide(1a)

To a stirred solution of aniline in DCM at 0 °C in inert atmosphere was added triethylamine (2 eq) followed by acetyl chloride (1.4 eq) . Reaction monitored by TLC (thin layer chromatography) after completion of reaction the reaction mixture were poured into the ice cold water white solid crystalline pure acetanilide formed. Yield: 70%, m.p-114.3°C. ^{1}HNMR ($CDCl_3$, 500 MHz) ppm:7.6 (db, 2H, Ar-H), 7.35-7.30 (m, 2H, Ar-H), 7.10 (m,1H, Ar-H), 2.0 (s, 3H, -CH_3)



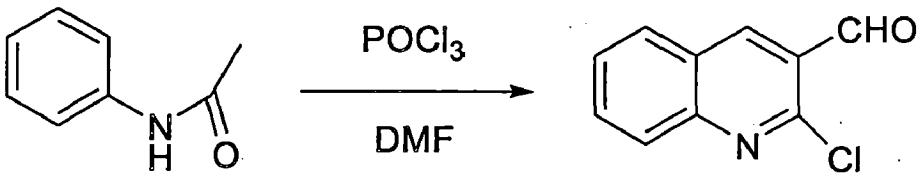
Scheme 1



TLC (1st-S.M, 2nd-Rxn mix)

2A.3 Synthesis of 2-chloroquinoline-3-carbaldehyde(2a)

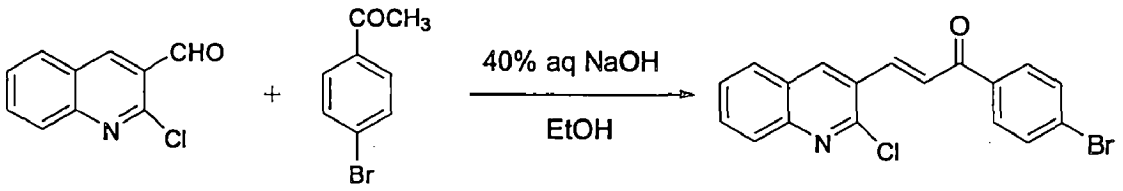
In a ovendried R.B. was taken DMF (2.5 eq) solvent to this solution at 0 °C was added $POCl_3$ (7eq) the resulting solution at this temperature was stirred 15 min. Then warmed to room temperature added acetanilide and the resulting solutions were heated at 75 °C for 2 h. Reaction monitored by TLC after completion of reaction the reaction mixture was poured into ice water and extracted by DCM. The organic layer was dried over Na_2SO_4, purified crude mixture by using silicagel column chromatography as eluents 1:10 ethylacetate:Hexane. Yield: 60%, m.p-148-150°C ^{1}H NMR ($CDCl_3$,500MHz) ppm: 9.61(s,1H,-CHO),8.71(s,1H,Ar-H),8.05(d,1H, Ar-H),7.68(d,1H,Ar-H),7.61(m,1H ,Ar-H),7.43(m,1H,Ar-H)



2A.4 Synthesis of (E)-1-(4-Bromophenyl)-3-(2-chloroquinolin-3-yl)prop-2-en-1-one(3a)

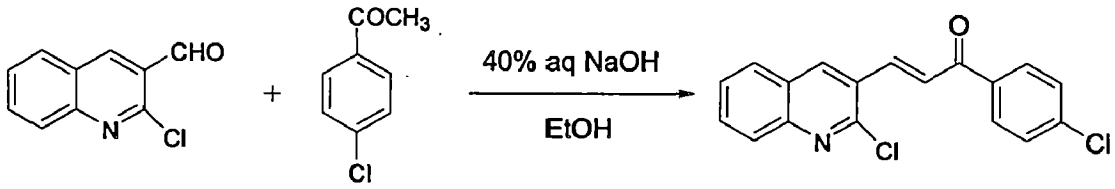
A mixture of substituted 2-chloro-3-formylquinolines (0.01 mmol), bromoacetophenone,and sodium hydroxide(2 mL, 40% aqueous) in 50mL ethanol was stirred at room temperature for 24 h.The resulting precipitate was collected by filtration,washed with water and recrystallize from ethylacetate. Yield 70%, m.p-223°C, ^{1}HNMR ($CDCl_3$, 500 MHz), 8.50 (s, 1H,

H_4quinoline), 8.24 (d, 1H, Hβ), 8.05 (d, 1H, H_5quinoline), 7.95-7.77 (m, 3H, 2Hphenyl, H_8quinoline) 7.69-7.70(m, 2H, phenyl), 7.58-7.69 (m, 2H, H6, H7), 7.60 (s, 1H, Hα)



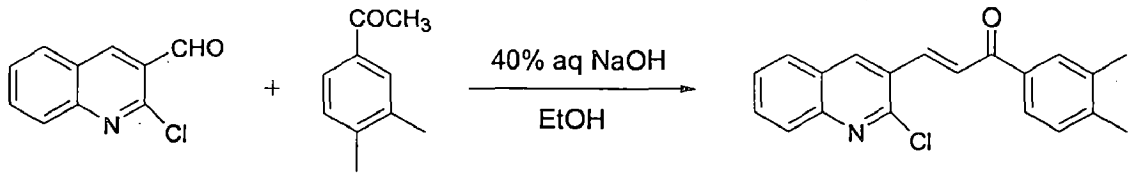
2A. 5 Synthesis of (E)--1-(4-chlorophenyl)-3-(2-chloroquinolin-3-yl)prop-2-en-1-one(4a)

A mixture of substituted 2-chloro-3-formylquinolines(0.01 mmol),bromoacetophenone,and sodium hydroxide(2ml, 40% aquous) in 50ml ethanol was stirred at room temperature for 24 h.The resulting precipitate was collected by filtration,washed with water and recrystallize from ethylacetate.yield = 72%, m.p = 180°C, ^{1}H NMR ($CDCl_3$, 500MHz), ppm δ (8.50(s, 1H, H_4quinoline), 8.24 (d, 1H, Hβ), 8.05 (d,1H, H_5quinoline), 7.95 (m, 3H, 2Hphenyl, H_8quinoline), 7.70 (m, 2H, phenyl), 7.69 (m, 2H, H6, H7), 7.60 (s, 1H, Hα)



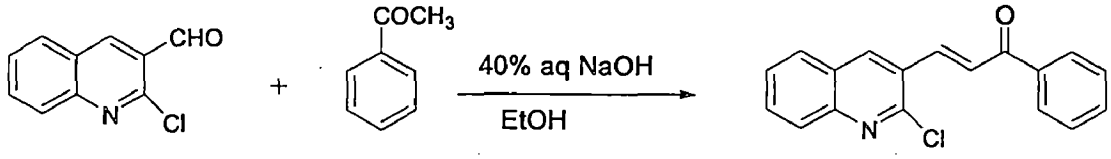
2A. 6 Synthesis of (E)-3-(2-chloroquinolin-3-yl)-1-(3,4-dimethyl phenyl)prop-2-en-1-one(5a)

A mixture of substituted 2-chloro-3-formylquinolines(0.01 mmol),3,4dimethyl acetophenone,and sodium hydroxide(2 mL, 40% aquous) in 50mL ethanol was stirred at room temperature for 24 h.The resulting precipitate was collected by filtration,washed with water and recrystallize from ethylacetate. Yield = 76 %, m.p. = 160 °C ^{1}HNMR ($CDCl_3$, 500MHz) δ ppm: 8.5 (s, Ar-H, 1H), 8.2 (d, Ar-H, 1H), 7.68-7.61 (m,Ar-H, 3H), 7.2-7.1 (m, ,2 =C-H,Ar-H, 3H), 7.35 (s, CH3, 6H)



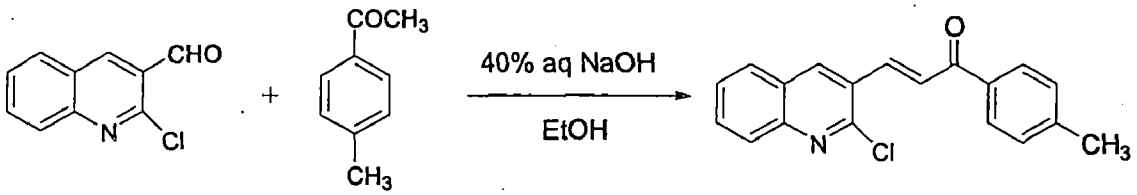
2A.7 Synthesis of (E)-3-(2-chloroquinolin-3-yl)-1-phenylprop-2-en-1-one(6a)

. A mixture of substituted 2-chloro-3-formylquinoline (0.01 mmol), acetophenone,and sodium hydroxide (2 mL, 40% aquous) in 50 mL ethanol was stirred at room temperature for 24 h.The resulting precipitate was collected by filtration,washed with water and recrystallize from ethylacetate. Yield = 73%, m.p. = 150 ^{0}C ^{1}HNMR ($CDCl_3$, 500MHz) δ ppm: 8.2 (s, Ar-H, 1H), 8.0(d, Ar-H, 1H), 7.81-7.82 (d,Ar-H, 2H), 7.6-7.4 (m,Ar-H,6H), 7.2 (m, =C-H, 2H)



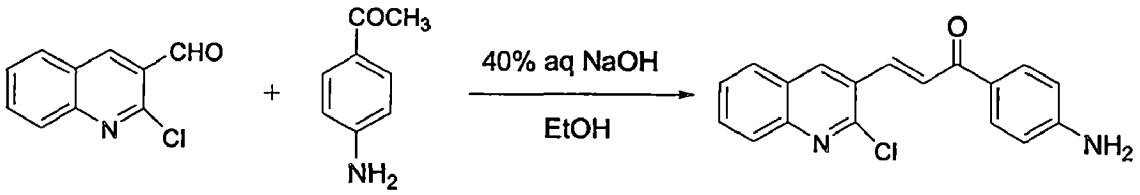
3A.8 Synthesis of (E)-3-(2-chloroquinolin-3-yl)-1-p-tolylprop-2-en-1-one(7a)

. A mixture of substituted 2-chloro-3-formylquinolines(0.01 mmol),4-methyl acetophenone,and sodium hydroxide(2 mL, 40% aquous) in 50ml ethanol was stirred at room temperature for 24 h.The resulting precipitate was collected by filtration,washed with water and recrystallize from ethylacetate. Yield = 75%, m.p. = 170 °C ^{1}HNMR ($CDCl_3$, 500MHz) δ ppm: 8.2 (s, Ar-H, 1H), 8.05(d, Ar-H, 1H), 7.9 (d,Ar-H, 1H), 7.6-7.7 (m,Ar-H,=C-H,5H), 7.43(m, Ar-H,1H),7.25(d,Ar-H,2H),2.35(s,CH3,3H); IR (ν_{max}, cm^{-1}): 1651 (C=O), 1586 (C=C), 1346 (C=N).



3A.9 Synthesis of (E))-1-(4-aminophenyl)-3-(2-chloroquinolin-3-yl)prop-2-en-1-one(8a)

A mixture of substituted 2-chloro-3-formylquinolines(0.01 mmol),4-amino acetophenone,and sodium hydroxide(2 mL, 40% aquous) in 50ml ethanol was stirred at room temperature for 24 h.The resulting precipitate was collected by filtration,washed with water and recrystallize from ethylacetate. Yield = 75%, m.p. = 170 °C ^{1}HNMR ($CDCl_3$, 500MHz) δ ppm: 8.5 (s, Ar-H, 1H), 8.2(d, Ar-H, 1H), 8.0 (d, Ar-H, 1H), 7.9(m, Ar-H,=C-H,2H), 7.6-7.9(m, Ar-H,=C-H,4H),6.8(s,Ar-H,2H),4.00(s,NH2,2H); IR (ν_{max}, cm^{-1}): 1651 (C=O), 1586 (C=C), 1346 (C=N).



Reference:

1. Bandgar, B. P.; Gawande, S. S.; Bodade, R. G.; Gawande, N. M. *Bioorg. Med. Chem.* **2009**, *17*, 8168-8173.

2. Jungshin, Y. K. K,; Yoo, K.; Seo, K. J. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 2385-2390.

3. Insusasty, B.; Tigreros, A.; Quiroga, F. *Bioorg. Med. Chem.* **2010**, *18*, 4965-4974.

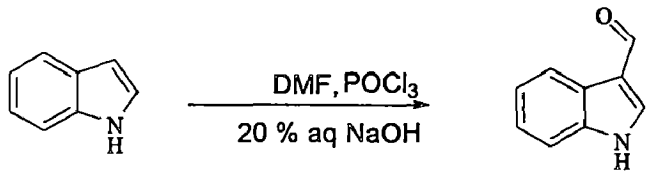
4. Kumar, D.; Kumar, N. M.; Akamatsu, K.; Kaska, E.; Harada, H. *Bioorg. Med. Chem.* **2010**, *20*, 3916-3919.

5. Bsanagounda, M.; Kulkarni, M. V.; .Kalkhambkar, R. G.; Kulkarni, G. M. *Synth. Commun.* **2008**, *38*, 2929-2940.

2B. SYNTHESIS AND CHARACTERISATION OF INDOLE BASED CHALCONE

2B.1 Synthesis of indole-3-carbaldehyde

To DMF (7 mL), $POCl_3$ (1 mL) was added at 0 °C. The mixture was stirred at 20 minute. Then a solution of indole(10 mmol) in DMF(3 mL) was added dropwise. After the mixture was stirred at 35 °C for 1 h. Ice was added,followed by 20% aq. NaOH,and the mixture was refluxed for 6 h.On cooling ,the mixture was poured into ice water,and the precipitate product was collected,wash by water and dried.yield-70% m.p. 190-192 °C, ^1H NMR ($CDCl_3$, 500Mz) δ (ppm): 9.9 (s, 1H), 8.7 (s, 1H), 8.4 (s, 1H), 7.8 (s, 1H), 7.5 (d,1H), 7.3 (m, *2H*),

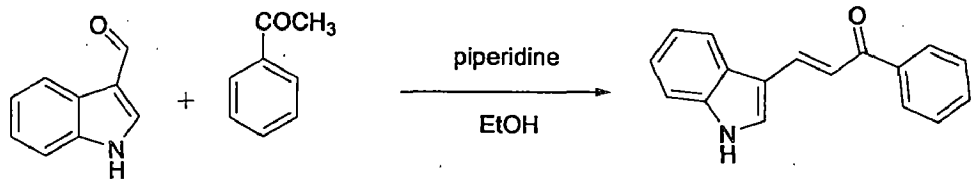


Scheme 2

2B.2 Synthesis of (E)-3-(1H-indol-3-yl)-1-phenyl-prop-2-en-1-one (2b)

Indole-3-carbaldehyde (6.89 mmol) was dissolved in EtOH (14 mL).Then acetophenone(6.89 mmol) and afterwards piperidine were added. The resulting solution was refluxed for 16 h. The reaction mixture was neutralized with 10% HCl to p^H-7.The formed precipitate was collected by vaccum filtration and purified from MeOH to give deep yellow solid. yield-70%, m.p. 137 °C

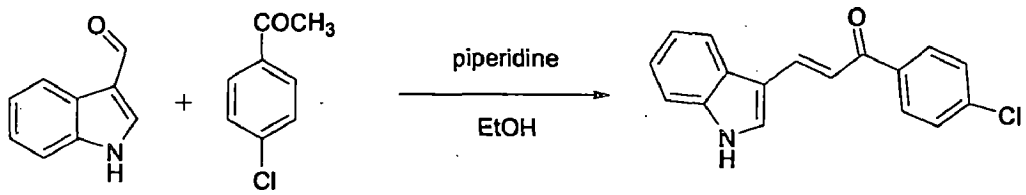
^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.60 (1H, s, br, NH), 7.11- 7.89 (9H, m, Ar-H), 6.86 (1H, d, J = 14.8 Hz, =CH-Ar), 5.82 (1H, d, J = 14.8 Hz, CO-CH]). IR (KBr) (cm^{-1}): 3160 (NH), 3020 (aromatic, C-H), 1710 (C=O), 1630 (-CH=CH).



2B.3 Synthesis of (E)-1-(4-chlorophenyl)-3-(1H-indol-3-yl)prop-2-en-1-one(3b)

Indole-3-carbaldehyde (6.89 mmol) was dissolved in EtOH(14 mL).Then 4-chloro acetophenone(6.89 mmol) and afterwards piperidine were added. The resulting solution was refluxed for 16 h. The reaction mixture was neutralized with 10% HCl to pH-7.The formed precipitate was collected by vaccum filtration and purified from MeOH to give deep yellow solid.yield 72%, m.p=151 °C

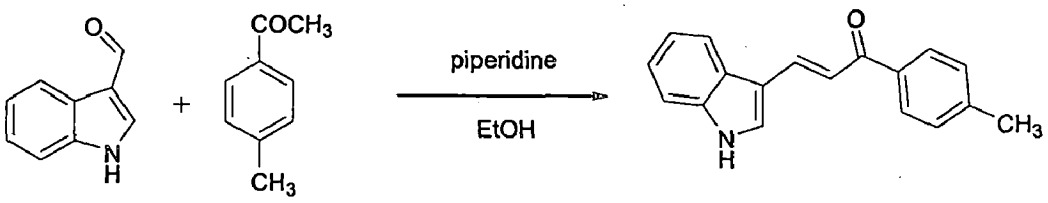
^{1}H NMR ($CDCl_3$ 500 MHz) δ: 8.71 (1H, bs), 8.04 (1H, d, J = 15.4 Hz), 8.00-7.94 (3H, m), 7.55-7.49 (2H, m), 7.46-7.43 (2H, m), 7.40-7.36 (1H, m), 7.26-7.22 (2H, m) ^{13}C NMR (125 MHz, CDCl3) δ 191.4, 139.4, 139.3, 137.6, 132.6, 130.7, 128.9, 128.7, 125.7, 123.9, 122.1, 121.1, 121.0, 118.2, 114.8, 112.3 IR (KBr) (cm^{-1}): 3147 (NH), 2927 (C-H), 1713 (C=O), 1640 (C=C).



2B.4 Synthesis of(E)-3-(1H-indol-3-yl)-1-p-tolylprop-2-en-1-one(4b)

Indole-3-carbaldehyde (6.89 mmol) was dissolved in EtOH (14 mL).Then methyl acetophenone(6.89 mmol) and afterwards piperidine were added. The resulting solution was refluxed for 16 h. The reaction mixture was neutralized with 10% HCl to pH-7.The formed precipitate was collected by vaccum filtration and purified from MeOH to give deep yellow solid.yield-68% ,m.p = 141 °C

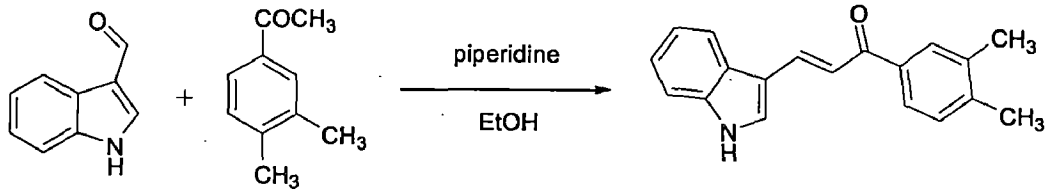
^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.69 (1H, s, br), 8.03 (1H, d, J = 15.4 Hz), 8.01-7.95 (3H, m), 7.58-7.47 (2H, m), 7.44-7.41 (2H, m), 7.39-7.35 (1H, m), 7.25-7.21 (2H, m), 2.12 (3H, s); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 193.5, 138.5, 139.3, 137.6, 132.6, 130.7, 128.9, 128.7, 125.7, 123.9, 121.16, 121.14, 121.01, 118.2, 113.8, 112.3, 24.2. IR (KBr) (cm^{-1}): 3147 (NH), 2927 (C-H), 1713 (C=O), 1640 (C=C).



2B. 5 Synthesis of (E)-1-(3,4-dimethylphenyl)-3-(1H-indol-3-yl)prop-2-en-1-one(5b)

Indole-3-carbaldehyde (6.89 mmol) was dissolved in EtOH(14 mL).Then the 3,4di methyl acetophenone(6.89 mmol) and afterwards piperidine were added. The resulting solution was refluxed for 16 h. The reaction mixture was neutralized with 10% HCl to pH-7.The formed precipitate was collected by vaccum filtration and purified from MeOH to give deep yellow solid.yield 65%, m.p. 145 °C

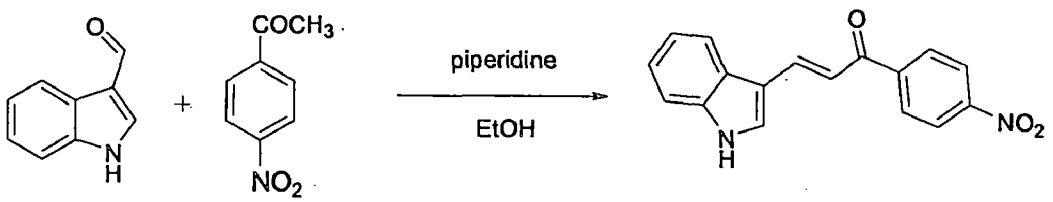
^{1}H NMR ($CDCl_3$ 500 MHz) δ: 8.70 (1H, bs), 8.01 (1H, d, J = 15.4 Hz), 7.96-7.93 (3H, m), 7.45-7.44 (2H, m), 7.41-7.38 (2H, m), 7.36-7.34 (1H, m), 7.24-7.20 (2H, m), 2.32 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (125 MHz, CDCl3) δ 191.4, 139.4, 139.3, 137.6, 132.6, 130.7, 128.9, 128.7, 125.7, 123.9, 122.1, 121.1, 121.0, 118.2, 114.8, 112.3, 23.21, 22.56. IR (KBr) (cm^{-1}): 3147 (NH), 2927 (C-H), 1713 (C=O), 1640 (C=C).



2B.6 Synthesis of (E)-1-(1H-indol-3-yl)-1-(4-nitrophenyl)prop-2-en-1-one(6b)

Indole-3-carbaldehyde (6.89 mmol) was dissolved in EtOH (14 mL). Then 4-nitro acetophenone (6.89 mmol) and afterwards piperidine were added. The resulting solution was refluxed for 16 h. The reaction mixture was neutralized with 10% HCl to p^H-7.The formed precipitate was collected by vaccum filtration and purified from MeOH to give deep yellow solid.yield 80%, m.p. 195 °C

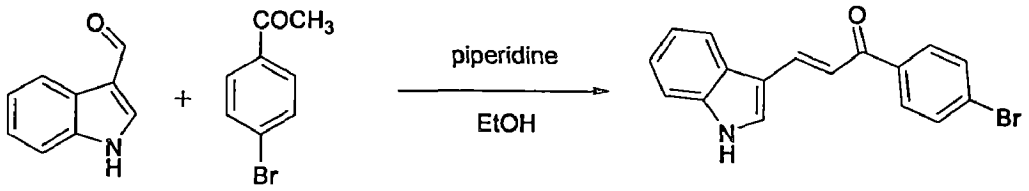
^{1}H NMR ($CDCl_3$ 500 MHz) δ: 8.71 (1H, bs), 8.38 (2H, d, J = 15.4 Hz), 8.07 (2H, d, J = 15.4 Hz) 7.94 (1H, d, 16 Hz), 7.56 (1H, d, 16 Hz), 7.55-7.49 (2H, m), 7.46-7.43 (2H, m). ^{13}C NMR (125 MHz, CDCl3): δ 188.4, 185.4, 144.5, 139.3, 137.6, 132.6, 130.7, 128.9, 128.7, 125.7, 123.9, 122.1, 121.1, 121.0, 118.2. IR (KBr) (cm^{-1}): 3147 (NH), 2927 (C-H), 1713 (C=O), 1662, 1640 (C=C).



2B.7 Synthesis of (E)-1-(4-bromophenyl)-3-(1H-indol-3-yl)prop-2-en-1-one(7b)

Indole-3-carbaldehyde (6.89 mmol) was dissolved in EtOH (14 mL).Then the acetophenone (6.89 mmol) and afterwards piperidine were added. The resulting solution was refluxed for 16 h. The reaction mixture was neutralized with 10% HCl to p^H-7.The formed precipitate was collected by vaccum filtration and purified from MeOH to give deep yellow solid, yield 73%, m.p. 155 °C

^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.69 (1H, s, br), 8.03 (1H, d, J = 15.4 Hz), 8.01-7.95 (3H, m), 7.58-7.47 (2H, m), 7.44-7.41 (2H, m), 7.39-7.35 (1H, m), 7.25-7.21 (2H, m) ^{13}C NMR (125 MHz, CDCl3) δ 193.5, 138.5, 139.3, 137.6, 132.6, 130.7, 128.9, 128.7, 125.7, 123.9, 121.16, 121.14, 121.01, 118.2, 113.8, 112.3 IR (KBr) (cm^{-1}): 3147 (NH), 2927 (C-H), 1713 (C=O), 1640 (C=C).

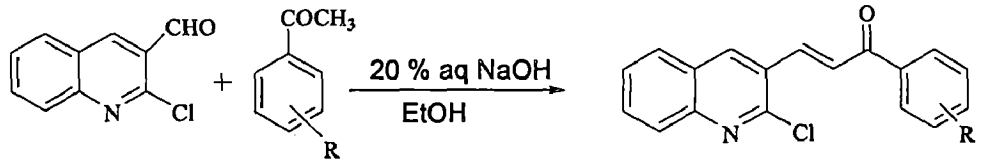


Reference:

1. Magdy, A. H. *J. Chem. Sci*. **2009**, *121*, 455-462.
2. Kumar, K.; Kumar, N. M.; Akamatsu, K.; Kaska, E.; Harada, H. *Bioorg. Med. Chem. Lett.* **2010**, *4*, 3916-3919.
3. (a) Ahmed, N.; Van Lier, J. E. *Tetrahedron Lett.* **2007**, *48*, 5407–5409. (b) Ahmed, N.; Van Lier, J. E. *Tetrahedron Lett.* **2007**, 48, 13–15. (c) Ahmed, N.; Van Lier, J. E.; *Tetrahedron Lett.* **2006**, *47*, 5345–5349. (d) Ahmed, N.; Van Lier, J. E. *Tetrahedron Lett.* **2006**, *47*, 2725–2729. (e) Ahmed, N.; Ali, H.; Van Lier, J. E. *Tetrahedron Lett.* **2005**, *46*,

253–256. (f) Ahmed, N. ; Ali, H. ; Van Lier, J. E. *J. Porphyrins Phthalocyanines* **2006,** *10*, 1172–1178.

TABLE 2: Condensation of 2-chloro quinoline aldehydes with aromatic acetophenones



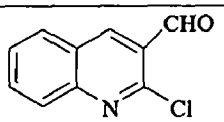
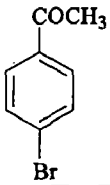
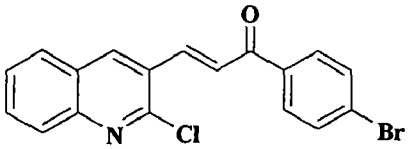
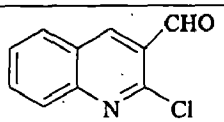
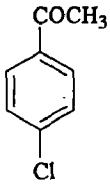
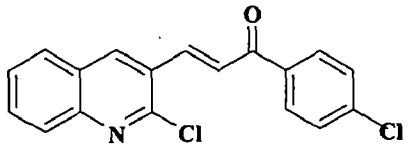
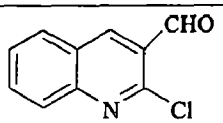
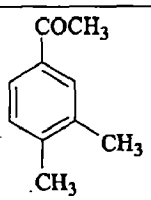
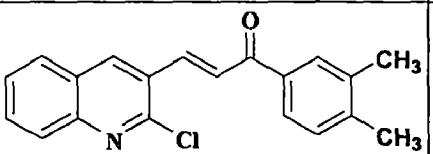
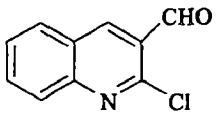
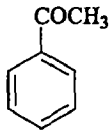
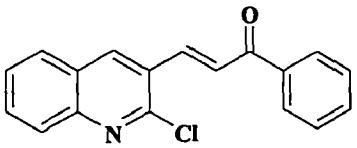
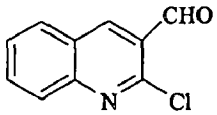
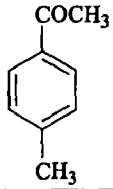
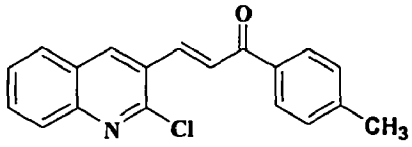
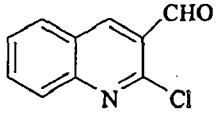
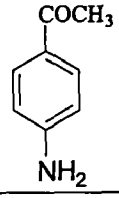
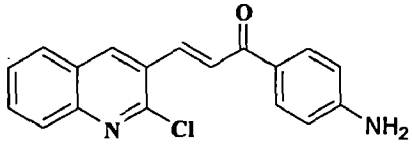
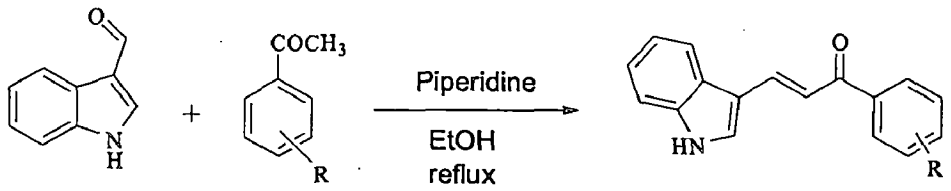
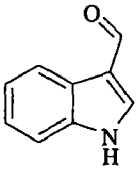
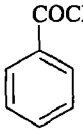
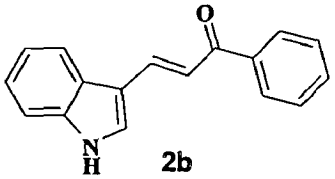
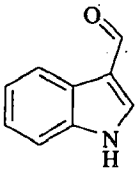
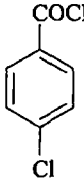
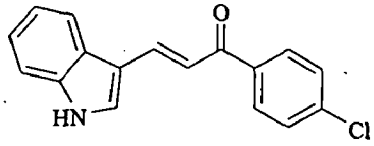
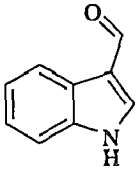
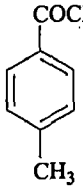
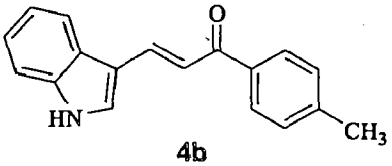
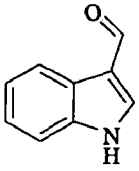
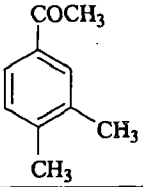
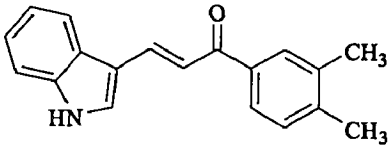
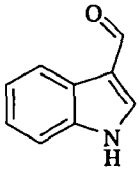
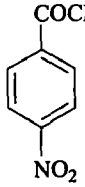
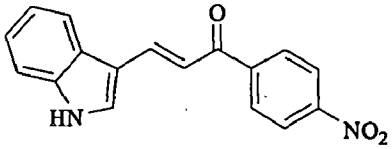
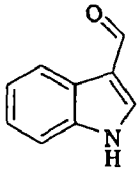
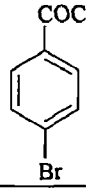
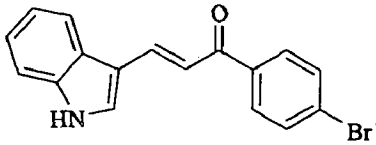
S.No	aldehyde	acetophenone	Reaction time (h)	product	Yield (%)
1			24 h	 **3a**	70
2			24 h	 **4a**	72
3			24 h	 **5a**	76
4			24 h	 **6a**	73
5			24 h	 **7a**	75
6			24 h	 **8a**	74

TABLE 3: Condensation of indole aldehydes with aromatic acetophenones



S.No	aldehyde	acetophenone	Reaction time (h)	product	Yield (%)
1			16 h	 **2b**	70
2			16 h	 **3b**	72
3			16 h	 **4b**	68
4			16 h	 **5b**	65
5			16 h	 **6b**	80
6			16 h	 **7b**	73

Chapter - 3

Conclusion

Conclusion

An efficient method developed for synthesis of hetero aromatic chalcones i.e indole based and 2-chloro quinoline based chalcones by using indole aldehyde or 2-chloro quinoline aldehyde condensation with various aromatic acetophenone given indole based chalcone, quinoline based chalcones respectively. indole based chalcone given 65-80 % yield and quinoline based chalcones 70-76 % yield. Indole aldehyde synthesized by using vilsmayer reaction and quinoline aldehyde was synthesized by reaction of N-acyl aniline with $DMF/POCl_3$.

Supporting information:

S.No	Title name
Figure1	^{1}HNMR spectrum of acetanilide
Figure2	^{1}HNMR spectrum of 2-chloro quinoline -3-carbaldehyde
Figure3	^{1}HNMR spectrum of (E)-1-(4-bromophenyl)-3-(2-chloroquinolin-3-yl)prop-2-en-1-one (3a)
Figure 4	^{1}HNMR spectrum of (E)-1-(4-chlorophenyl)-3-(2-chloroquinolin-3-yl)prop-2-en-1-one(4a)
Figure 5	^{1}HNMR spectrum of (E)-3-(2-chloroquinolin-3-yl)-1-(3,4-dimethyl phenyl)prop-2-en-1-one (5a)
Figure 6	^{1}HNMR spectrum of (E)-3-(2-chloroquinolin-3-yl)-1-phenylprop-2-en-1-one (6a)
Figure 7	^{1}HNMR spectrum of (E)-3-(2-choloroquinolin-3-yl)-1-p-tolylprop-2-en-1-one (7a)
Figure 8	^{1}HNMR spectrum of (E)-1-(4-aminophenyl)-3-(2-chloroquinolin-3-yl)prop-2-en-1-one (8a)
Figure 9	^{1}HNMR spectrum of indole-3-carbaldehyde (1b)
Figure 10	^{1}HNMR spectrum of (E)-3-(1H-indol-3-yl)-1-phenyl-prop-2-en-1-one (2b)
Figure 11	^{1}HNMR spectrum of (E)-1-(4-chlorophenyl)-3-(1H-indol-3-yl)prop-2-en-1-one (3b)
Figure 12	^{1}HNMR spectrum of (E)-3-(1H-indol-3-yl)-1-p-tolylprop-2-en-1-one (4b)
Figure 13	^{1}HNMR spectrum of (E)-1-(3,4-dimethylphenyl)-3-(1H-indol-3-yl)prop-2-en-1-one (5b)

Figure 14 ^{1}HNMR spectrum of (E)-1-(1H-indol-3-yl)-1-(4-nitrophenyl)prop-2-en-1-one (6b)

Figure 15 ^{1}HNMR spectrum (E)-1-(4-bromophenyl)-3-(1H-indol-3-yl)prop-2-en-1-one (7b)

Figure 16 ^{13}C NMR spectrum (E)-3-(1H-indol-3-yl)-1-phenyl-prop-2-en-1-one (2b)

Figure 17 ^{13}CNMR spectrum (E)-1-(4-chlorophenyl)-3-(1H-indol-3-yl)prop-2-en-1- one (3b)

Figure18 IR spectrum of (E)-1-(4-bromophenyl)-3-(2-chloroquinolin-3-yl)prop-2-en-1-one (3a)

Figure 19 IR spectrum of (E)-1-(4-chlorophenyl)-3-(2-chloroquinolin-3-yl)prop-2-en-1-one (4a)

Figure 20 IR spectrum of (E)-3-(2-chloroquinolin-3-yl)-1-(3,4-dimethyl phenyl)prop-2-en-1-one (5a)

Figure 21 IR spectrum of (E)-3-(2-chloroquinolin-3-yl)-1-phenylprop-2-en-1-one (6a)

Figure 22 IR spectrum of (E)-3-(2-choloroquinolin-3-yl)-1-p-tolylprop-2-en-1-one (7a)

Figure 23 IR spectrum of (E)-1-(4-aminophenyl)-3-(2-chloroquinolin-3-yl)prop-2-en-1-one (8a)

Figure 24 IR spectrum of (E)-3-(1H-indol-3-yl)-1-phenyl-prop-2-en-1-one (2b)

Figure 25 IR spectrum of (E)-1-(4-chlorophenyl)-3-(1H-indol-3-yl)prop-2-en-1-one (3b)

Figure 26 IR spectrum of (E)-3-(1H-indol-3-yl)-1-p-tolylprop-2-en-1-one (4b)

Figure 27 IR spectrum of (E)-1-(3,4-dimethylphenyl)-3-(1H-indol-3-yl)prop-2-en-1-one (5b)

Figure 28 IR spectrum of (E)-1-(1H-indol-3-yl)-1-(4-nitrophenyl)prop-2-en-1-one (6b)

Figure 29 IR spectrum of (E)-1-(4-bromophenyl)-3-(1H-indol-3-yl)prop-2-en-1-one (7b)

Spectra -

figure-1

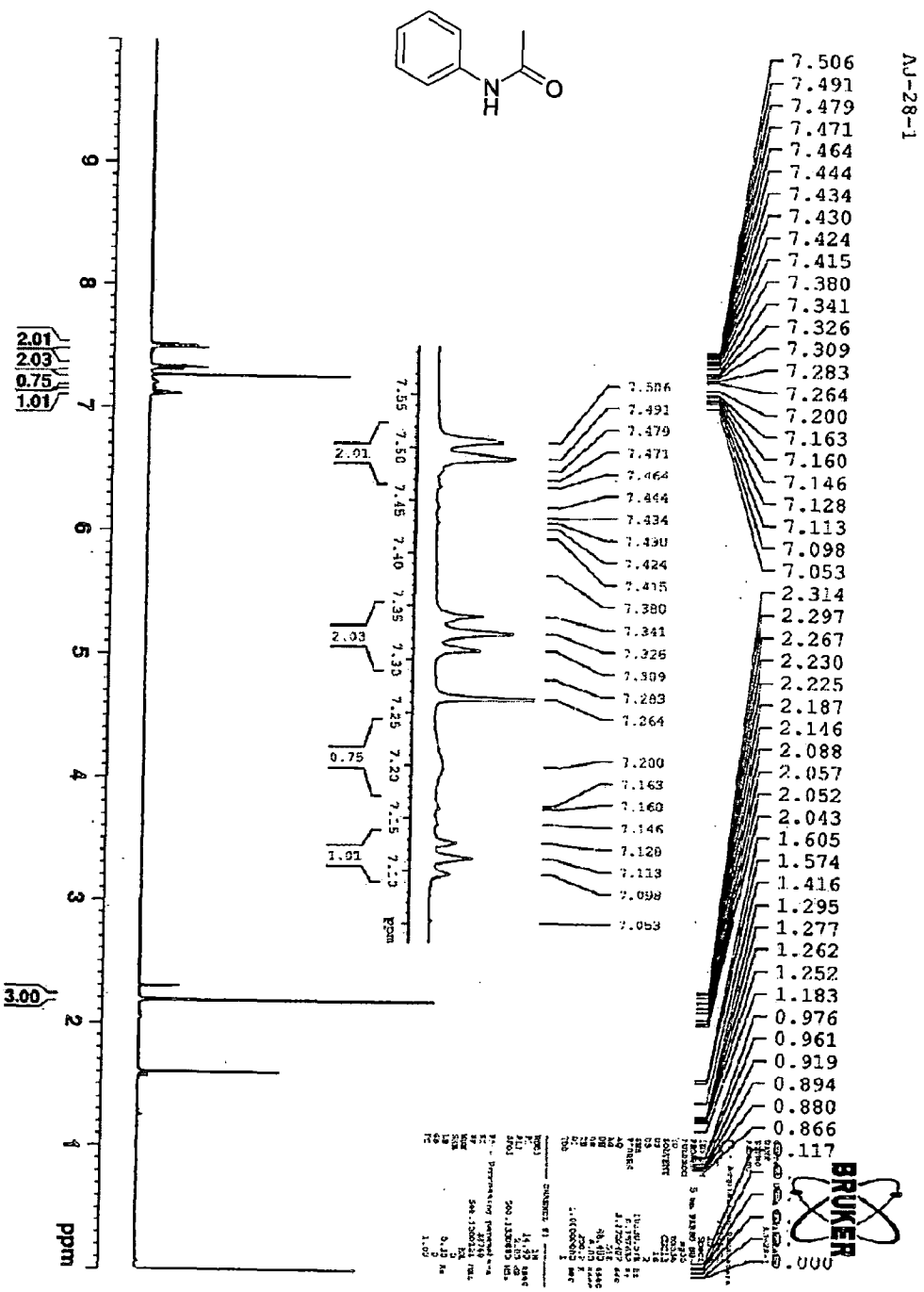
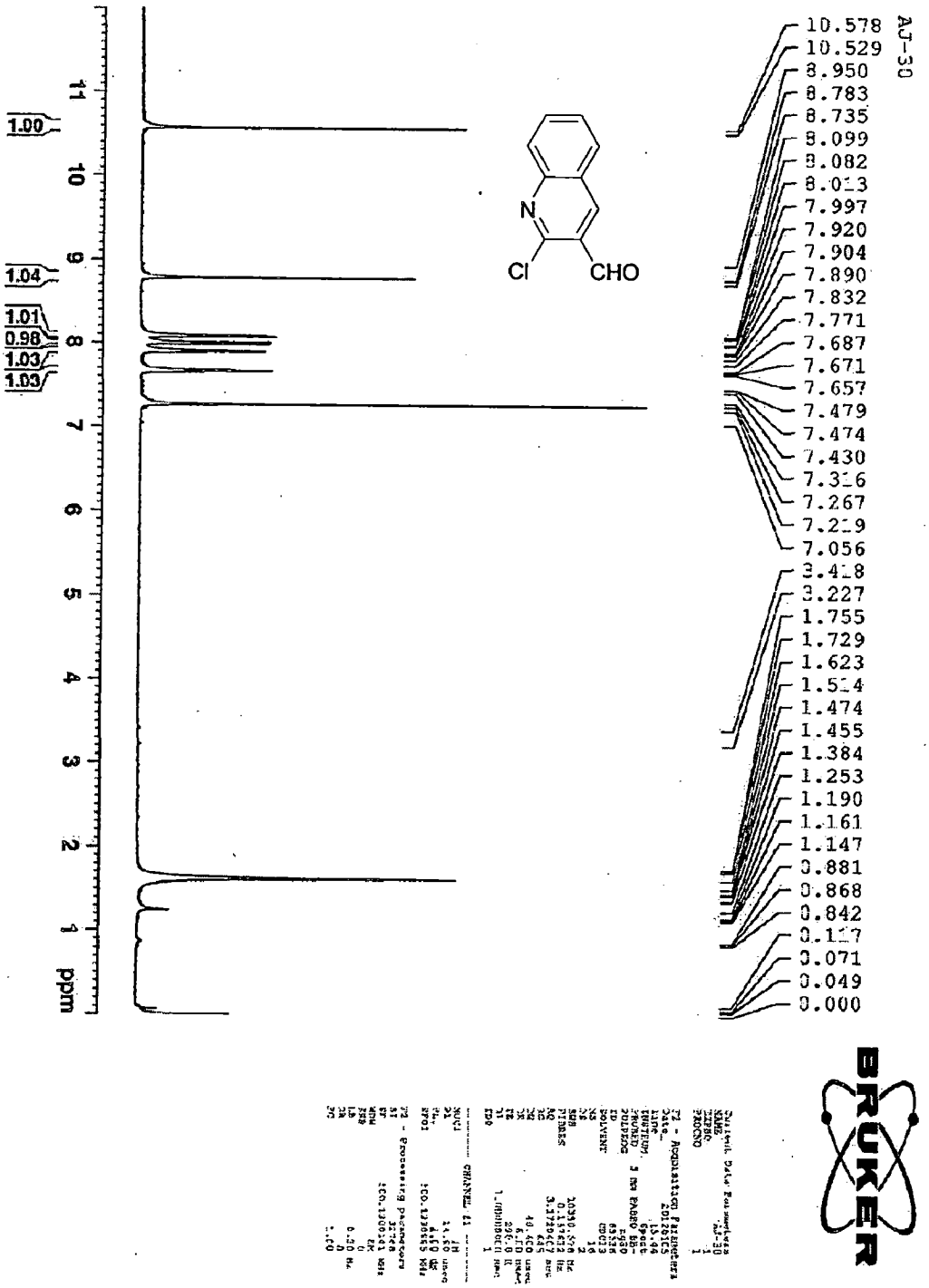


figure-2


AJ-30
10.578
10.529
8.950
8.783
8.735
8.099
8.082
8.013
7.997
7.920
7.904
7.890
7.832
7.771
7.687
7.671
7.657
7.479
7.474
7.430
7.316
7.267
7.219
7.056
3.418
3.227
1.755
1.729
1.623
1.514
1.474
1.455
1.384
1.253
1.190
1.161
1.147
0.881
0.868
0.842
0.117
0.071
0.049
0.000
1.00
1.04
1.01
0.98
1.03
1.03
N
Cl
CHO
ppm
BRUKER

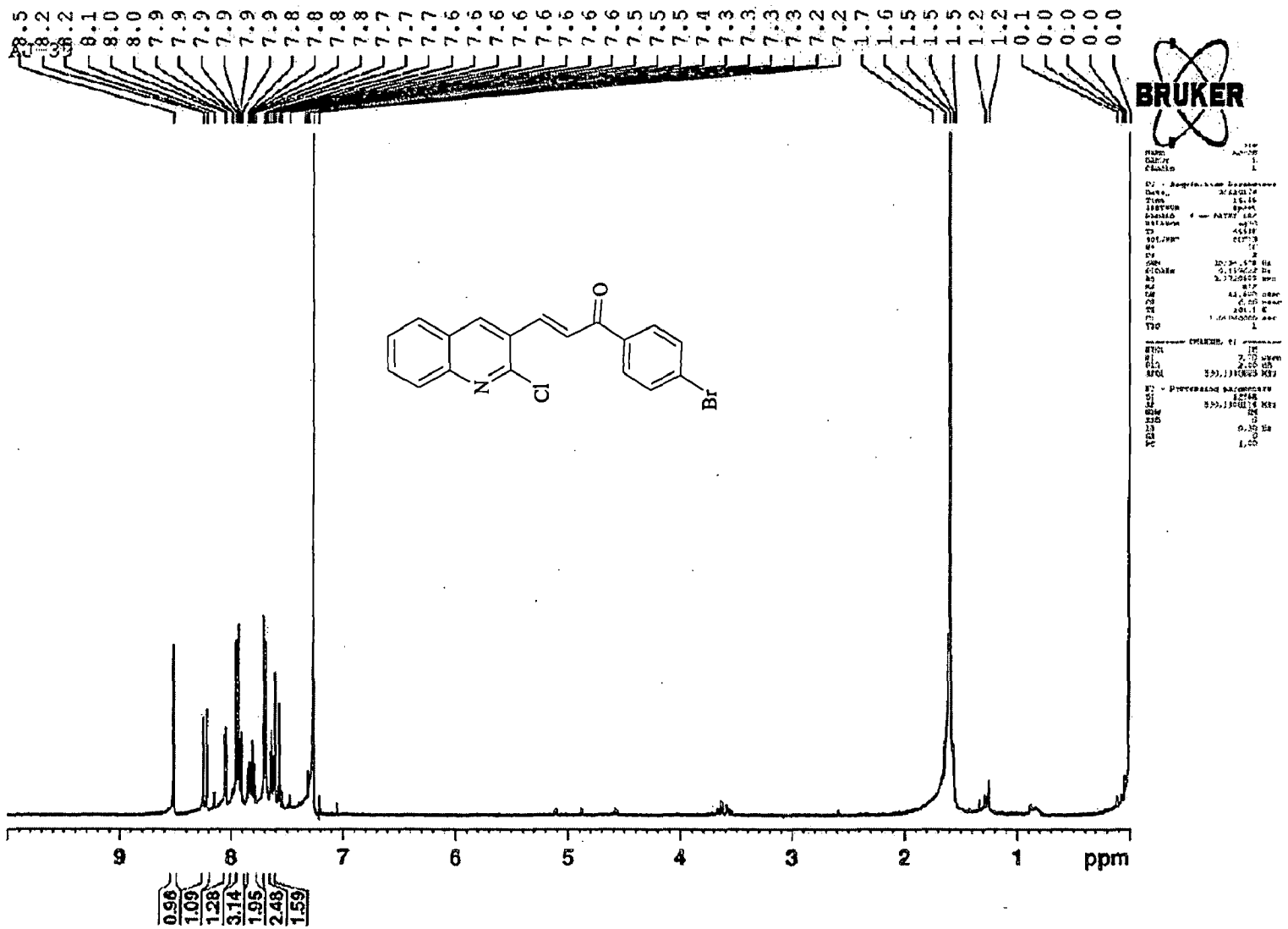


figure-3

figure-4

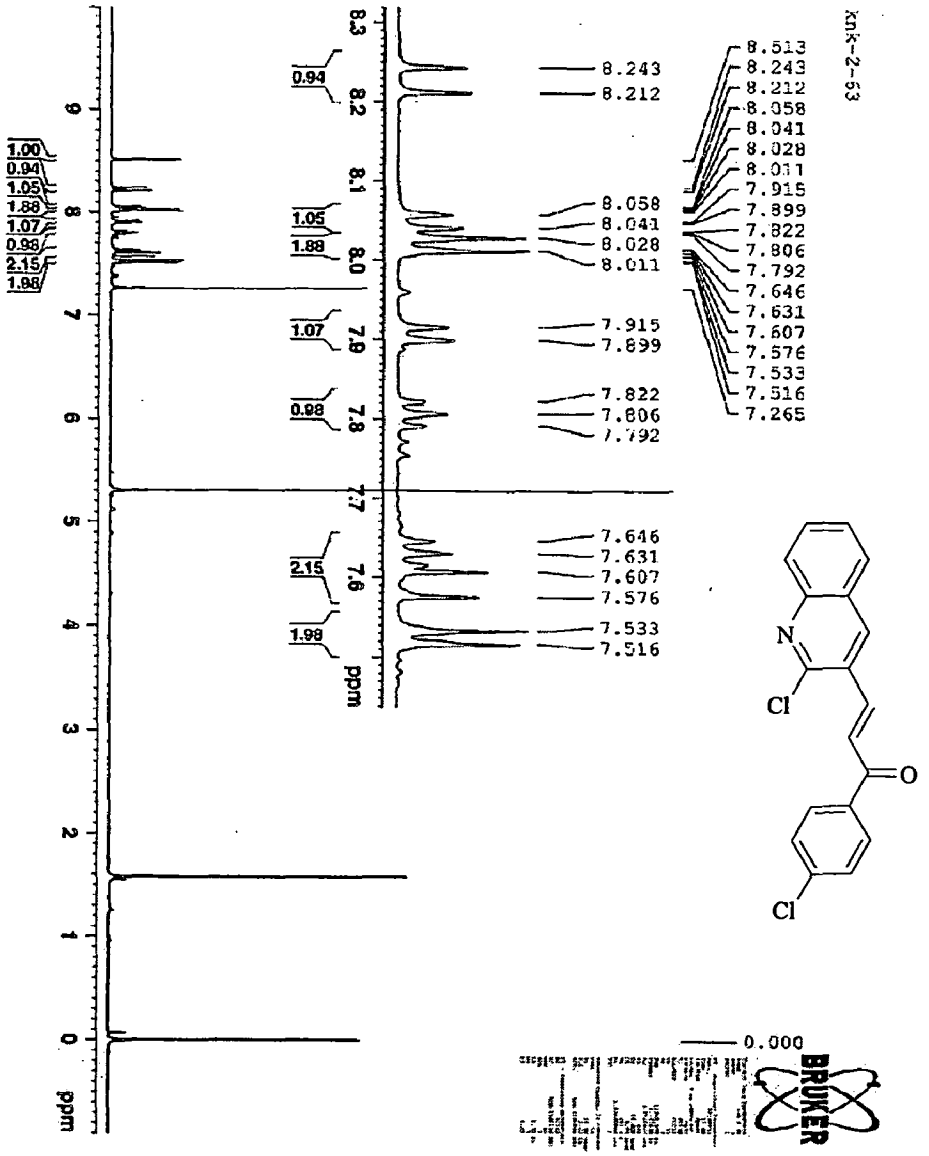

knk-2-53
8.513
8.243
8.212
8.058
8.041
8.028
8.011
7.915
7.899
7.822
7.806
7.792
7.646
7.631
7.607
7.576
7.533
7.516
7.265
1.00
0.94
1.05
1.88
1.07
0.98
2.15
1.98
ppm
0.000
BRUKER
N
Cl
O
Cl

figure-5

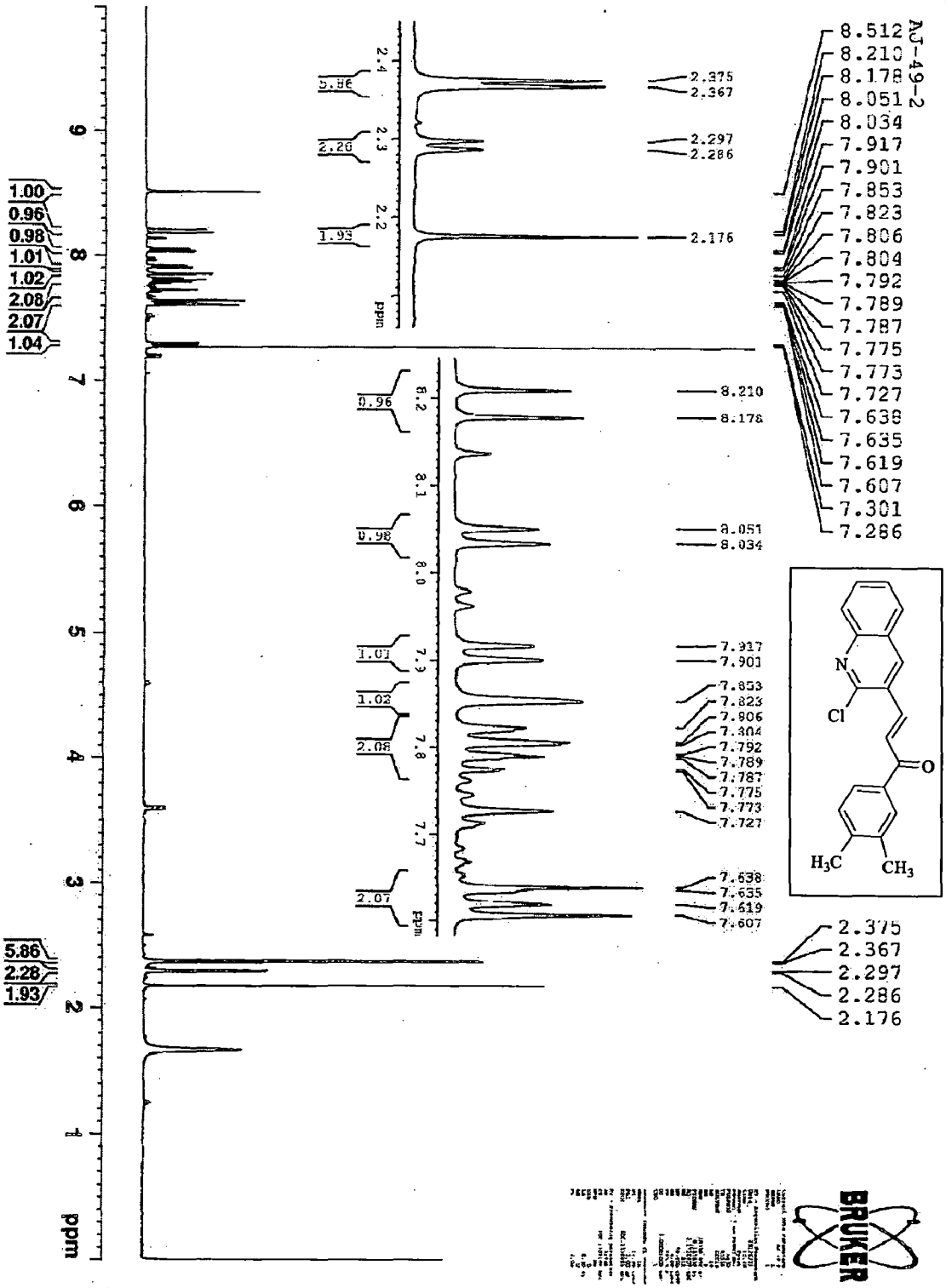

AJ-49-2
8.512
8.210
8.178
8.051
8.034
7.917
7.901
7.853
7.823
7.806
7.804
7.792
7.789
7.787
7.775
7.773
7.727
7.638
7.635
7.619
7.607
7.301
7.286
2.375
2.367
2.297
2.286
2.176
1.00
0.96
0.98
1.01
1.02
2.08
2.07
1.04
5.86
2.28
1.93
ppm
N
Cl
O
H3C
CH3
BRUKER

figure-6

AJ-50
7.266
8.173
7.988
7.973
7.971
7.786
7.769
7.700
7.697
7.686
7.683
7.669
7.666
7.580
7.566
7.551
7.528
7.474
7.458
7.443
4.639
4.626
4.612
N
Cl
O
BRUKER
ppm

figure-7

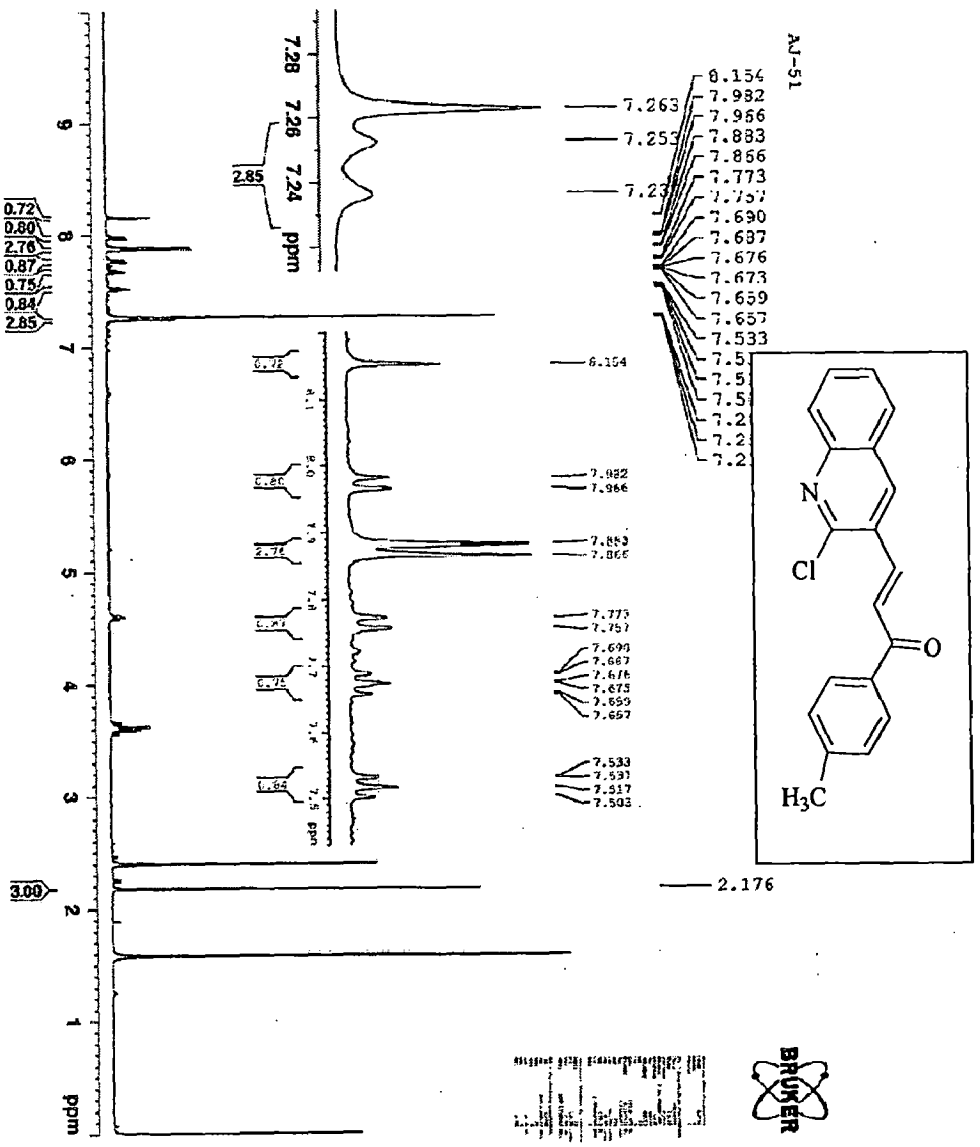

AJ-51
8.154
7.982
7.956
7.883
7.866
7.773
7.690
7.687
7.676
7.673
7.659
7.657
7.533
7.263
7.253
7.24
2.176
0.72
0.80
2.76
0.87
0.75
0.84
2.85
3.00
7.28 7.26 7.24 ppm
2.85
N
Cl
O
H3C
BRUKER
ppm

figure-8

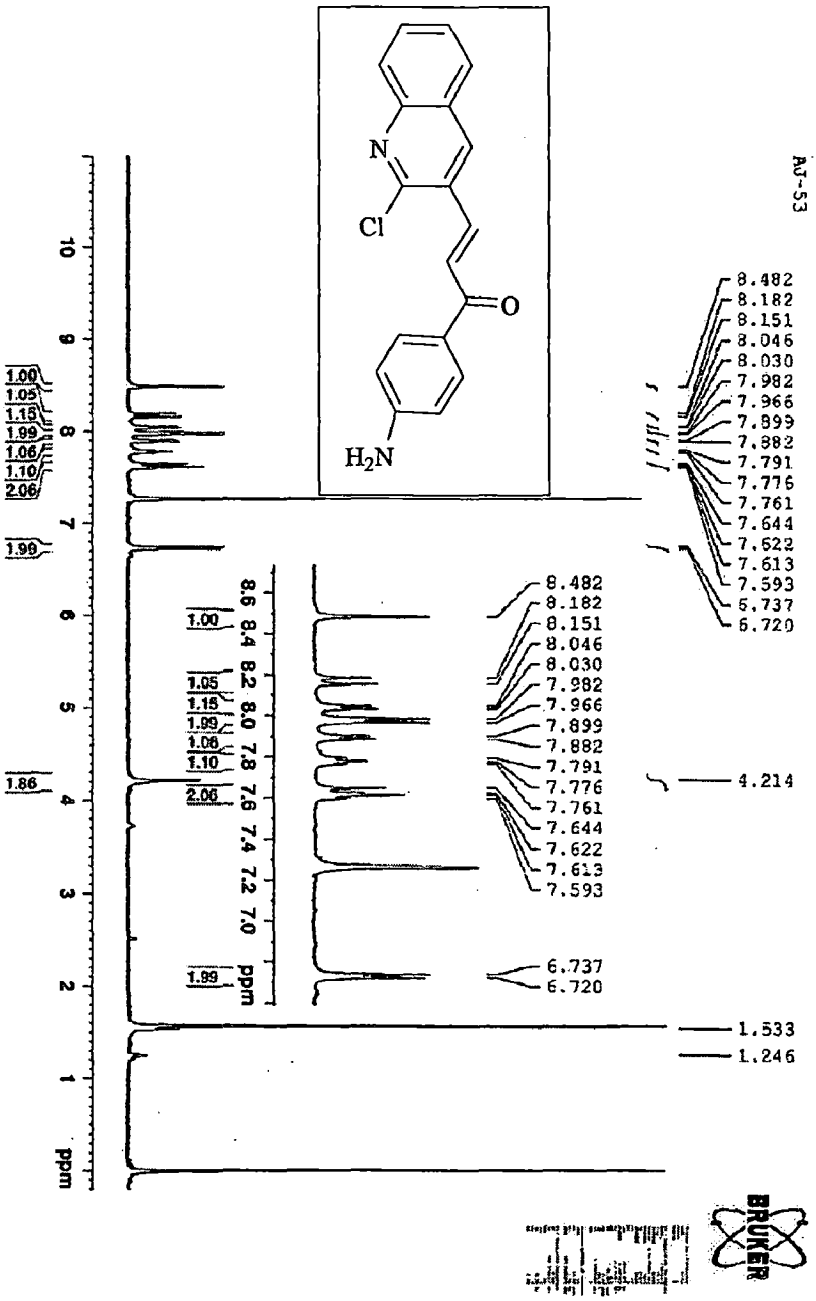
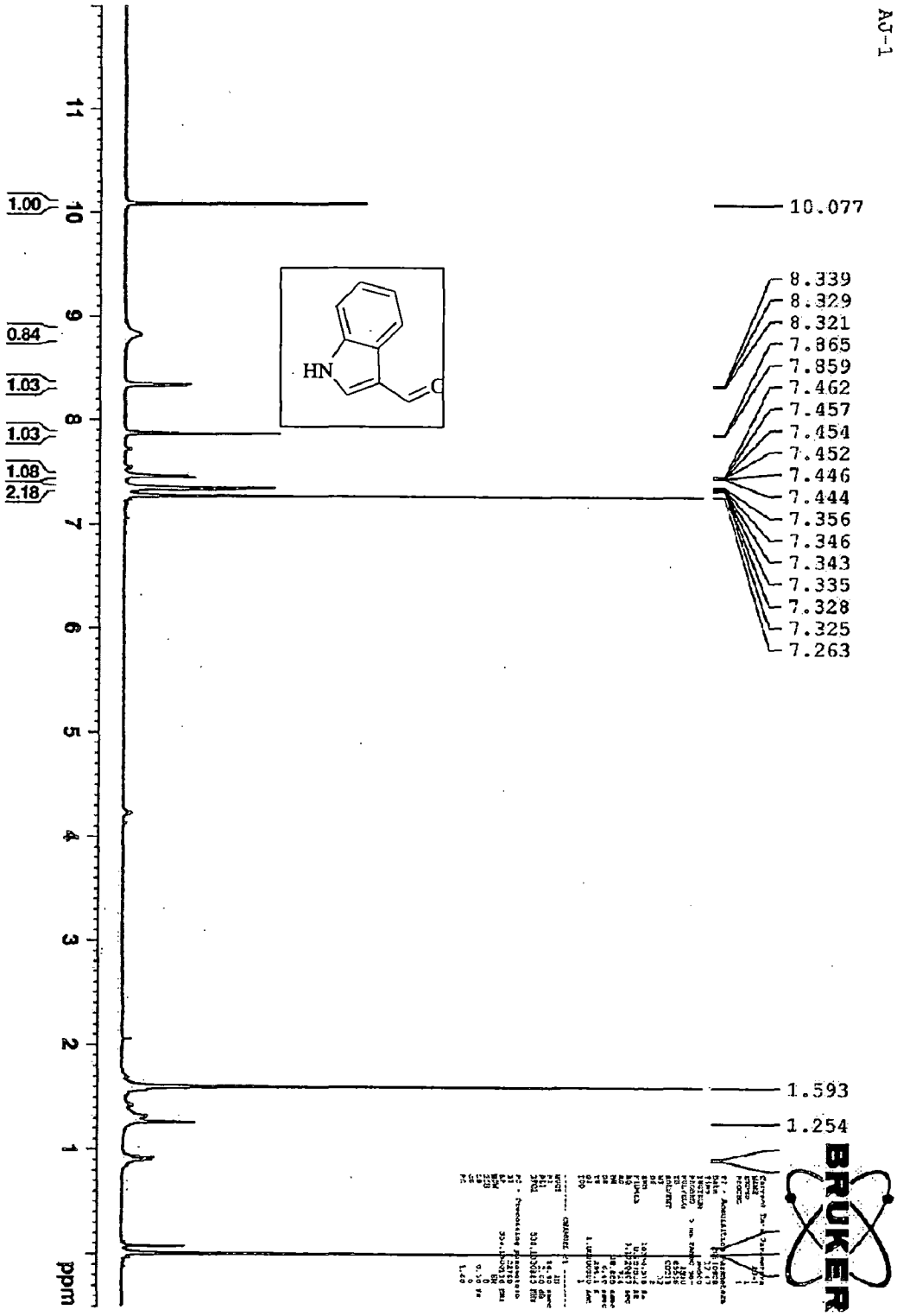

AJ-53
N
Cl
O
H_2N
8.482
8.182
8.151
8.046
8.030
7.982
7.966
7.899
7.882
7.791
7.776
7.761
7.644
7.622
7.613
7.593
6.737
6.720
4.214
1.533
1.246
1.00
1.05
1.15
1.99
1.06
1.10
2.06
1.86
1.99
ppm
BRUKER

figure-9


AJ-1
10.077
8.339
8.329
8.321
7.865
7.859
7.462
7.457
7.454
7.452
7.446
7.444
7.356
7.346
7.343
7.335
7.328
7.325
7.263
1.593
1.254
1.00
0.84
1.03
1.03
1.08
2.18
HN
ppm
BRUKER

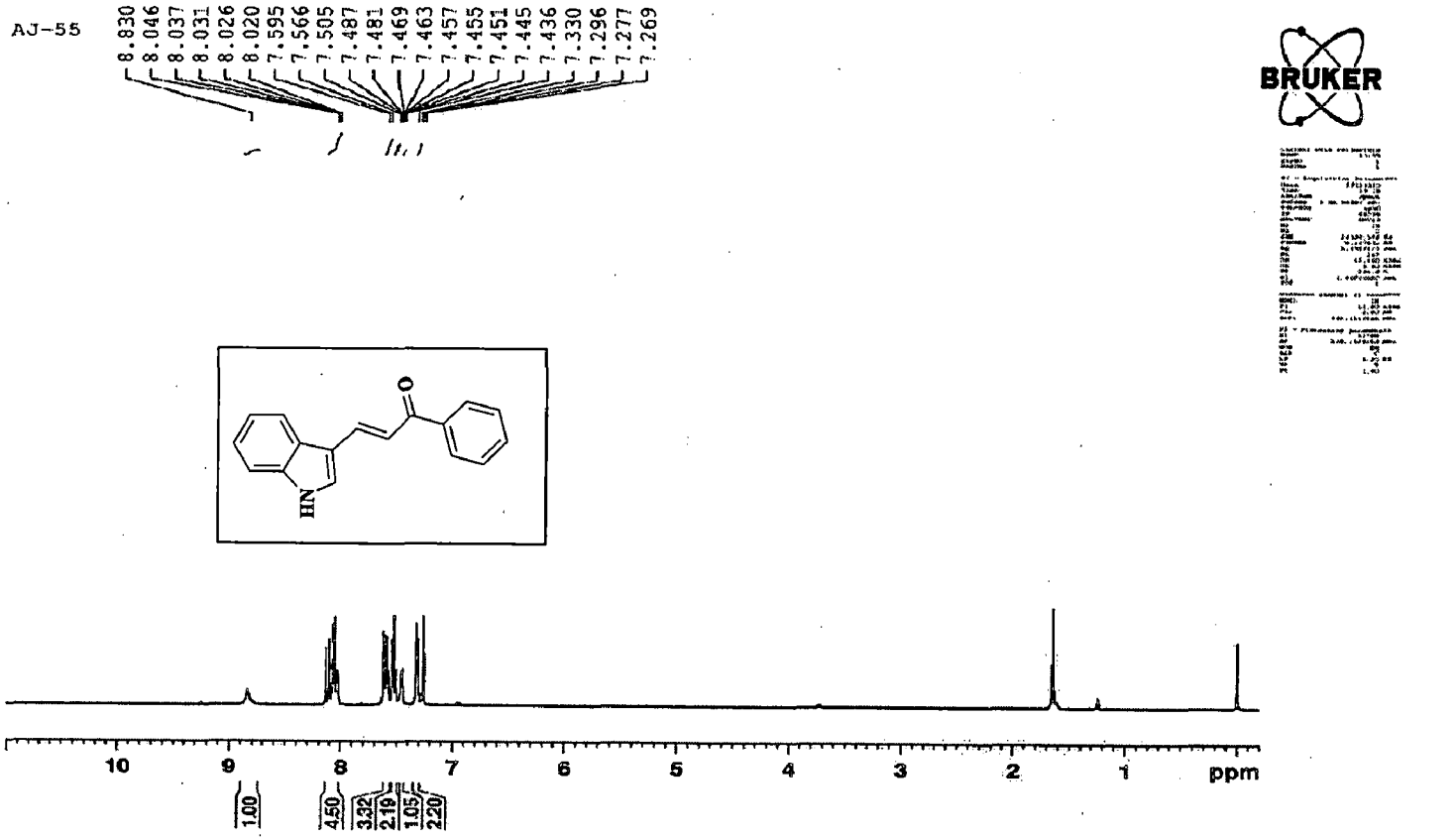

AJ-55
8.830
8.046
8.037
8.031
8.026
8.020
7.595
7.566
7.505
7.487
7.481
7.469
7.463
7.457
7.455
7.451
7.445
7.436
7.330
7.296
7.277
7.269
BRUKER
HN
O
10
9
8
7
6
5
4
3
2
1
ppm
1.00
4.50
3.32
2.19
1.05
2.20

figure-10

figure-11

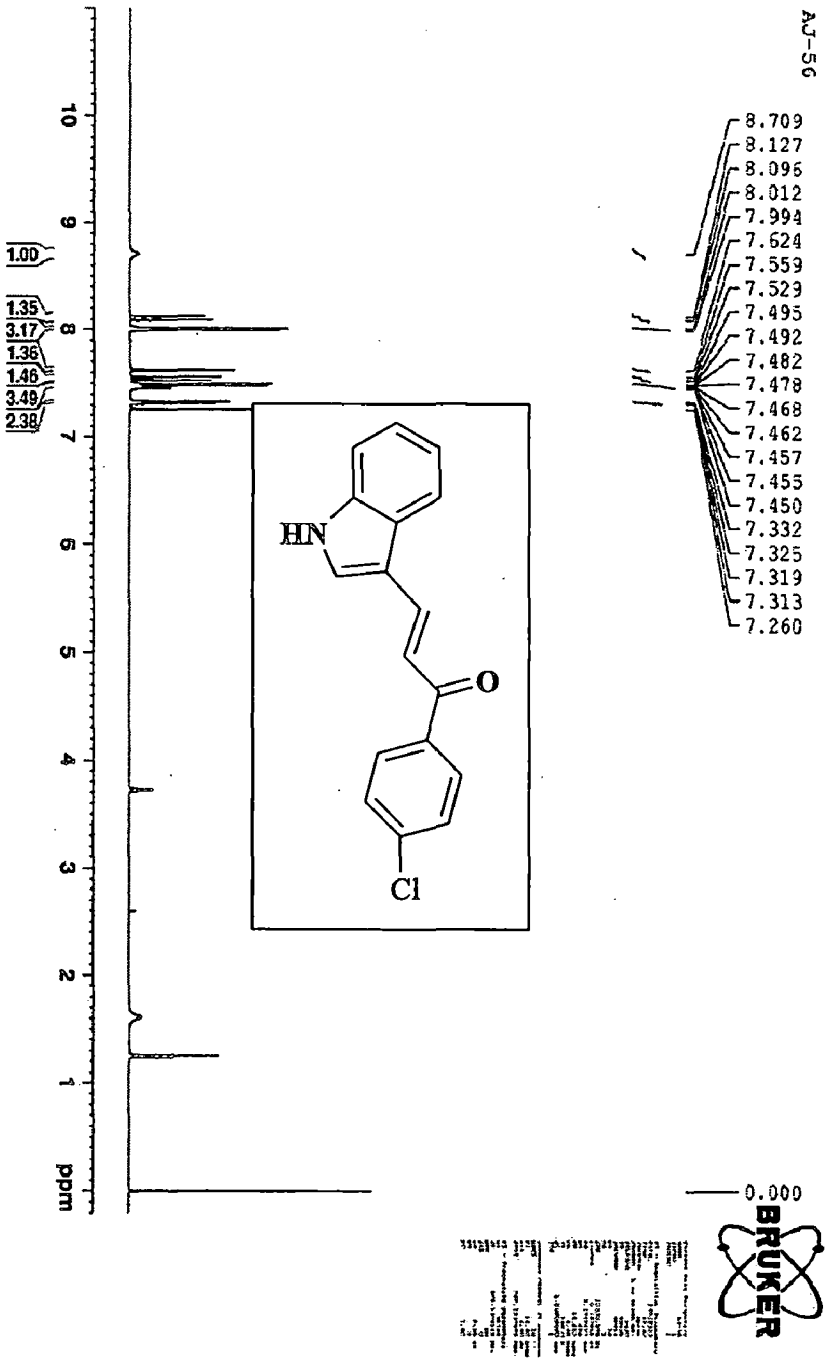

AJ-56
8.709
8.127
8.096
8.012
7.994
7.624
7.559
7.529
7.495
7.492
7.482
7.478
7.468
7.462
7.457
7.455
7.450
7.332
7.325
7.319
7.313
7.260
1.00
1.35
3.17
1.36
1.46
3.49
2.38
HN
O
Cl
ppm
0.000
BRUKER

figure-12

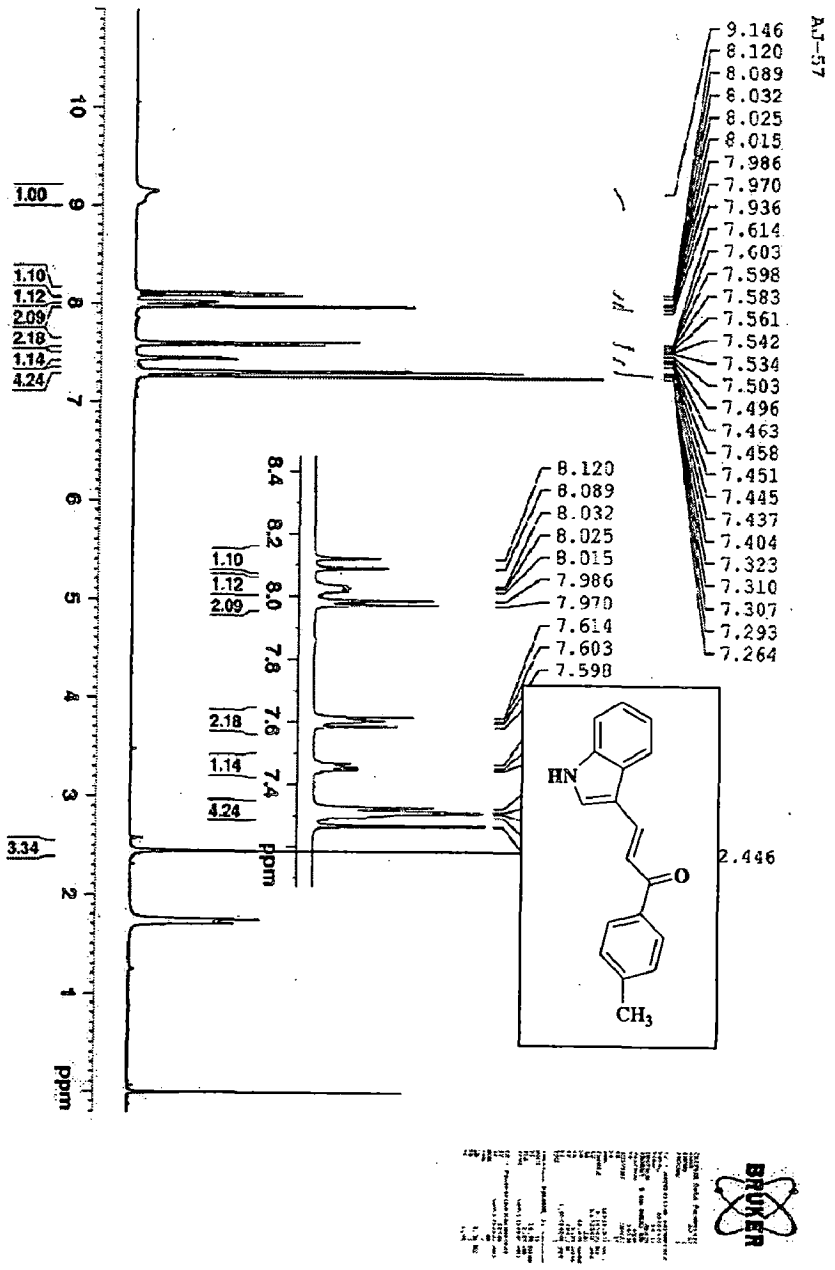

AJ-57
9.146
8.120
8.089
8.032
8.025
8.015
7.986
7.970
7.936
7.614
7.603
7.598
7.583
7.561
7.542
7.534
7.503
7.496
7.463
7.458
7.451
7.445
7.437
7.404
7.323
7.310
7.307
7.293
7.264
2.446
1.00
1.10
1.12
2.09
2.18
1.14
4.24
3.34
ppm
HN
O
CH3
BRUKER

figure-13

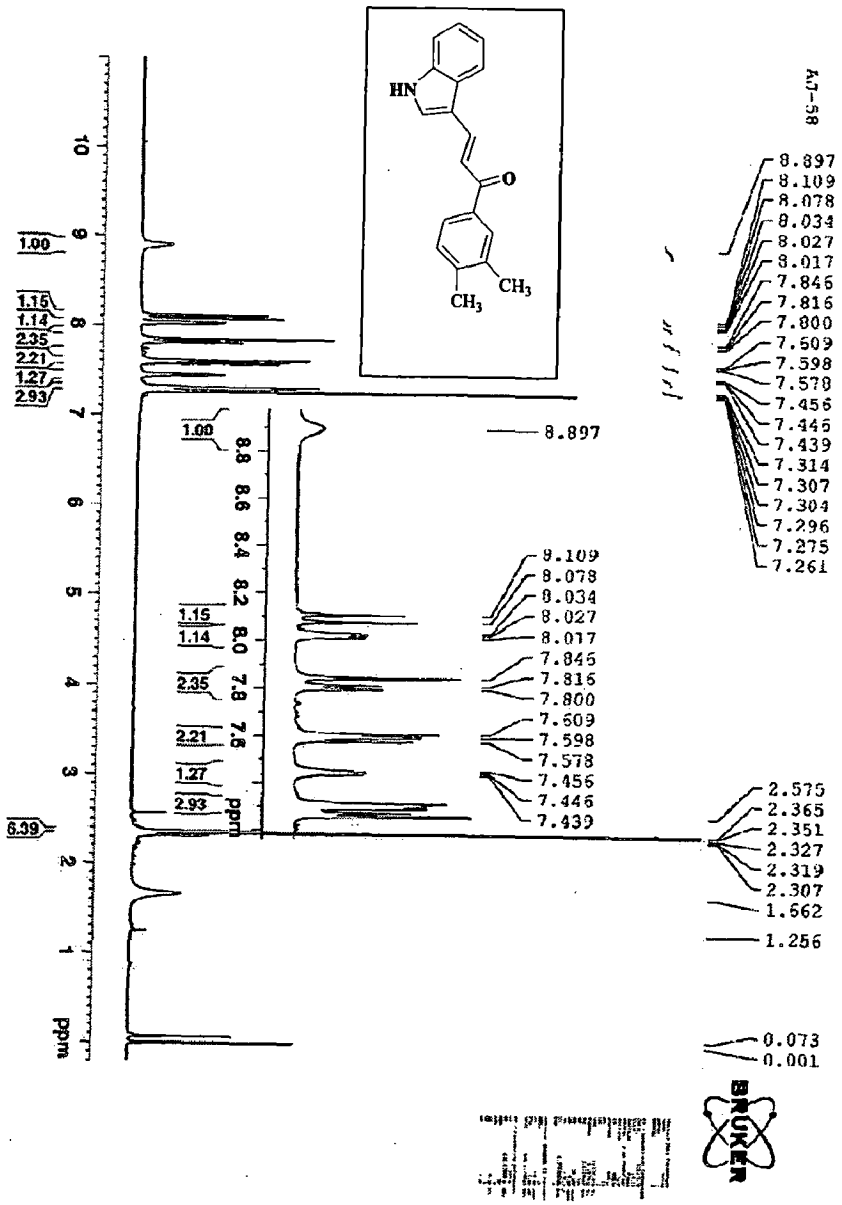

HN
O
CH3
CH3
A7-58
8.897
8.109
8.078
8.034
8.027
8.017
7.845
7.816
7.800
7.509
7.598
7.578
7.456
7.446
7.439
7.314
7.307
7.304
7.296
7.275
7.261
2.575
2.365
2.351
2.327
2.319
2.307
1.662
1.256
0.073
0.001
1.00
1.15
1.14
2.35
2.21
1.27
2.93
6.39
ppm
BRUKER

figure-14

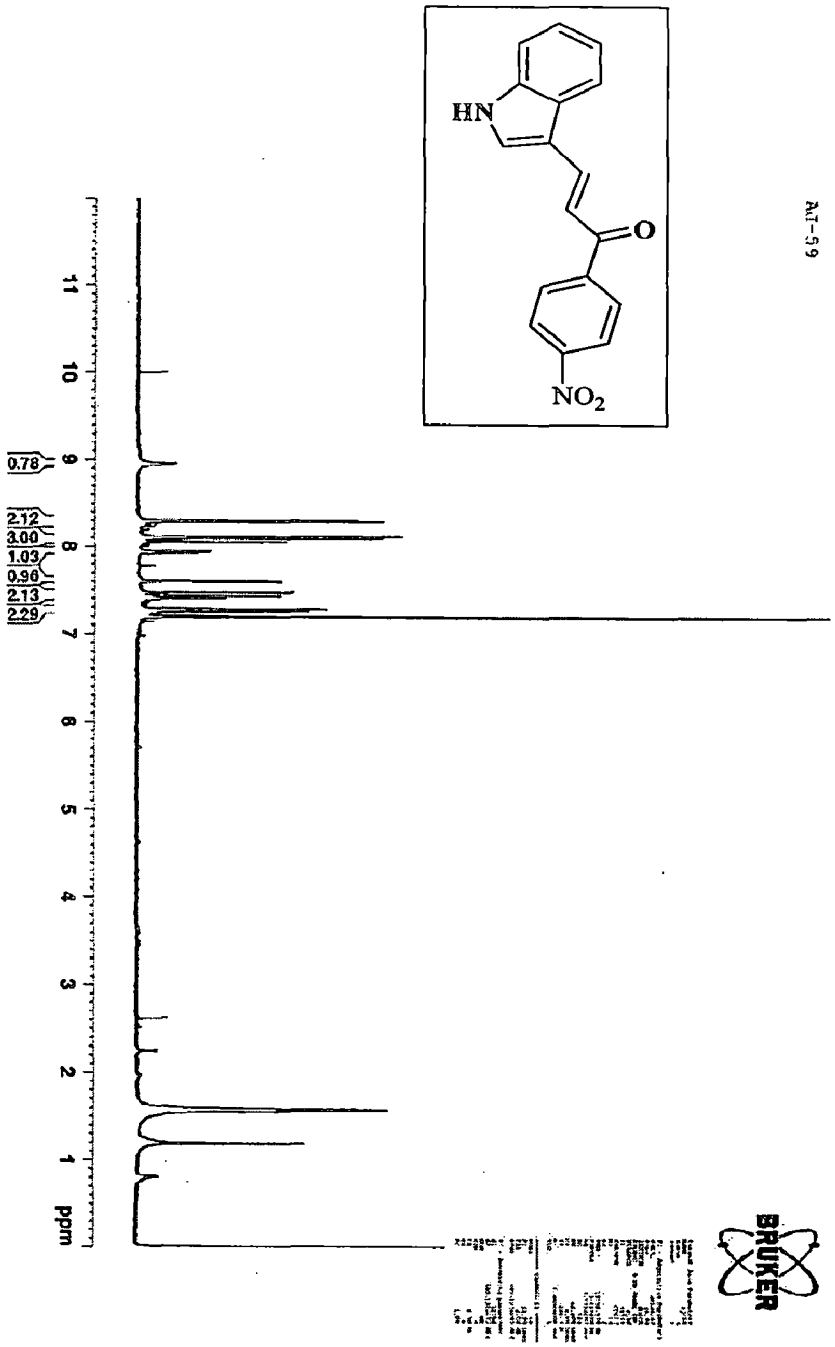

HN
O
NO2
AT-59
0.78
2.12
3.00
1.03
0.96
2.13
2.29
11
10
9
8
7
6
5
4
3
2
1
ppm
BRUKER

figure-15

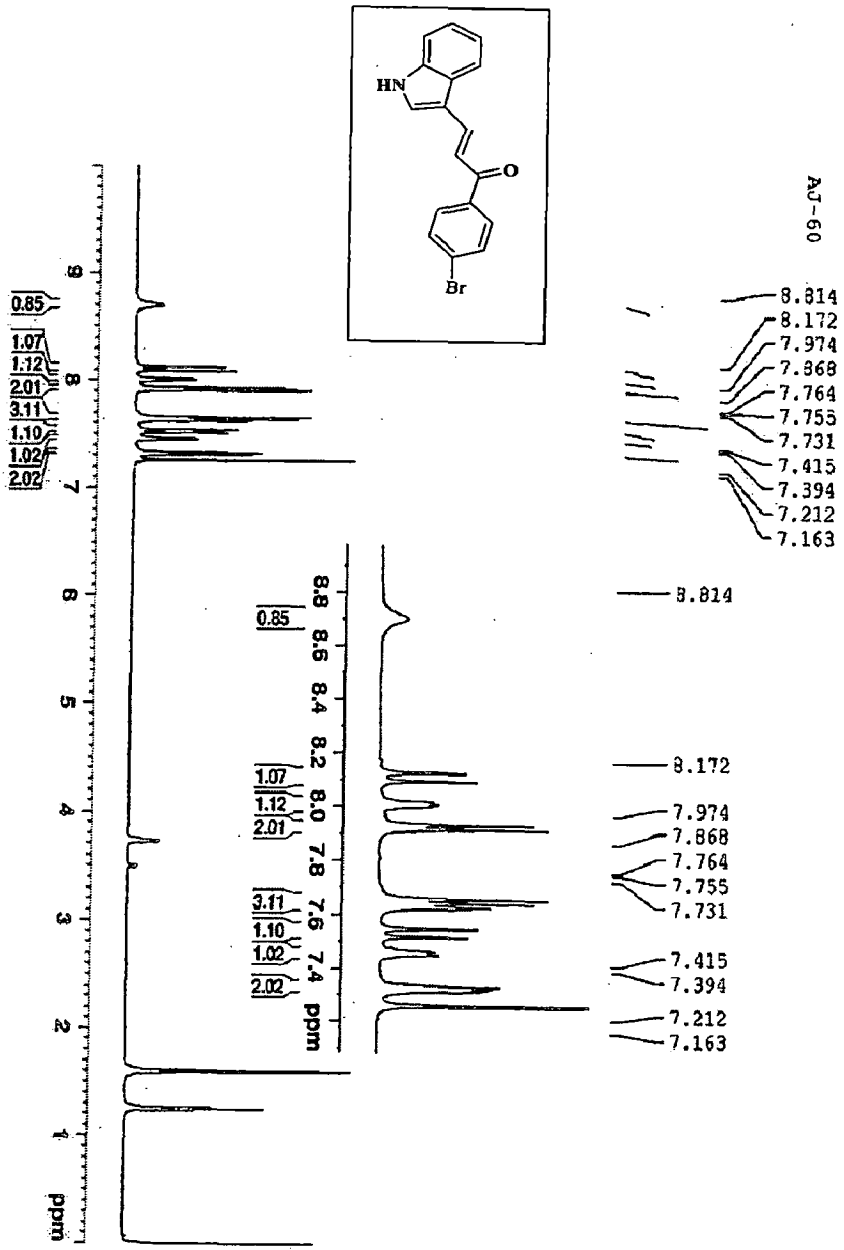

AJ-60
HN
O
Br
0.85
1.07
1.12
2.01
3.11
1.10
1.02
2.02
8.814
8.172
7.974
7.868
7.764
7.755
7.731
7.415
7.394
7.212
7.163
ppm
BRUKER

figure-16

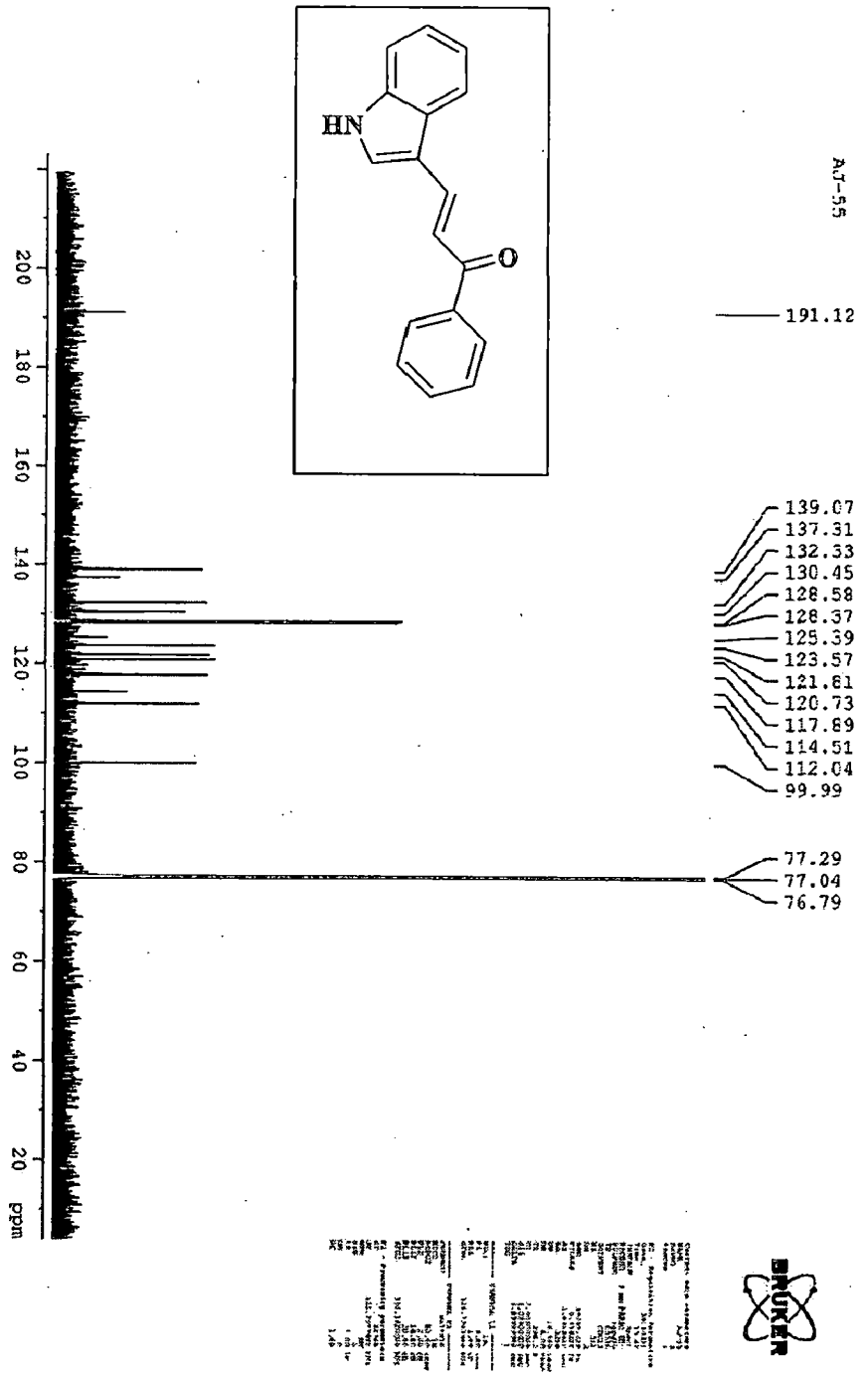

HN
O
AJ-55
191.12
139.07
137.31
132.53
130.45
128.58
128.37
125.39
123.57
121.81
120.73
117.89
114.51
112.04
99.99
77.29
77.04
76.79
200
180
160
140
120
100
80
60
40
20
ppm
BRUKER

figure-17

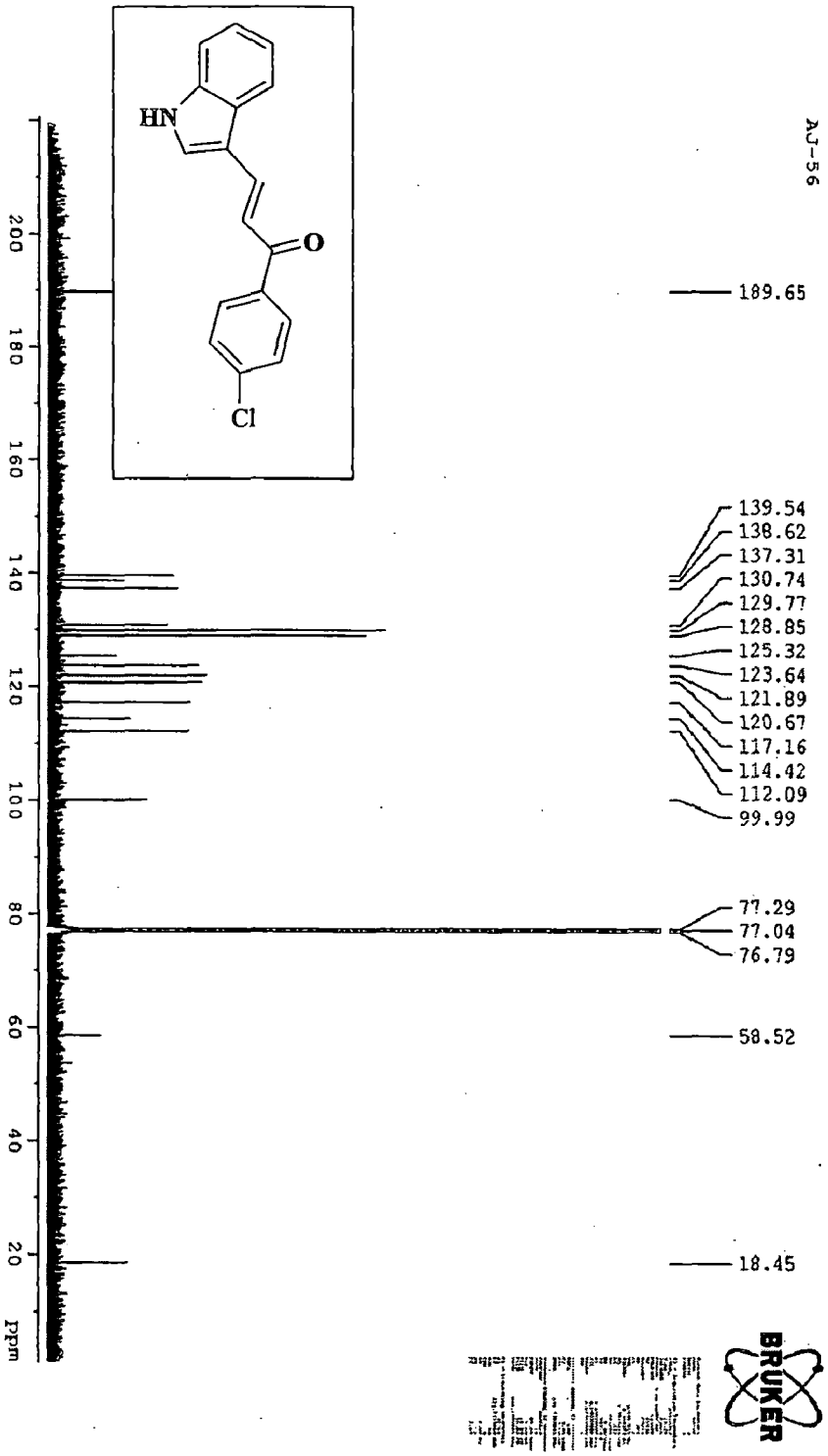

HN
O
Cl
AJ-56
189.65
139.54
138.62
137.31
130.74
129.77
128.85
125.32
123.64
121.89
120.67
117.16
114.42
112.09
99.99
77.29
77.04
76.79
58.52
18.45
200
180
160
140
120
100
80
60
40
20
Ppm
BRUKER

Figure-18

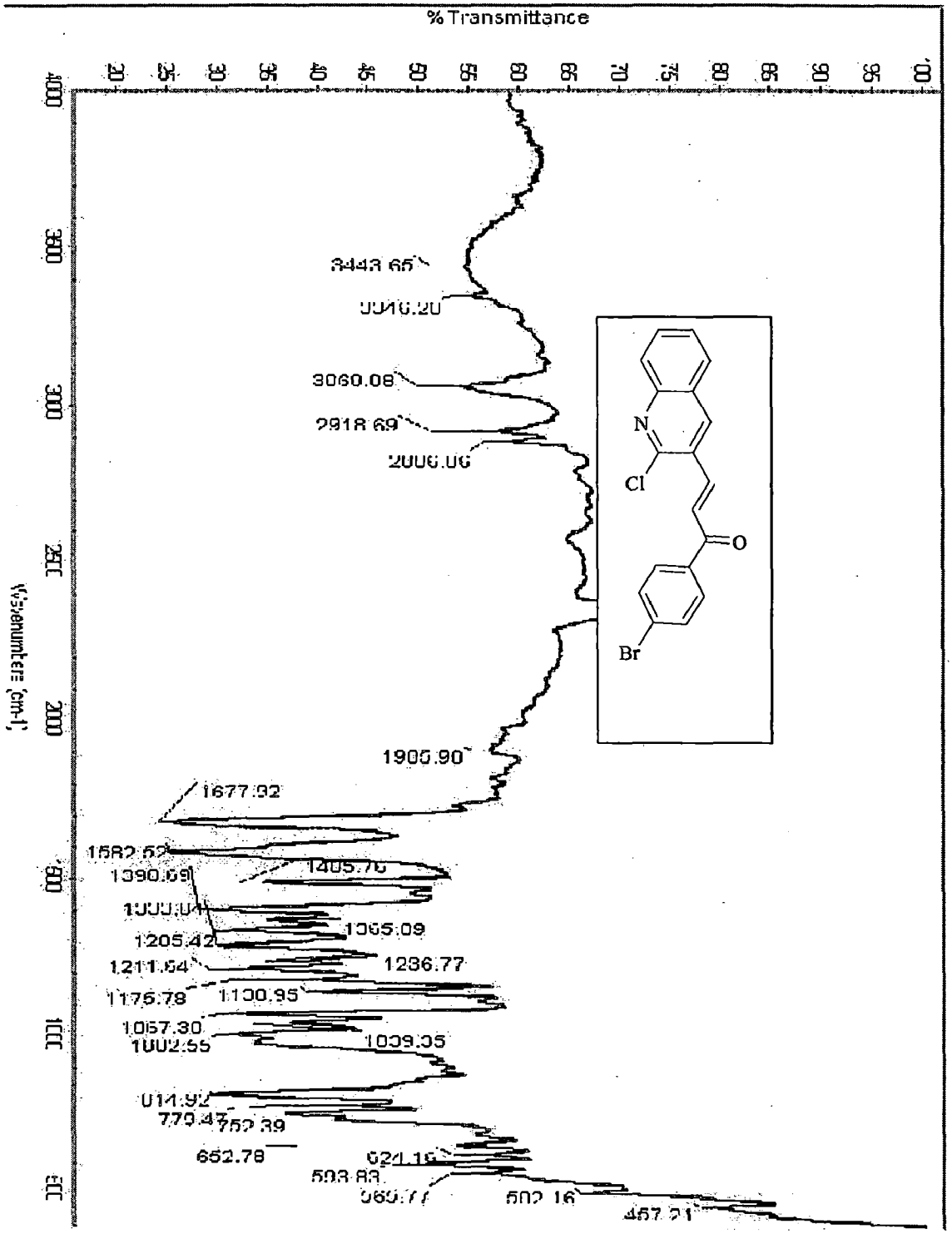

%Transmittance
Wavenumbers (cm-1)
3060.08
2918.69
1677.92
1582.52
1390.09
1205.42
1211.64
1236.77
1175.78
1100.95
1057.30
1002.55
1039.35
779.47
752.39
652.78
N
Cl
O
Br

figure-19

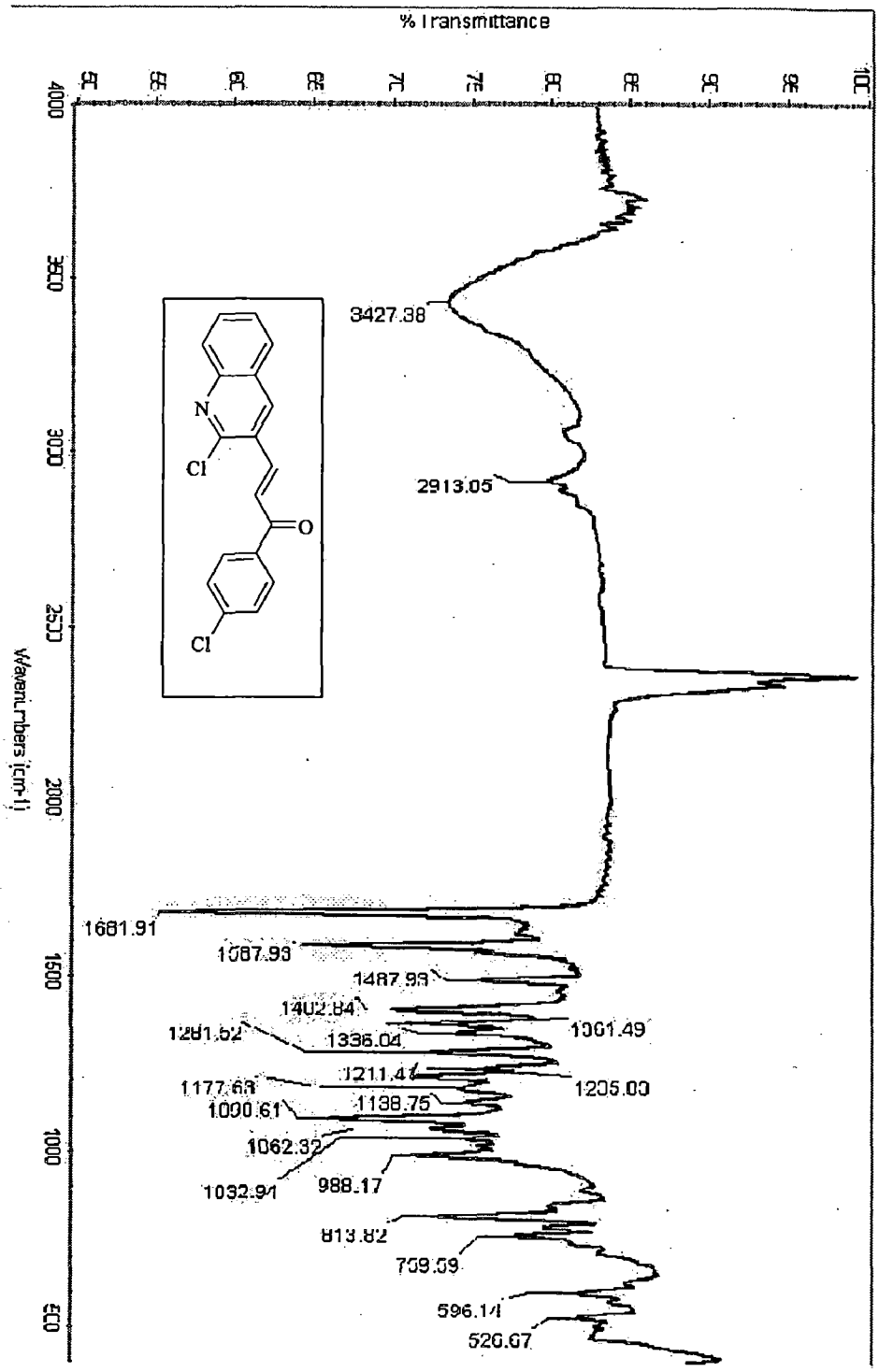

% Transmittance
Wavenumbers (cm-1)
4000
3500
3000
2500
2000
1500
1000
500
3427.38
2913.05
1681.91
1587.93
1487.93
1402.84
1361.49
1281.62
1336.04
1211.41
1205.00
1177.68
1138.75
1090.61
1062.32
1032.91
988.17
813.82
759.09
596.14
526.67
N
Cl
O
Cl

figure-20

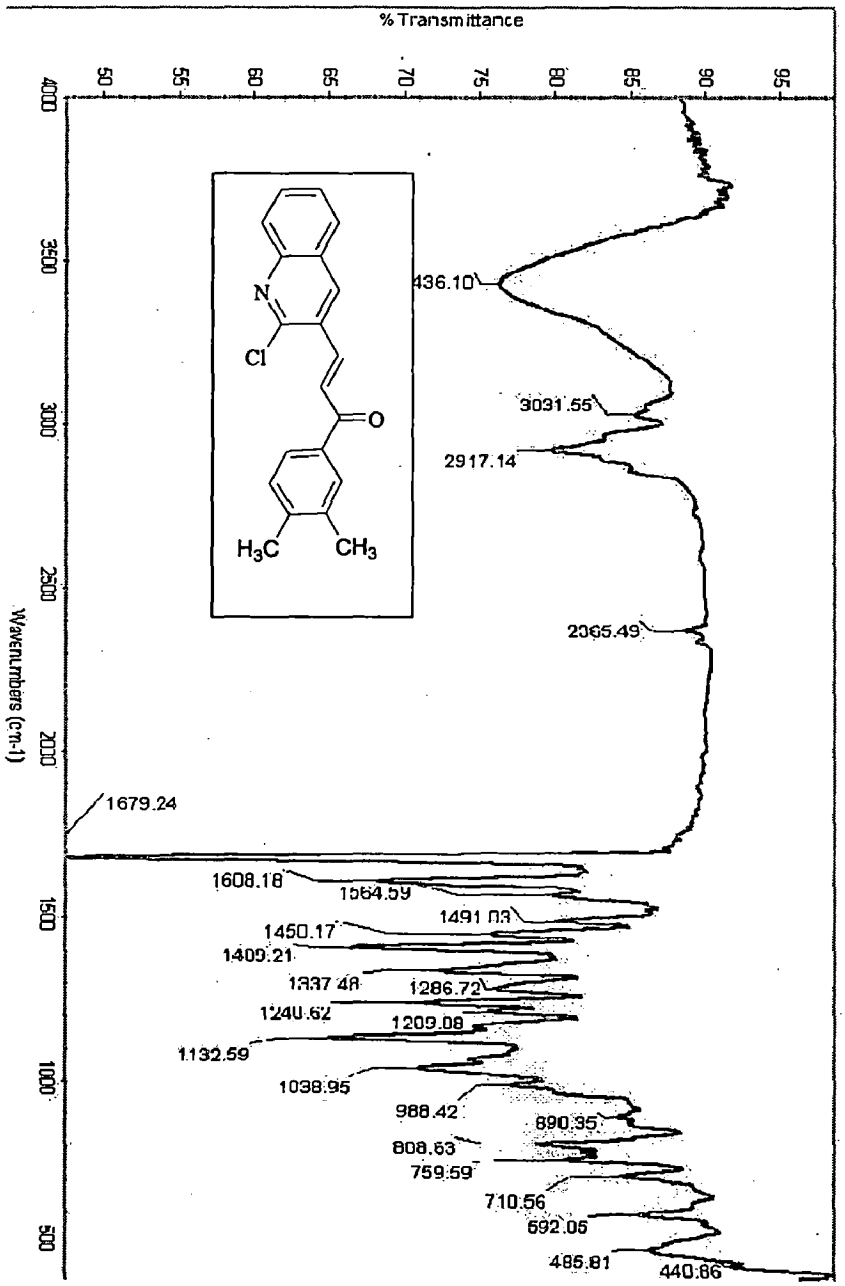

% Transmittance
50
55
60
65
70
75
80
85
90
95
4000
3500
3000
2500
2000
1500
1000
500
Wavenumbers (cm-1)
N
Cl
O
H3C
CH3
436.10
3031.55
2917.14
2065.49
1679.24
1608.18
1564.59
1491.03
1450.17
1409.21
1337.48
1286.72
1240.62
1209.08
1132.59
1038.95
988.42
890.35
808.63
759.59
710.56
692.05
485.81
440.86

figure-21

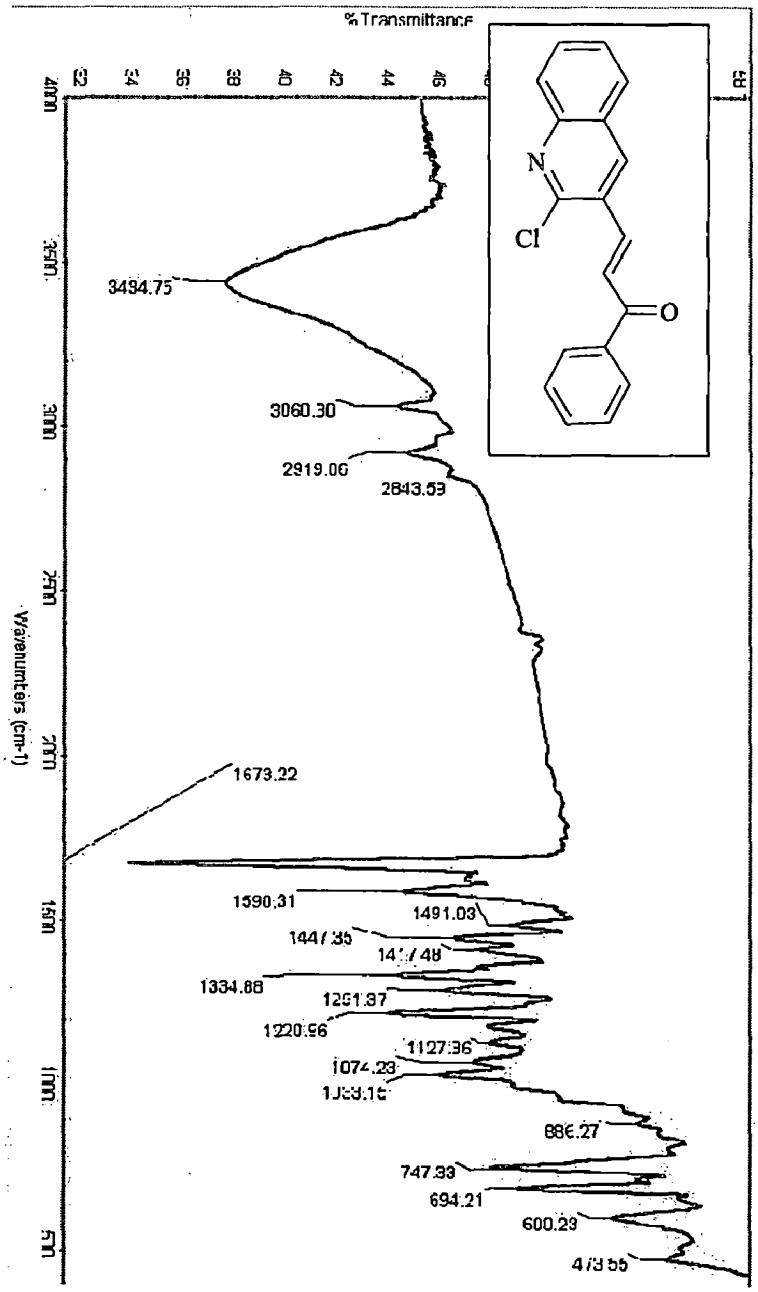

%Transmittance
Wavenumbers (cm-1)
3434.75
3060.30
2919.06
2843.59
1673.22
1590.31
1491.03
1334.88
1291.87
1220.96
1127.36
747.33
694.21
600.23
N
Cl
O

figure-22

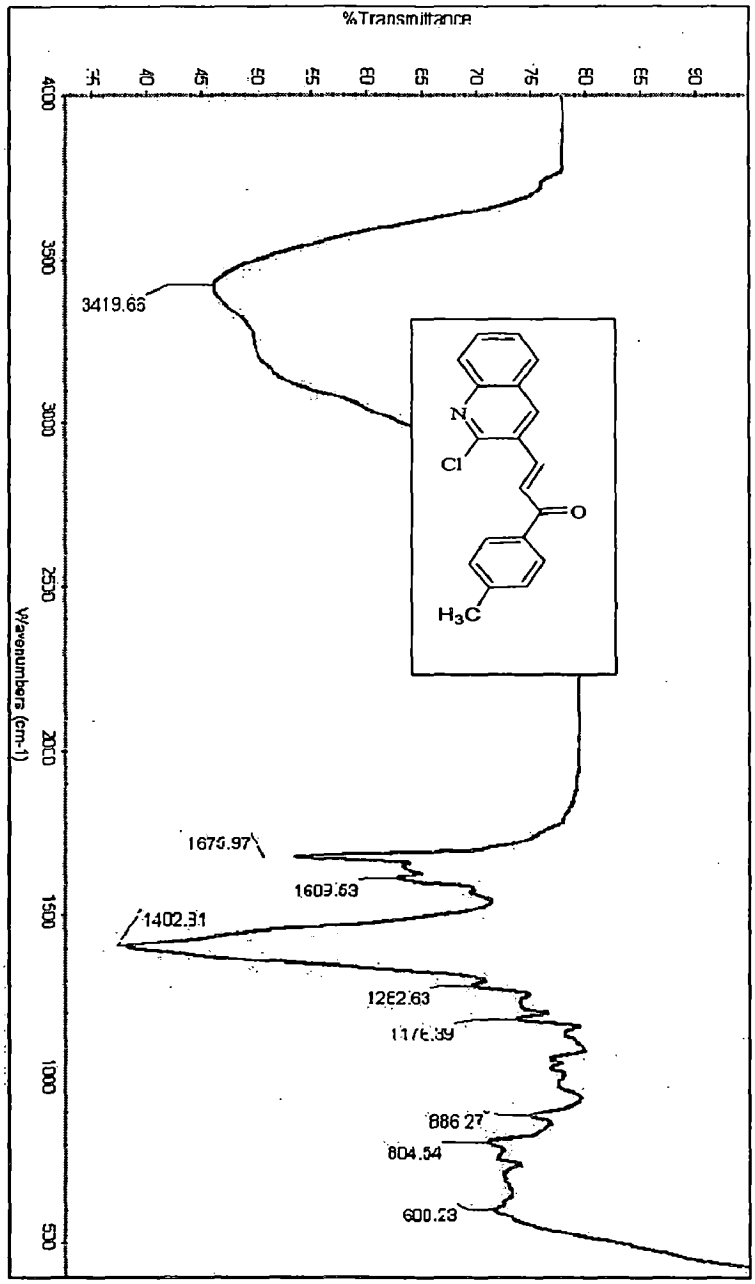

%Transmittance
Wavenumbers (cm-1)
3419.65
1675.97
1609.63
1402.31
1262.63
886.27
804.54
600.23
N
Cl
O
H3C

figure-23

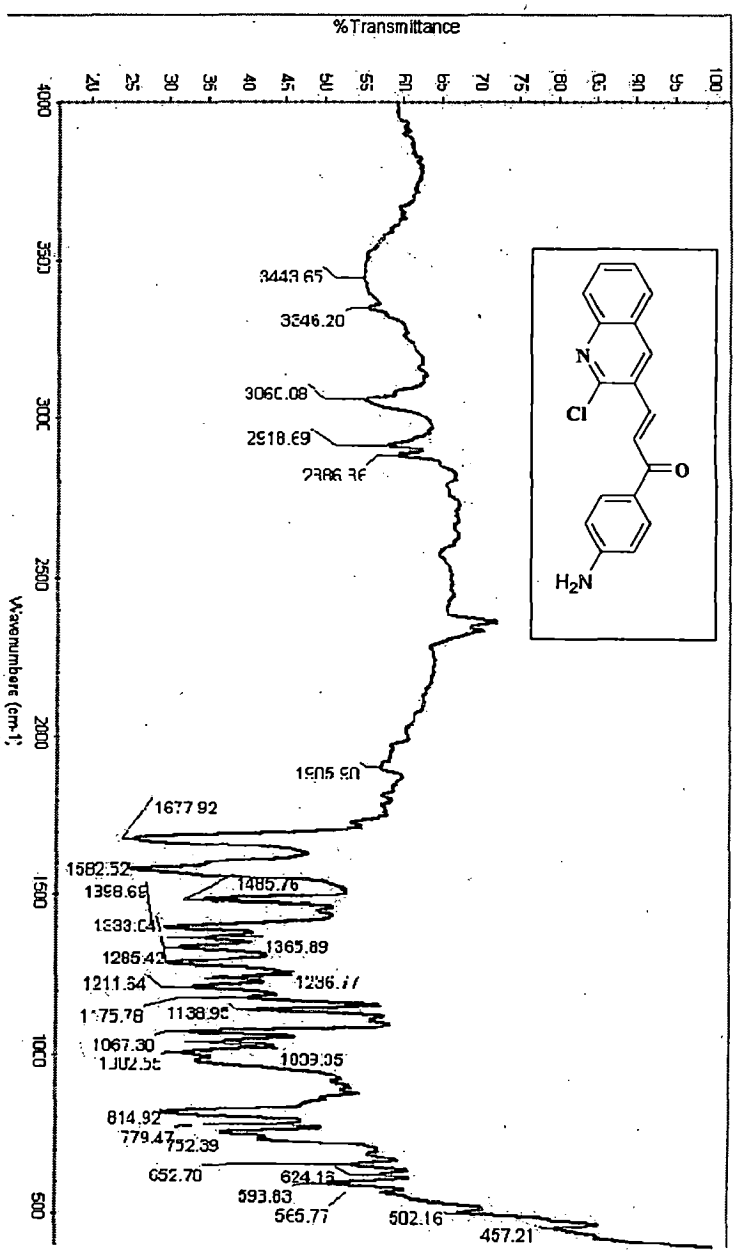

%Transmittance
Wavenumbers (cm-1)
3448.65
3346.20
3060.08
2918.69
1677.92
1582.52
1485.76
1365.89
1211.54
1067.30
1009.35
814.92
779.47
752.39
652.70
624.15
593.63
565.77
502.16
457.21
N
Cl
O
H2N

figure-24

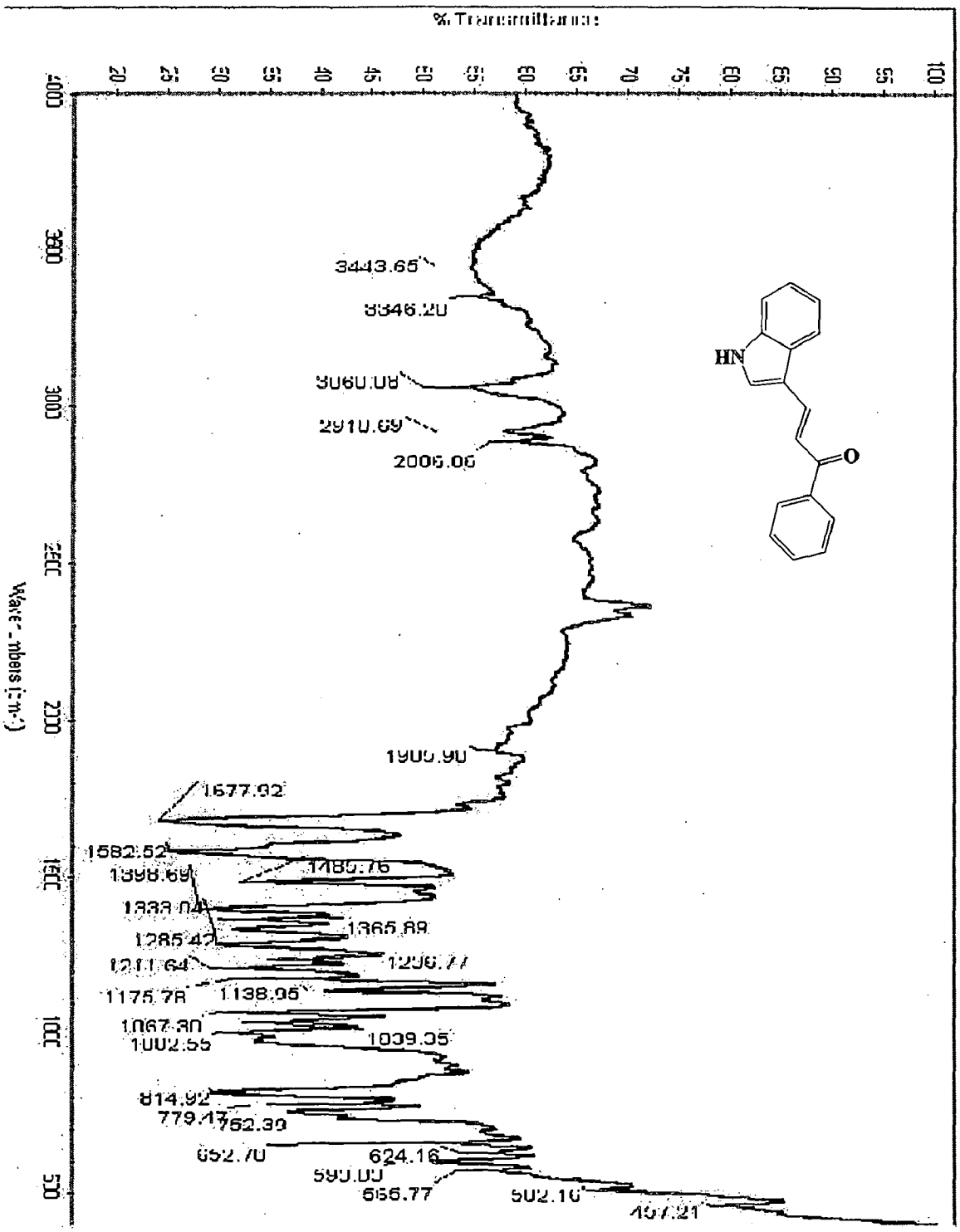

% Transmittance
Wave - nbers (cm-1)
4000
3500
3000
2500
2000
1500
1000
500
3443.65
3346.20
3060.08
2910.69
2005.06
1900.90
1677.92
1582.52
1398.69
1485.76
1365.89
1296.77
1138.95
1039.05
814.92
779.47
752.39
652.70
624.16
590.00
555.77
502.10
457.21
HN
O

figure-25

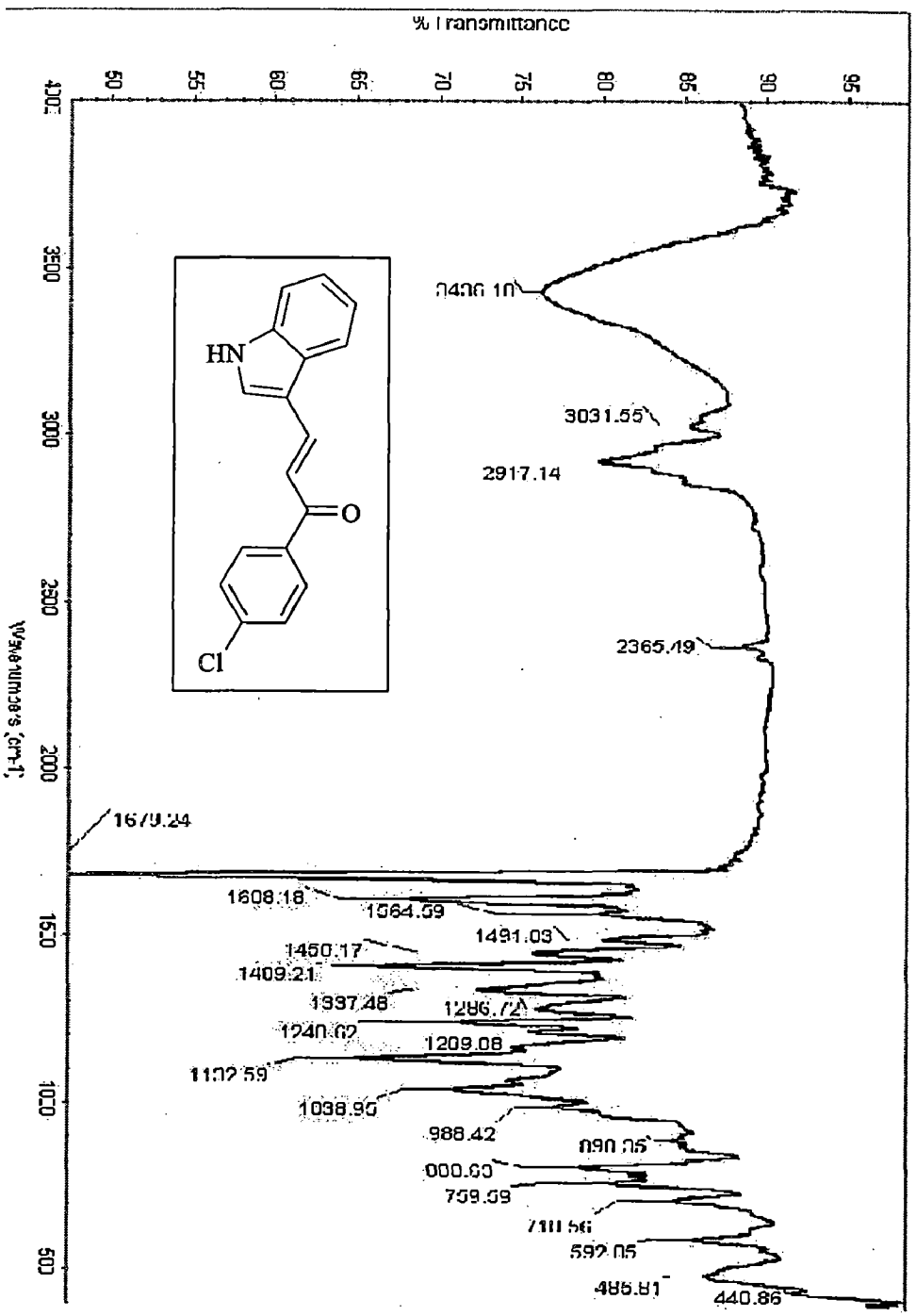

% Transmittance
50
55
60
65
70
75
80
85
90
95
4000
3500
3000
2500
2000
1500
1000
500
Wavenumbers (cm-1)
HN
O
Cl
3400.10
3031.55
2917.14
2365.49
1679.24
1608.18
1564.59
1491.03
1450.17
1409.21
1337.48
1286.72
1240.62
1209.08
1102.59
1038.90
988.42
890.05
800.00
759.59
711.56
592.05
485.81
440.86

figure-26

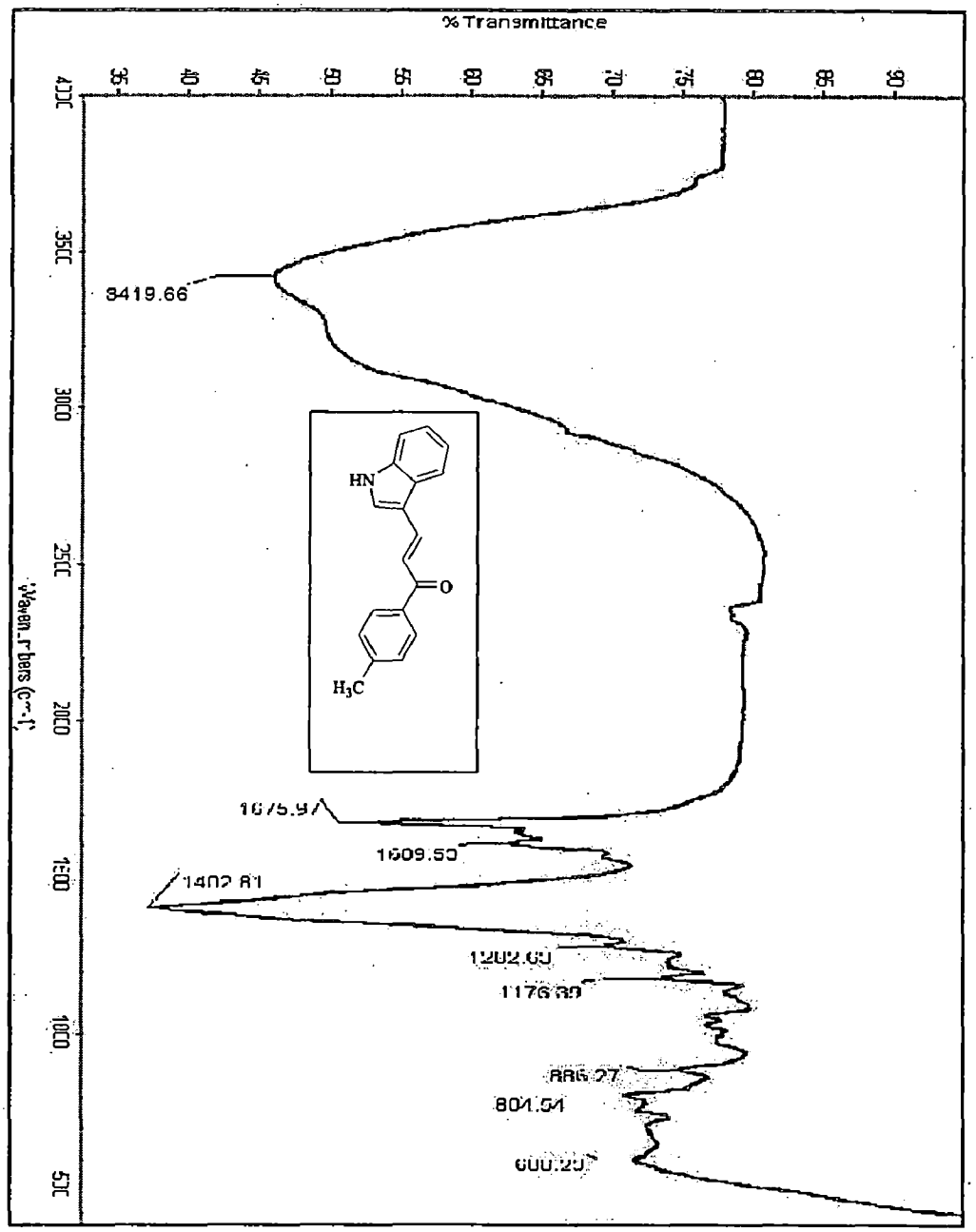

% Transmittance
Wavenumbers (cm-1)
3419.66
1675.97
1609.50
1402.81
1202.60
1176.89
801.54
HN
O
H3C

figure-27

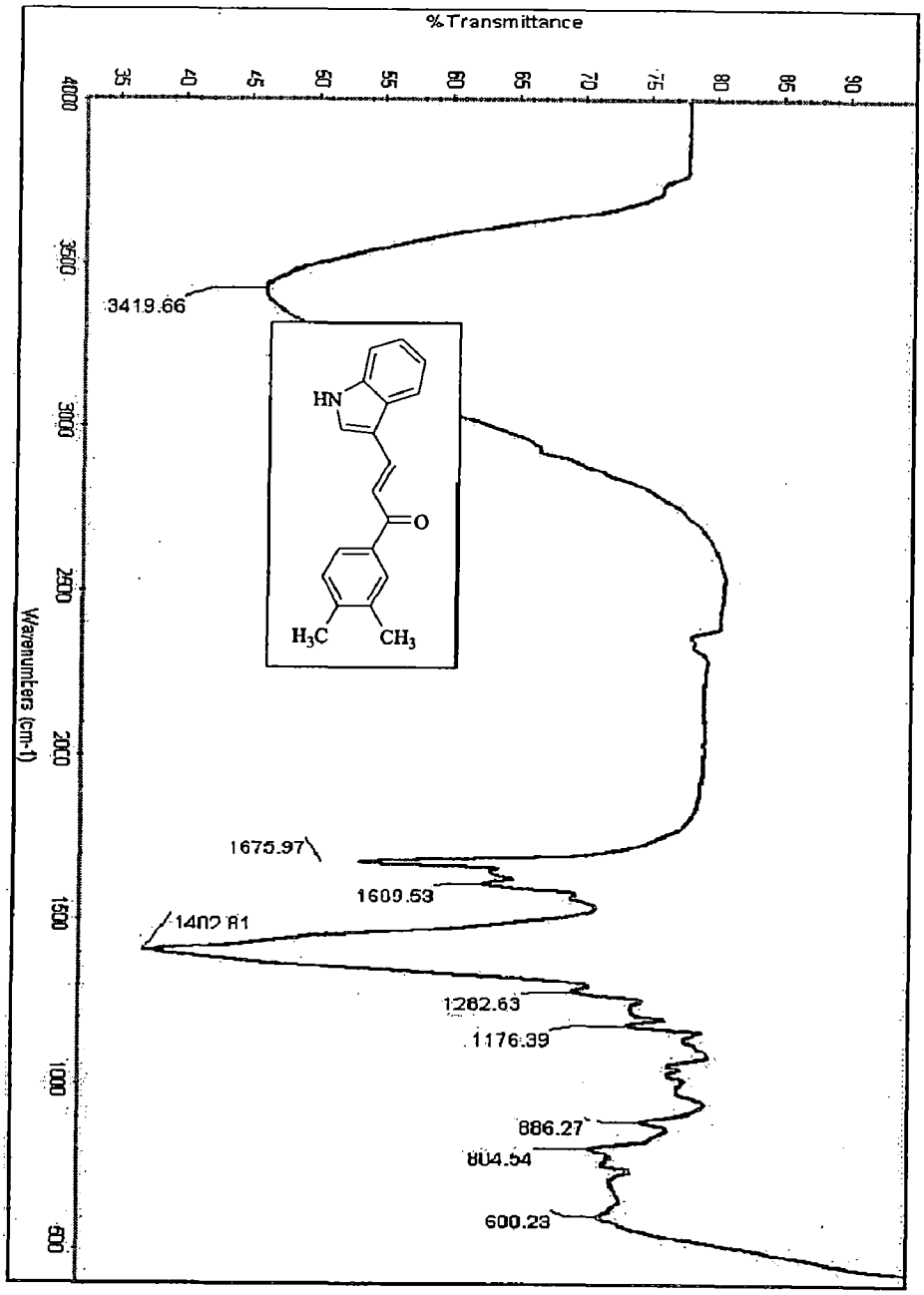

%Transmittance
Wavenumbers (cm-1)
3419.66
1675.97
1609.53
1262.63
1176.39
886.27
804.54
600.23
HN
O
H3C
CH3

figure-28

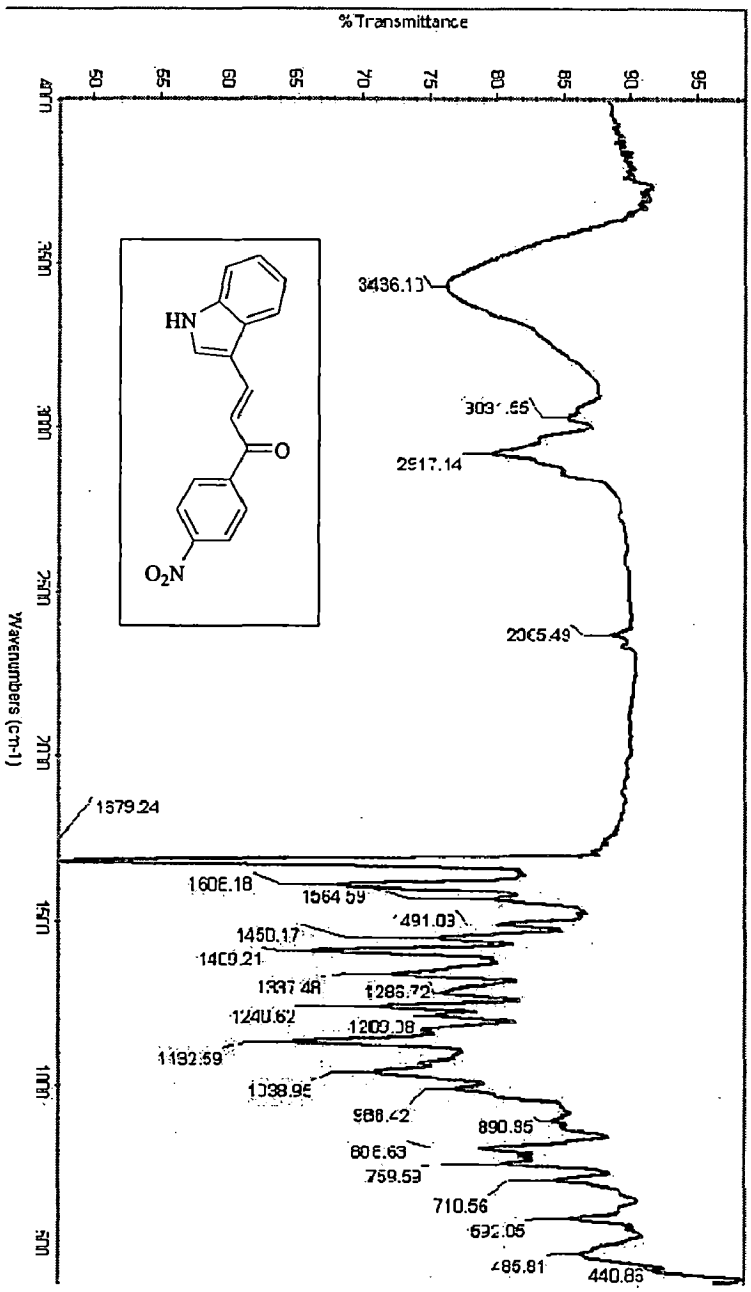
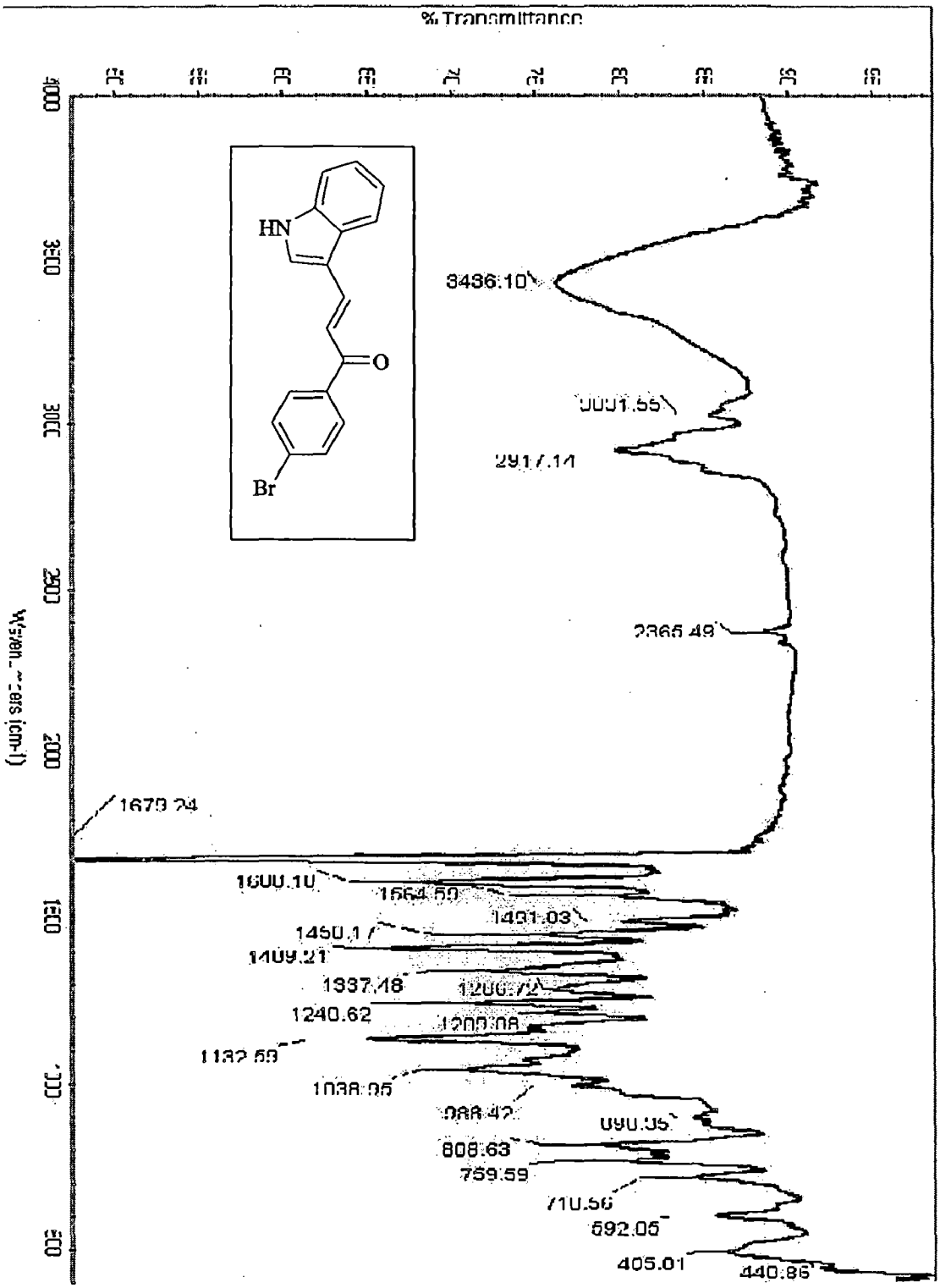

%Transmittance
Wavenumbers (cm-1)
3436.13
2917.14
2065.49
1579.24
1560.18
1564.59
1491.03
1450.17
1409.21
1337.48
1286.72
1240.62
1209.08
1192.59
1038.95
988.42
890.85
806.63
759.59
710.56
685.81
440.83
HN
O
O2N

figure-29


% Transmittance
Wave numbers (cm-1)
HN
O
Br
3436.10
2917.14
2365.49
1679.24
1600.10
1564.59
1491.03
1450.17
1409.21
1337.48
1240.62
1182.59
1038.95
990.35
808.63
759.59
592.05
405.01
440.86

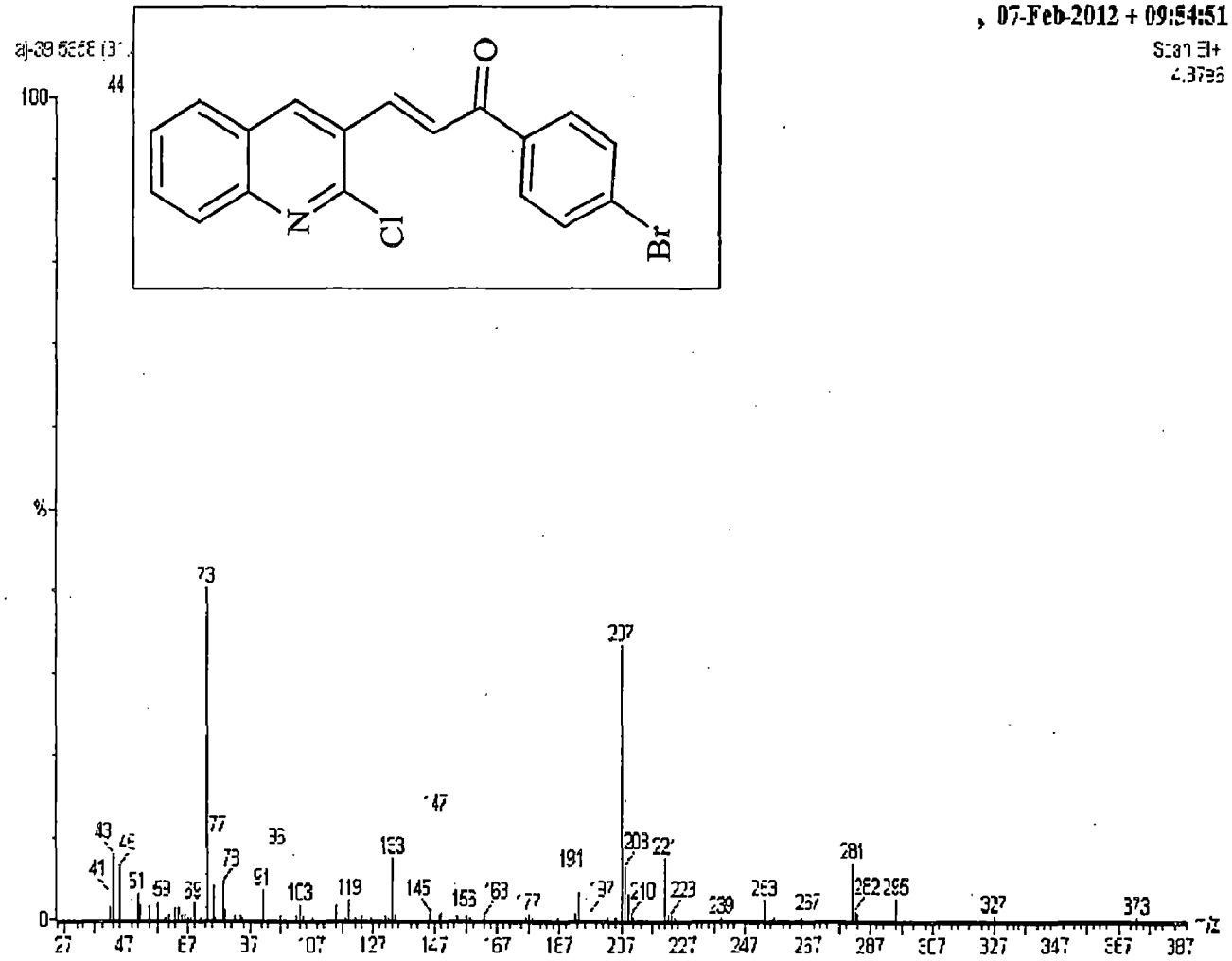
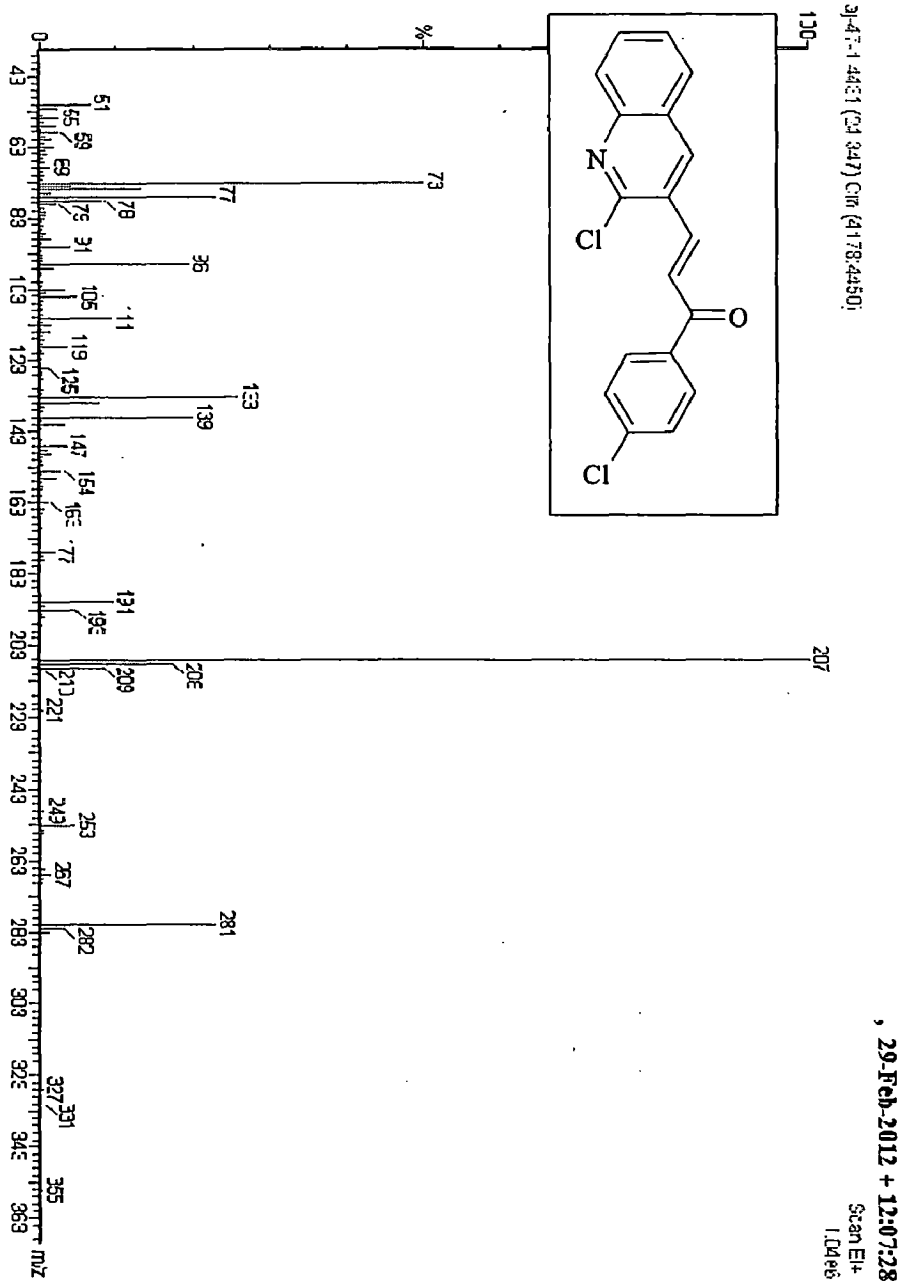


figure-30

figure-31


29-Feb-2012 + 12:07:28
Scan EI+
1.04e6
N
Cl
O
Cl
%
0
43
51
55
59
63
69
73
77
78
83
91
93
103
105
111
119
123
125
133
139
147
149
154
163
165
177
183
195
131
203
207
209
210
221
223
243
249
253
263
267
281
282
303
323
327
331
343
355
363
m/z

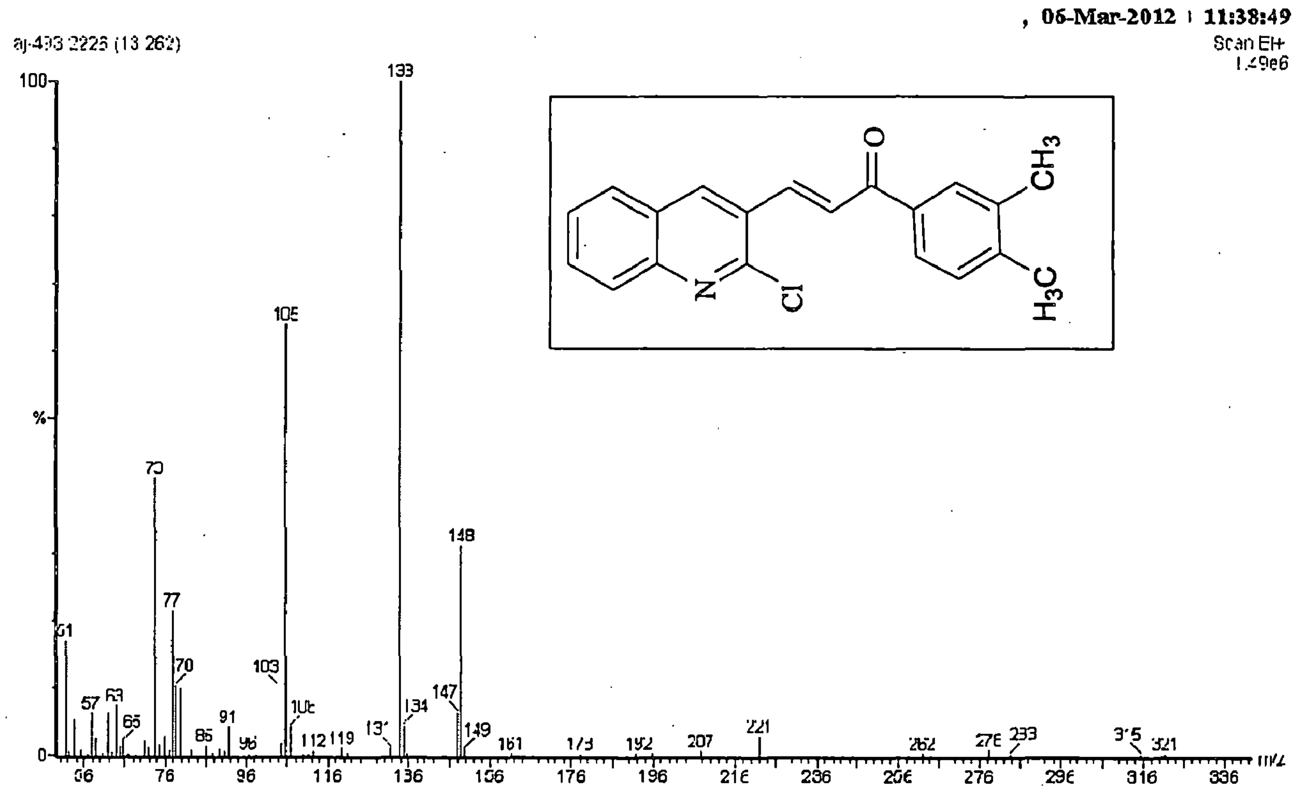
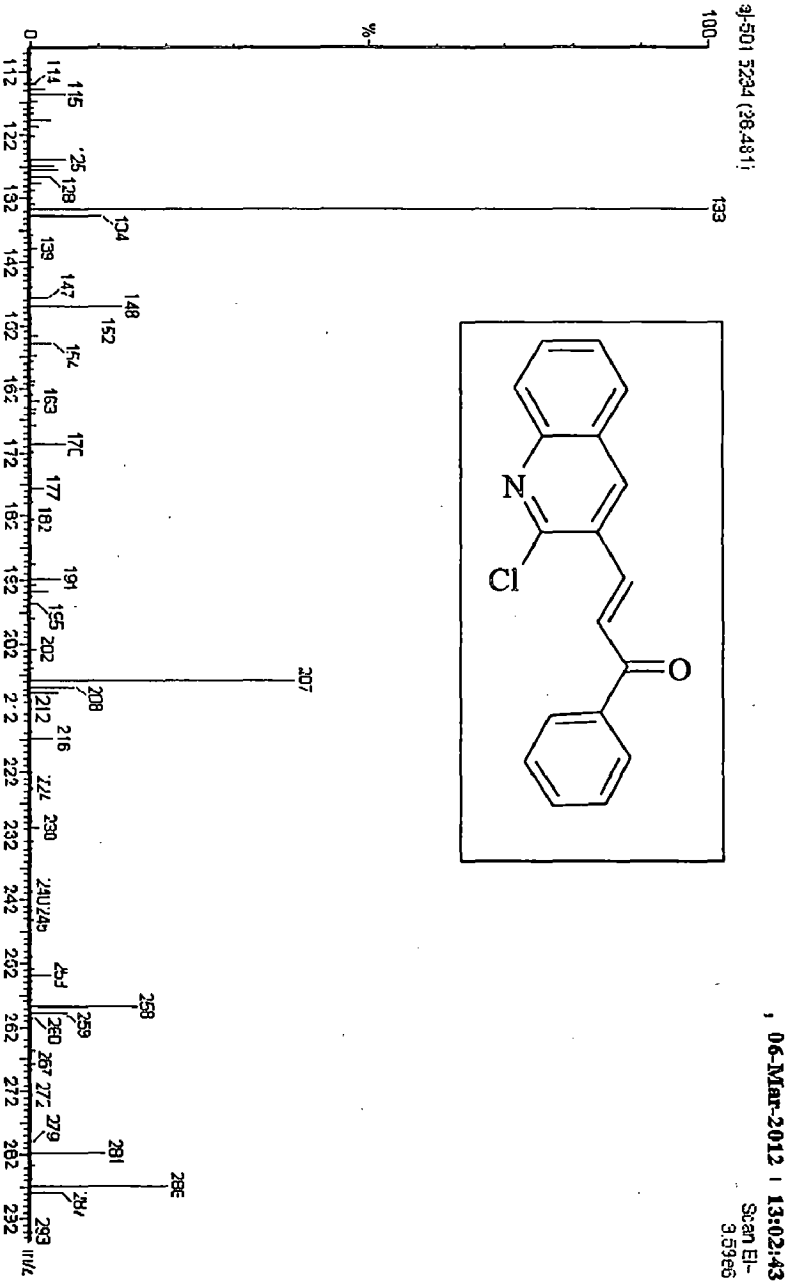

, 06-Mar-2012 11:38:49
Scan EI+
1.49e6
100
%
0
m/z
133
105
73
148
77
61
70
103
147
134
57
63
65
91
221
N
Cl
O
CH_3
H_3C

figure-32

figure-33


9j-501 5234 (36.481)
100
%
0
133
207
258
281
286
N
Cl
O
; 06-Mar-2012 ; 13:02:43
Scan EI-
3.59e6
m/z

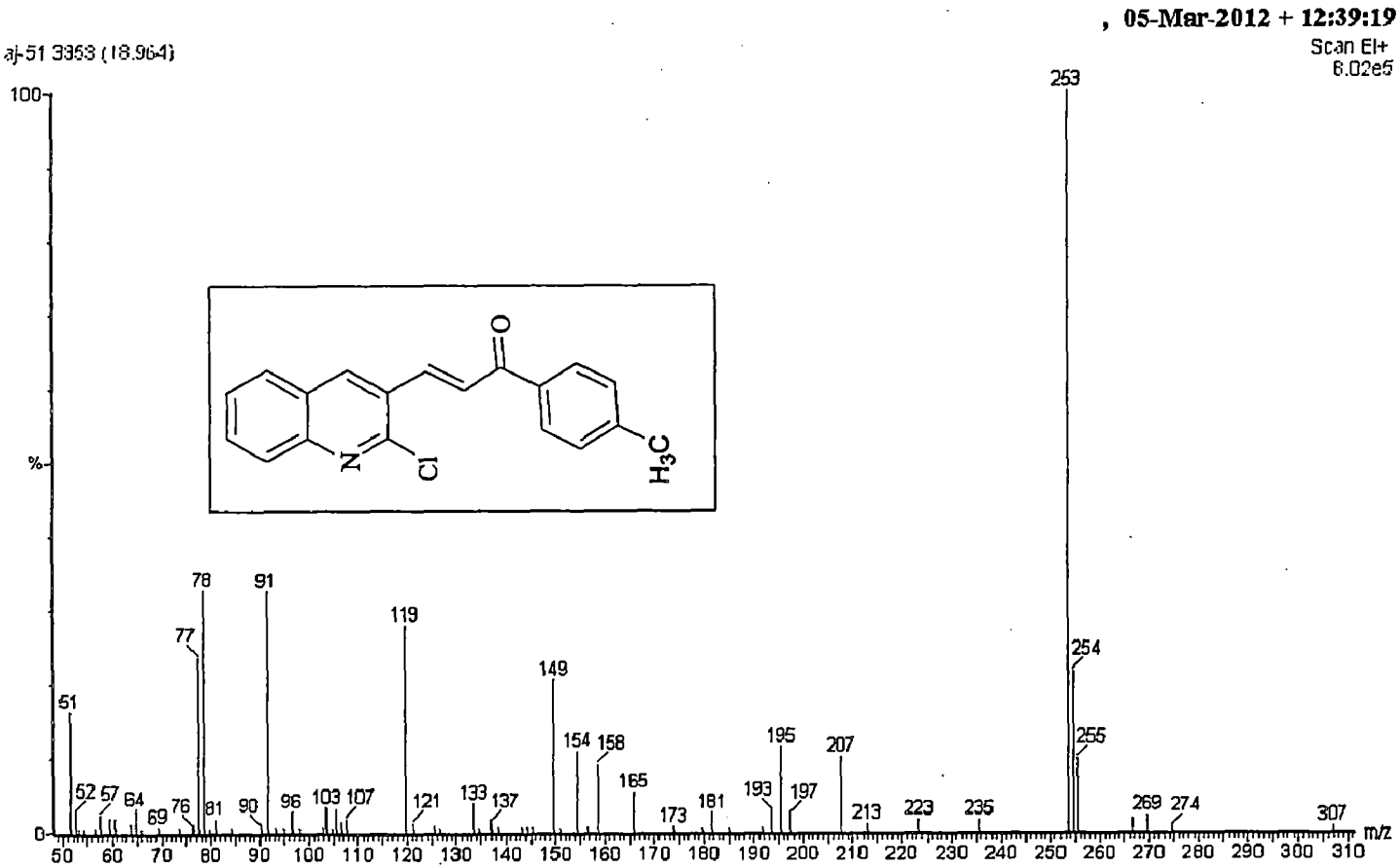

, 05-Mar-2012 + 12:39:19
Scan EI+
6.02e5
aj-51 3353 (18.964)
100
%
0
253
254
255
78
91
77
119
149
51
154
158
165
195
207
52
57
64
69
76
81
90
96
103
107
121
133
137
173
181
193
197
213
223
236
269
274
307
m/z
50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210 220 230 240 250 260 270 280 290 300 310
O
N
Cl
H3C

figure-34

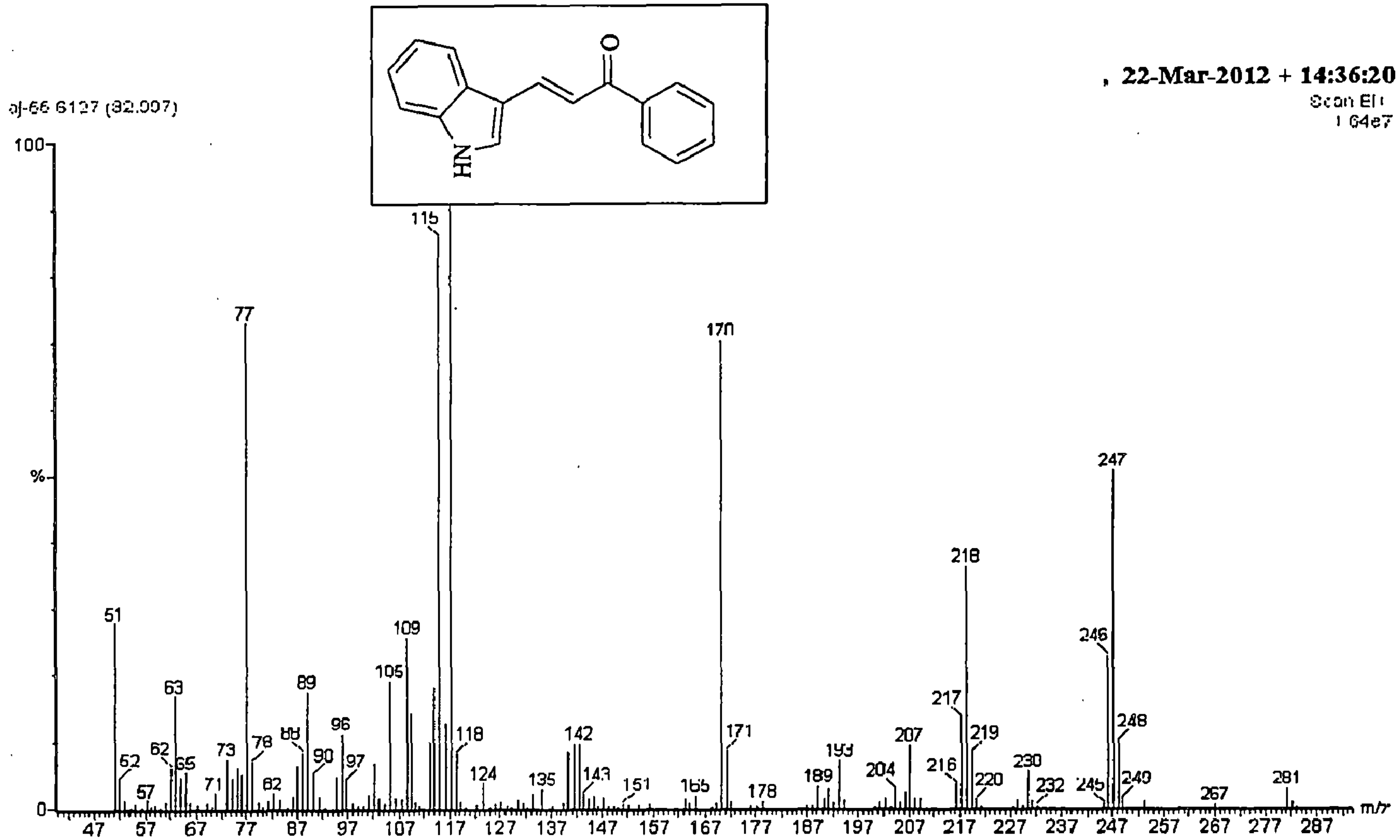

aj-66 6127 (82.007)
, 22-Mar-2012 + 14:36:20
Scan EI+
1.64e7
100
%
0
HN
O
m/z
51
63
77
89
105
109
115
118
142
170
171
207
217
218
219
246
247
248
281

figure-35

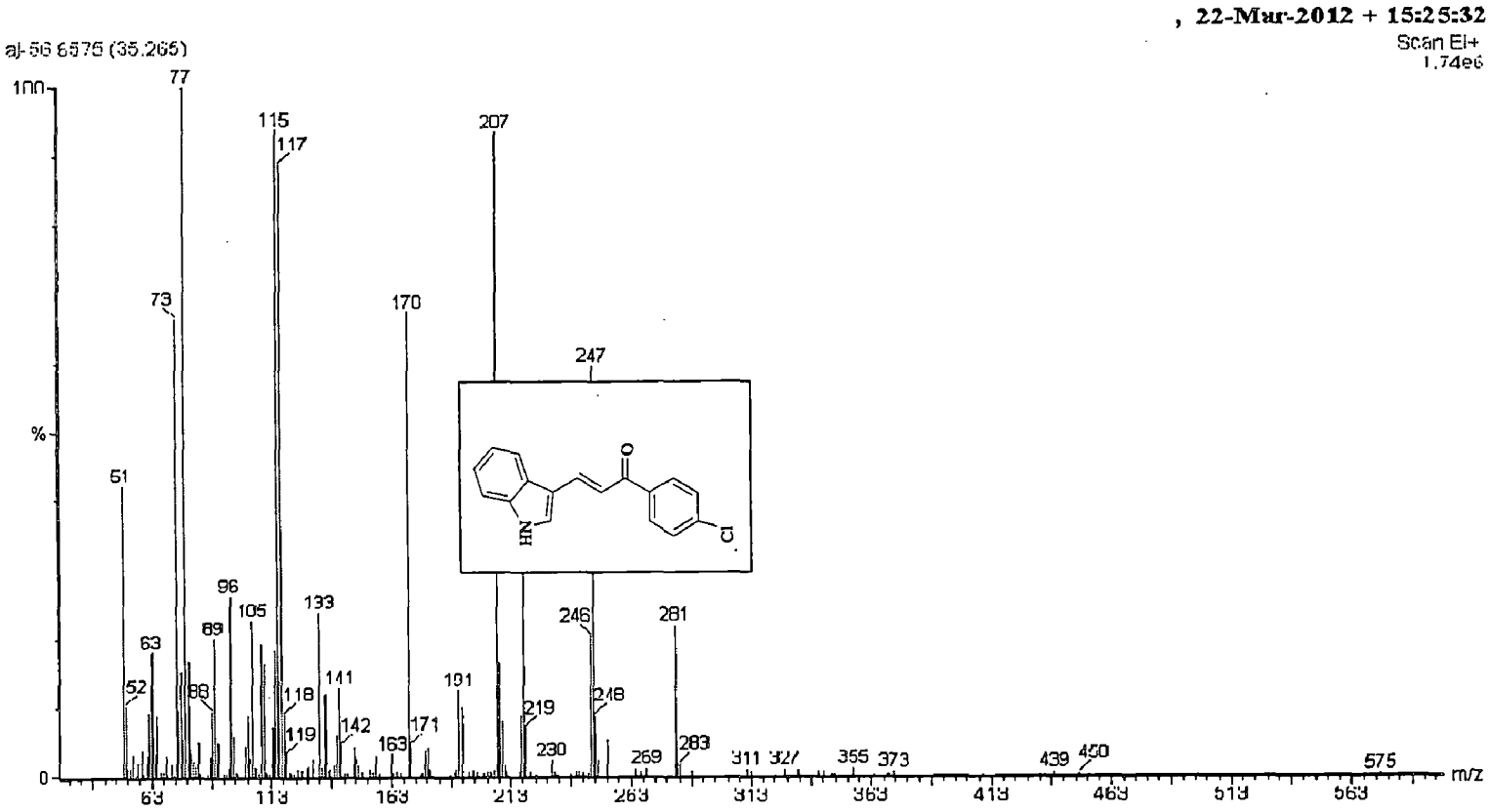

, 22-Mar-2012 + 15:25:32
Scan EI+
1.74e6
aj-56 6575 (35.265)
100
%
0
77
115
117
207
73
170
247
51
96
105
89
133
63
52
88
246
281
141
191
118
219
248
142
119
171
163
230
269
283
311
327
355
373
439
450
575
m/z
63
113
163
213
263
313
363
413
463
513
563
O
HN
Cl

figure-36

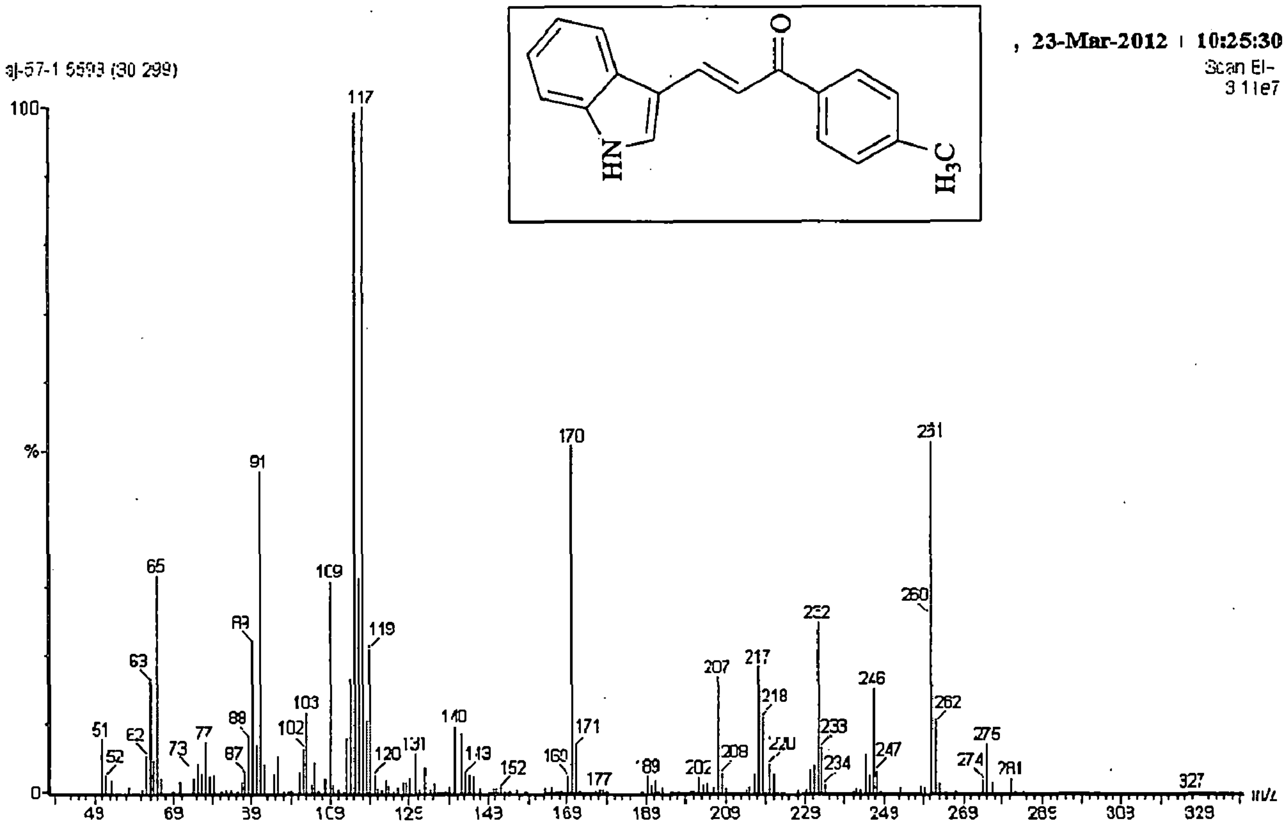

, 23-Mar-2012 ı 10:25:30
Scan EI-
3 11e7
sJ-57-1 5593 (30 299)
100
%
0
HN
O
H3C
m/z

figure-37