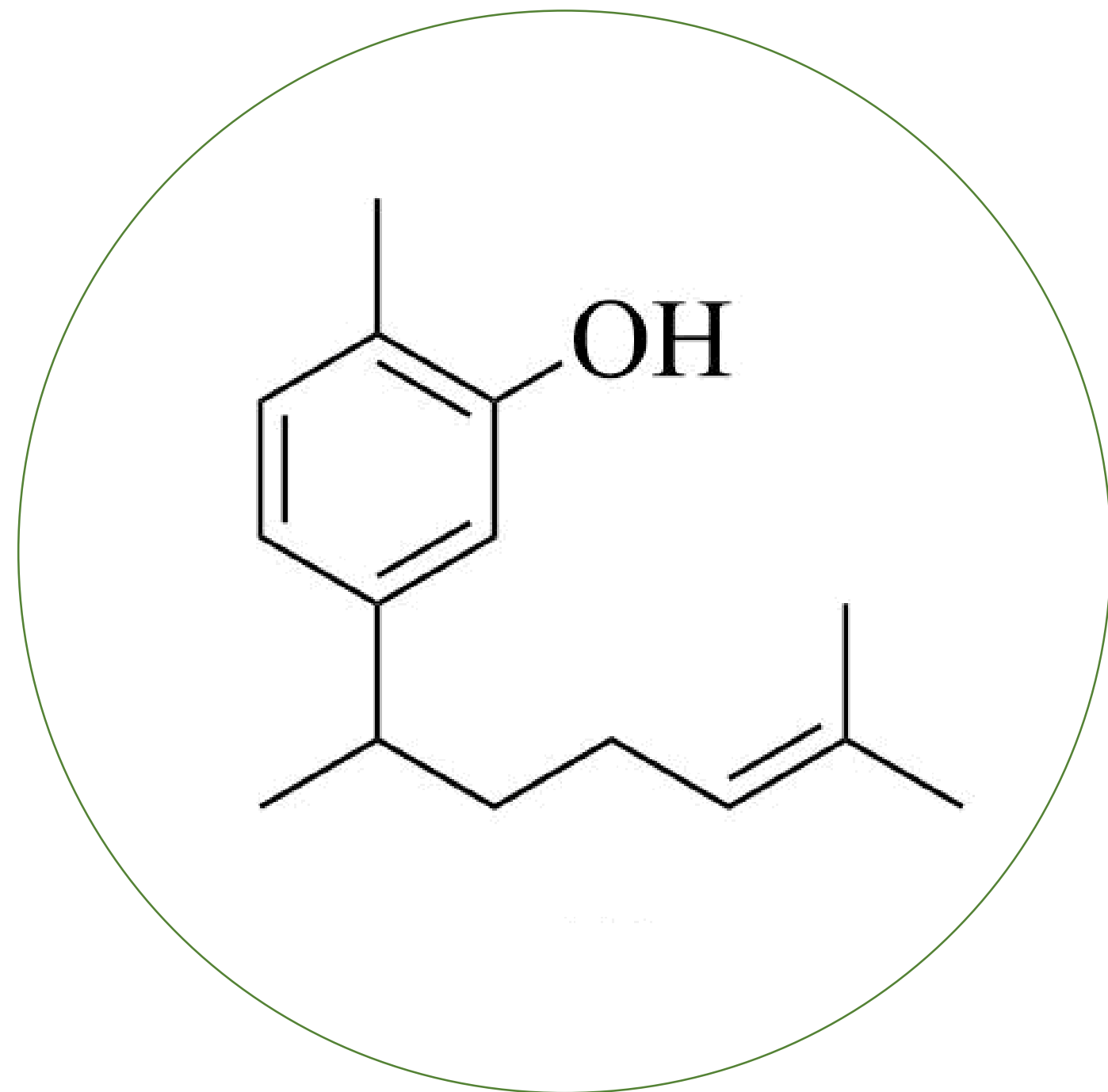


DESIGN AND SYNTHESIS OF XANTHORRHIZOL DERIVATIVES USING *IN SILICO* FRAGMENT- BASED DRUG DESIGN (FBDD) APPROACH AS HYALURONIDASE INHIBITOR

Tengku Kamilah Tengku Nazmi¹, Nurul Iman Aminudin*¹, Nurasyikin Hamzah¹, Mazura Md
Pisar², Siti Nur Aisyah Mohd Hashim²,

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Malaysia*



Xanthorrhizol (1)

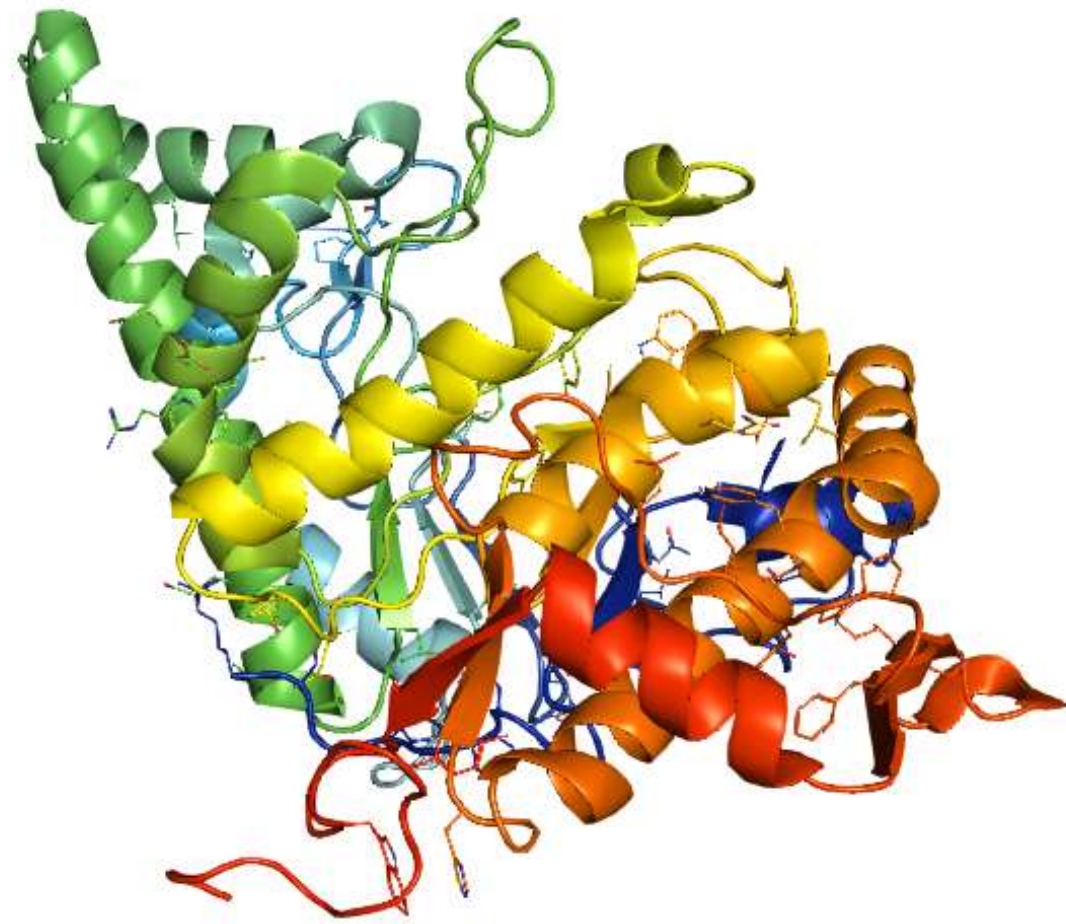
A type of **bisabolene sesquiterpenoids** isolated from rhizome part of ***Curcuma xanthorrhiza***

92 % in *Curcuma xanthorrhiza* essential oil¹

Molecular weight = 218.33 g/mol

Possessed various biological activities, including anti-inflammatory properties

Active against several pro-inflammatory enzymes, i.e., inducible nitric oxide synthase (iNOS)² and cyclooxygenase (COX)³



Crystal structure of human hyaluronidase-1 deposited in PDB⁵ (PDB ID: 2PE4)

- HA metabolism can result in **production of low molecular weight HA (LW-HA) fragments**⁴
- ✓ Increased expression of chemokines and iNOS
- ✓ Stimulate dendritic cell signaling pathways to produce IL-1 β , IL-12, and TNF- α
- Hyaluronidase-1 and 2 are the **key enzymes** in degradation of HA



- The whole process took 12 to 15 years⁵
- Cost more than one million USD for one drug to be approved
- Low success rate

Structure-based drug design (SBDD)

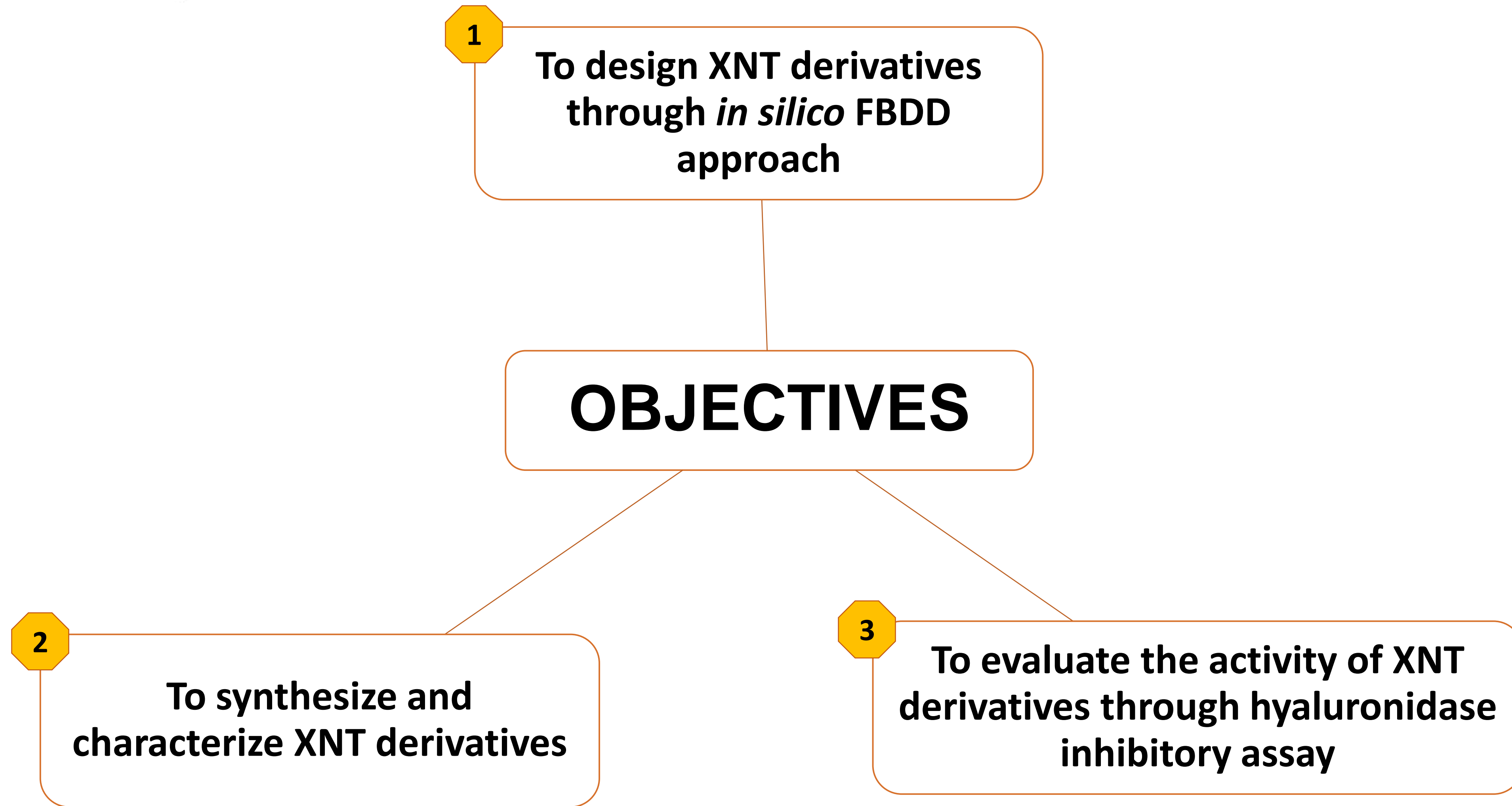
Relies on the knowledge of the 3D structure of the protein⁶

Fragment-based drug design (FBDD)

- New drug compounds will be designed through fragments of small molecules that exhibited weak affinity towards the protein target⁷

Molecular docking

- Predict binding affinity between a drug molecule and biological target⁸
- Binding affinity of each pose will be ranked using energy-based scoring function





Isolation and purification of XNT from *C. xanthorrhiza* essential oil

Structural modification of XNT using LigBuilder

Synthesis and characterization xanthorrhizol derivatives

***In vitro* hyaluronidase enzyme inhibitory assay**

4. Modification of XNT derivatives

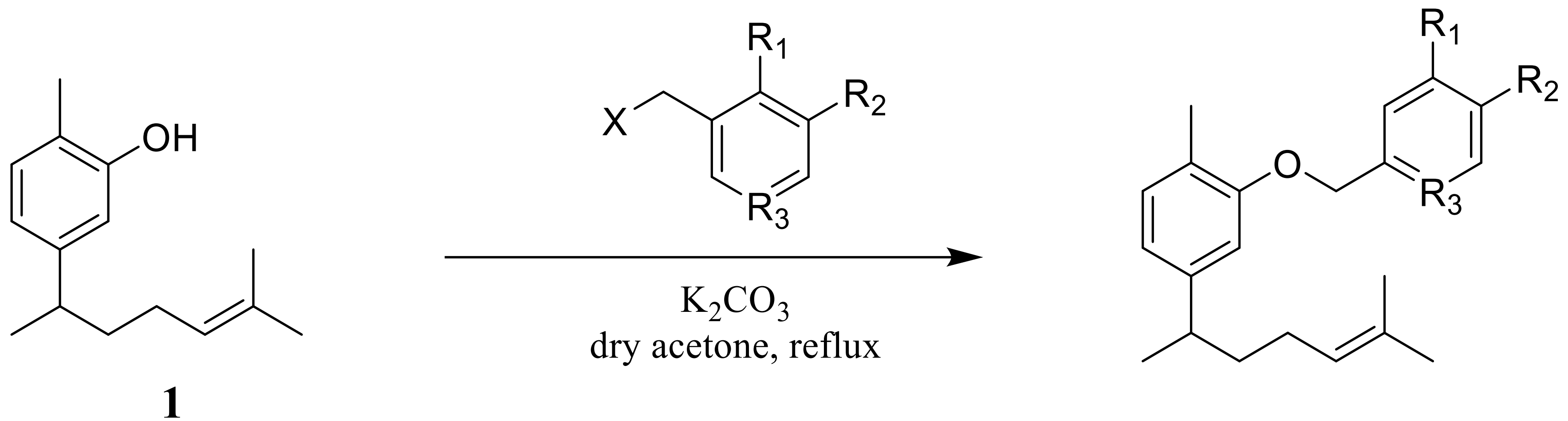
Further modification of XNT derivatives

1. Structure of the derivatives

2. Binding energy

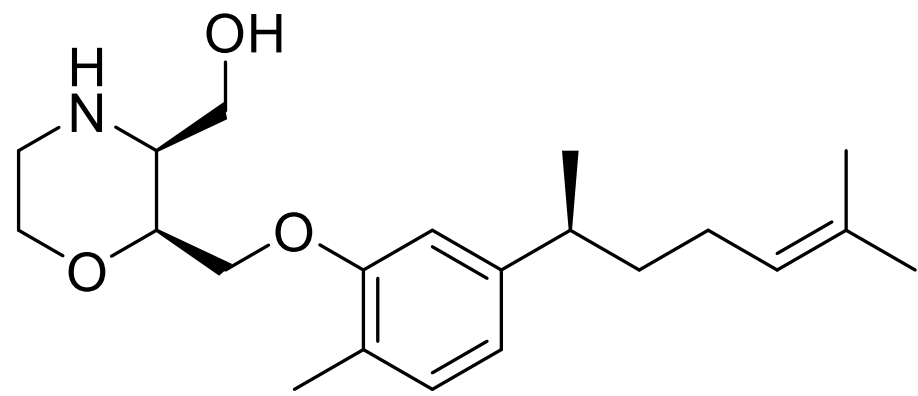
3. ADME properties

4. Synthetic tractability

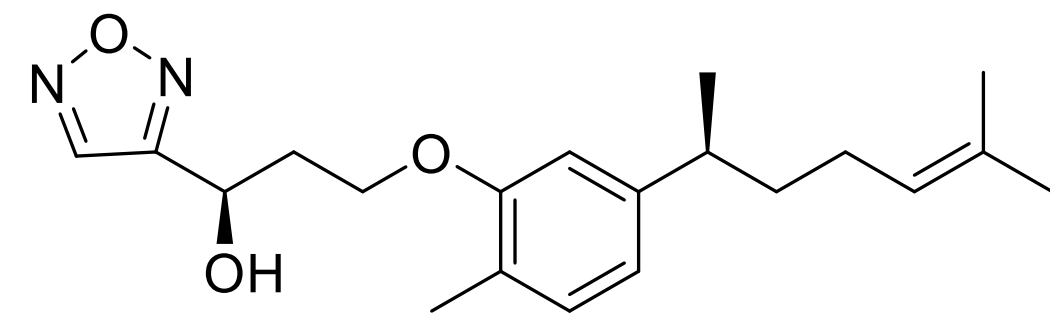


- 2** X = Br, R₁ = H, R₂ = H, R₃ = H
- 3** X = Cl, R₁ = H, R₂ = H, R₃ = N
- 4** X = Br, R₁ = H, R₂ = NO₂, R₃ = H
- 5** X = Cl, R₁ = CF₃, R₂ = H, R₃ = H

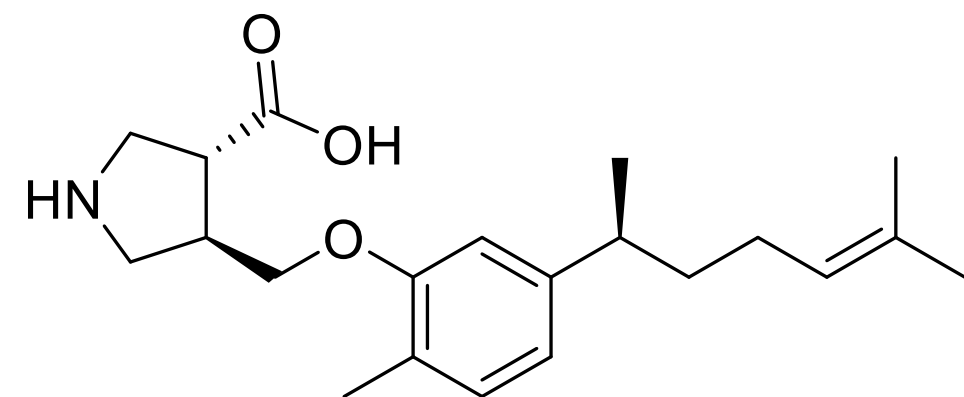
- A total of 1187 derivatives were generated in LigBuilder
- Top 50 derivatives with highest binding affinity were filtered



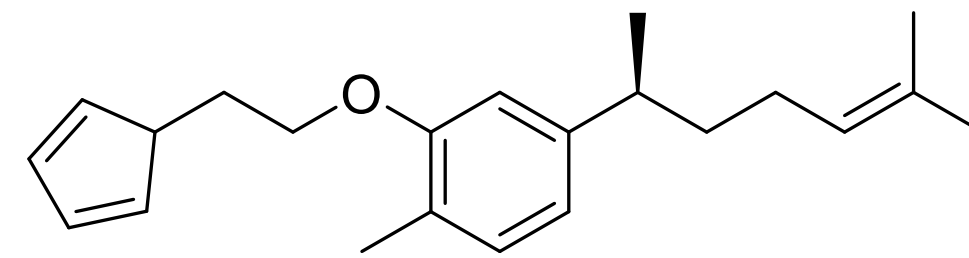
910 (BE = -8.2 kcal/mol)



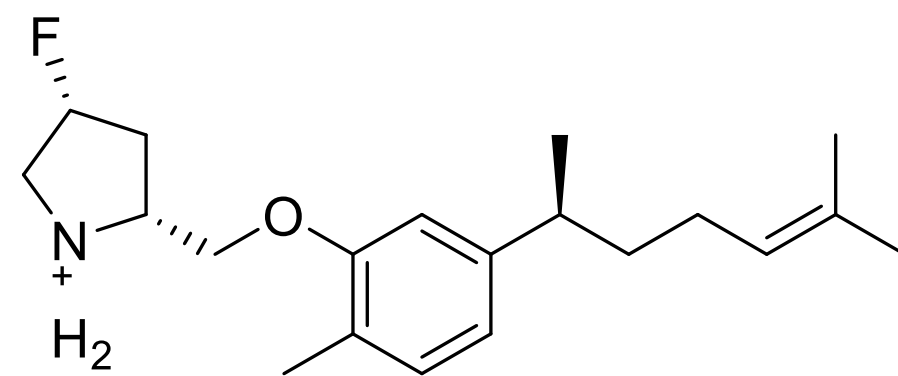
343 (BE = 8.1 kcal/mol)



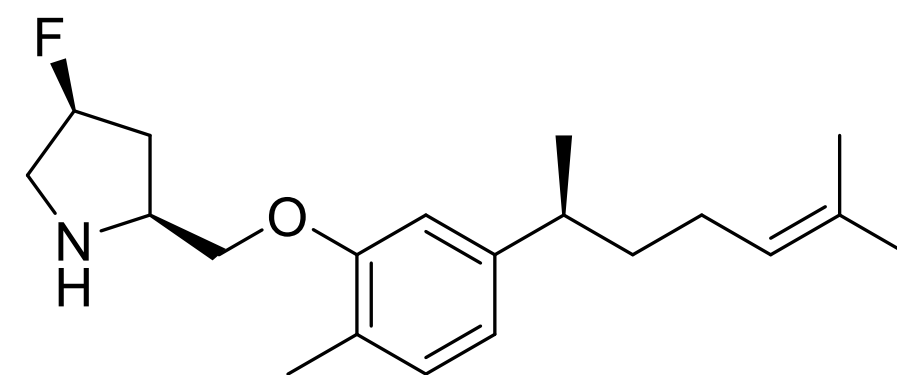
552 (BE = -8.5 kcal/mol)



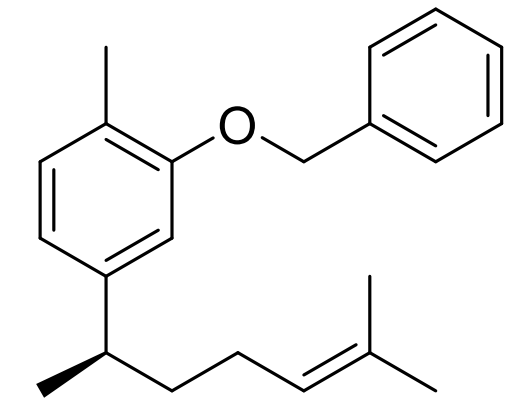
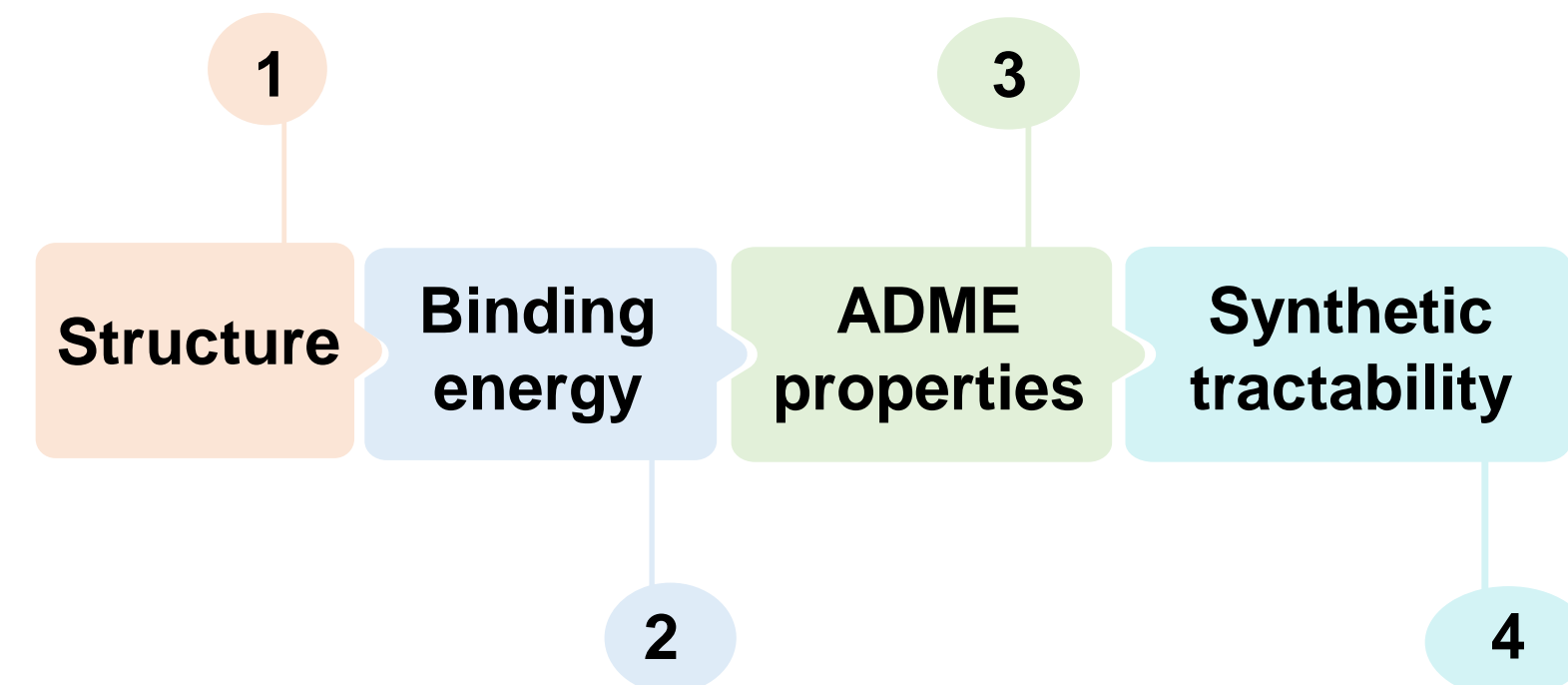
026 (BE = -8.0 kcal/mol)



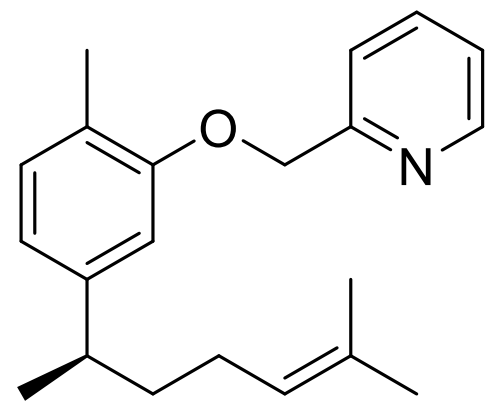
242 (BE = -8.0 kcal/mol)



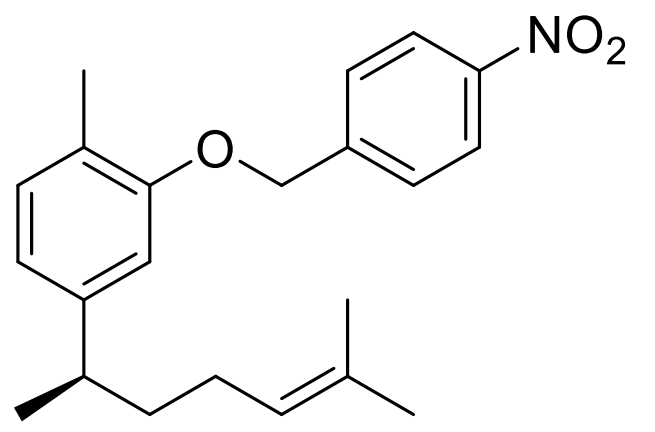
131 (BE = -7.9 kcal/mol)



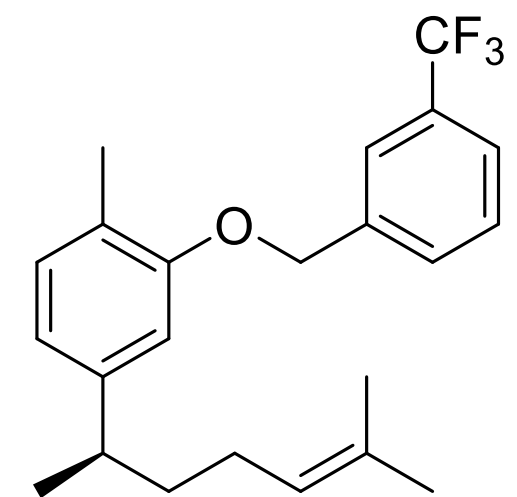
2



3


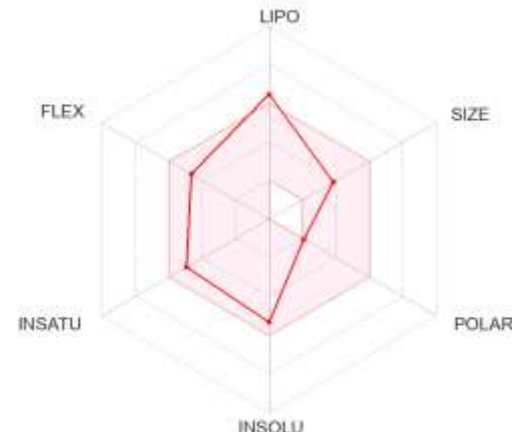
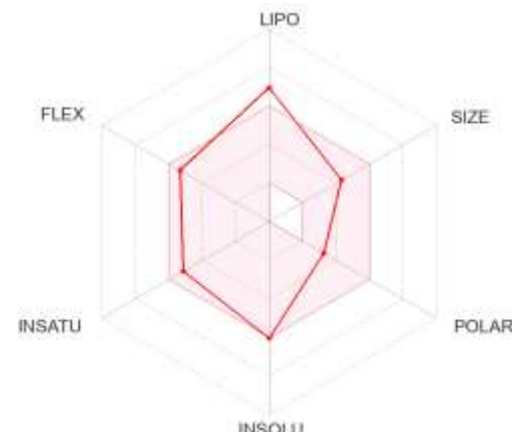


4



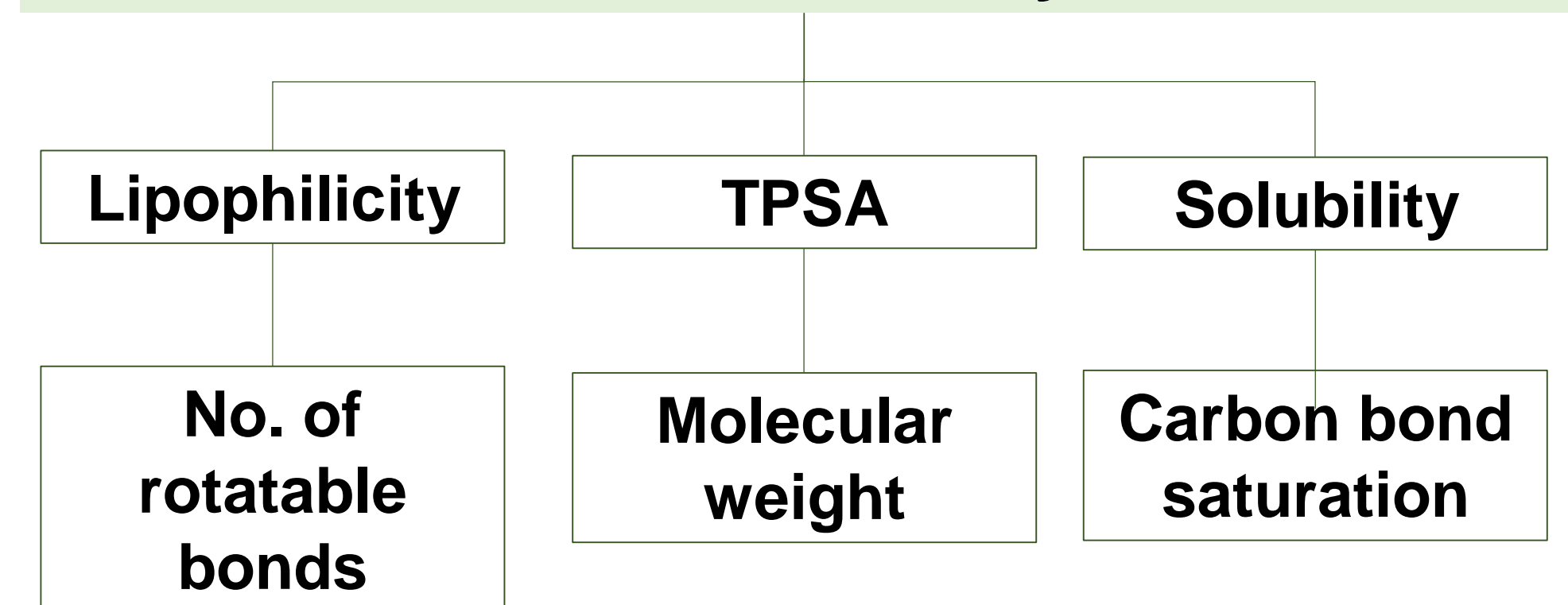
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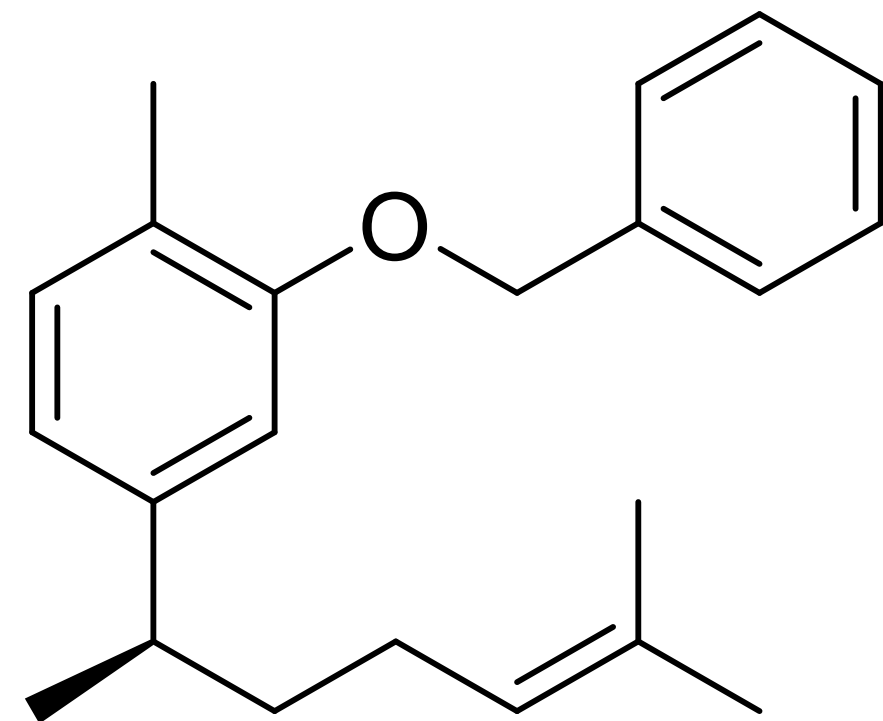
- Ring system
- Composed of heteroatoms (O and N) and fluorine atom

Compound	Substituent	Binding energies (kcal/mol)	Bioavailability radar
(2)	Benzyloxy	-8.0	
(3)	Methyleneoxy pyridine	-7.8	
(4)	5'-Nitrobenzyloxy	-8.1	
(5)	6'-(Trifluoromethyl) benzyl oxy	-8.9	

All derivatives exhibited improved binding affinity compared to XNT (-6.5 kcal/mol)

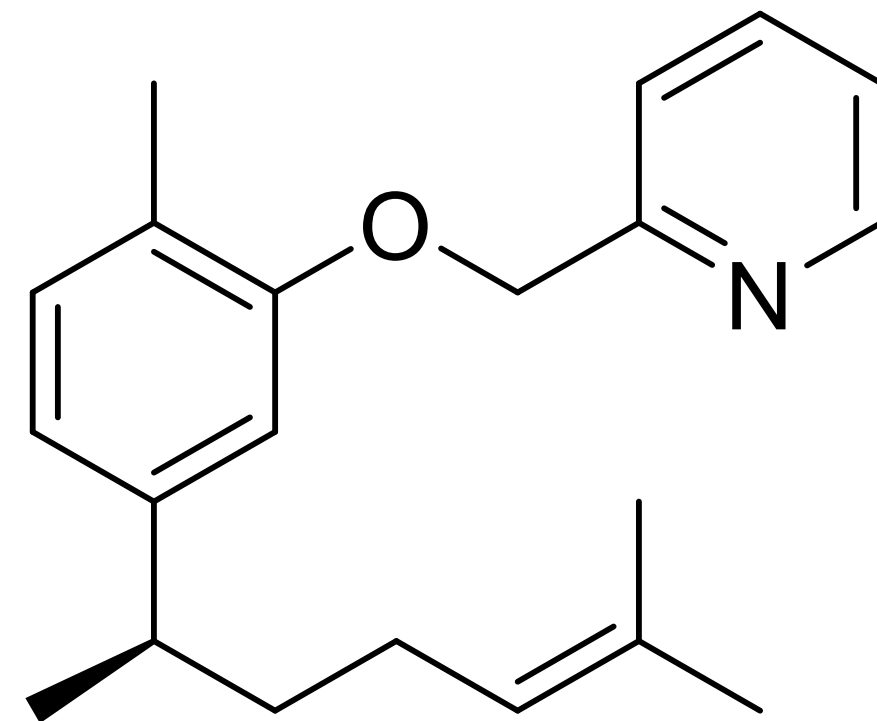
All derivatives adhered to most of the important parameters for drug absorption in human body





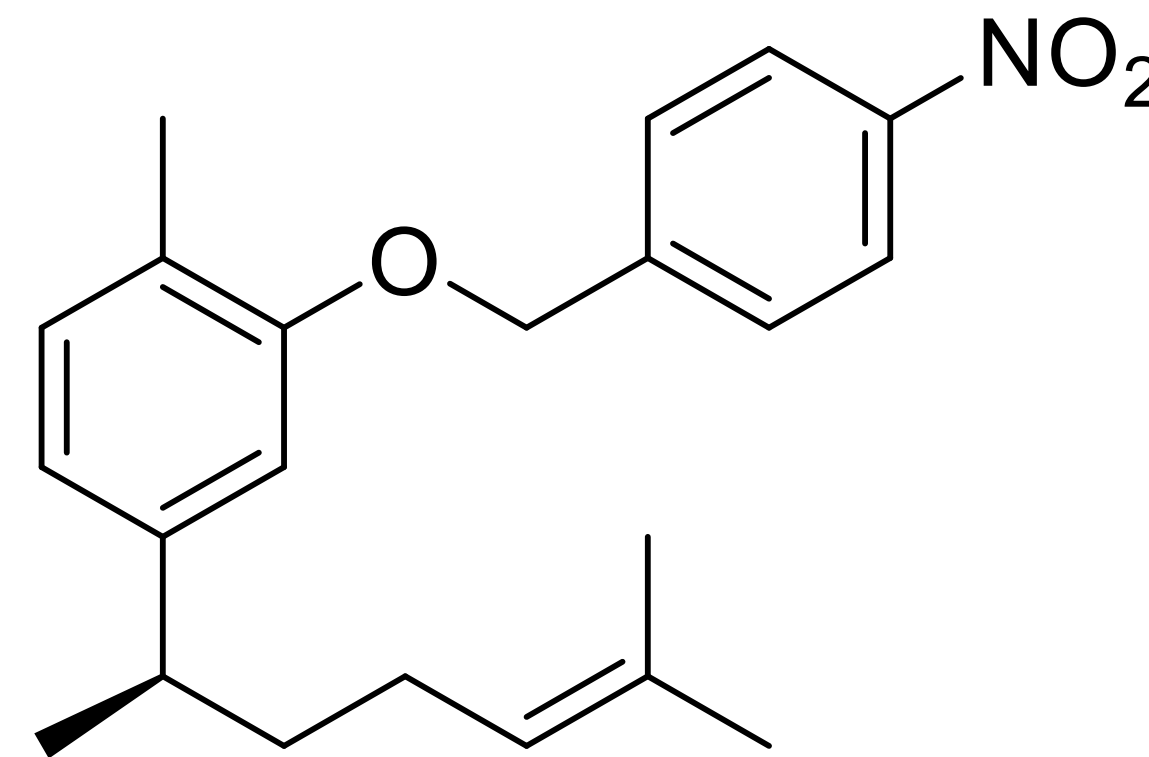
2

yellow oil
(315.10 mg, 63.02 %)



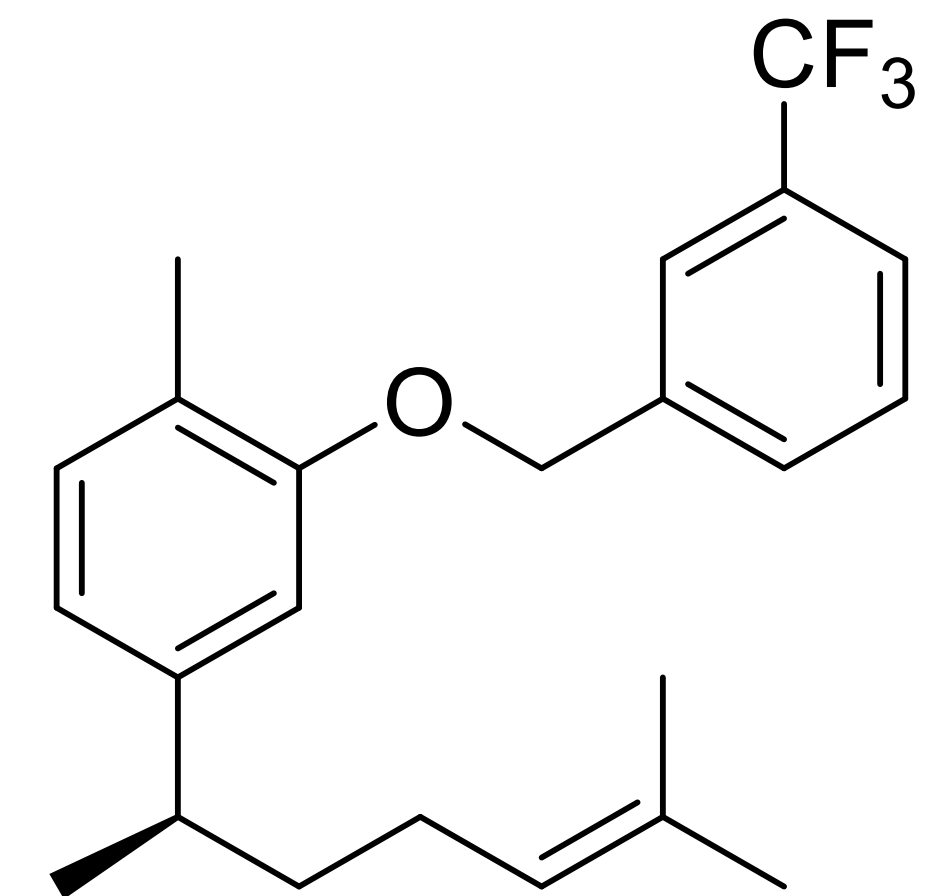
3

yellow oil
(289.10 mg, 40.79 %)



4

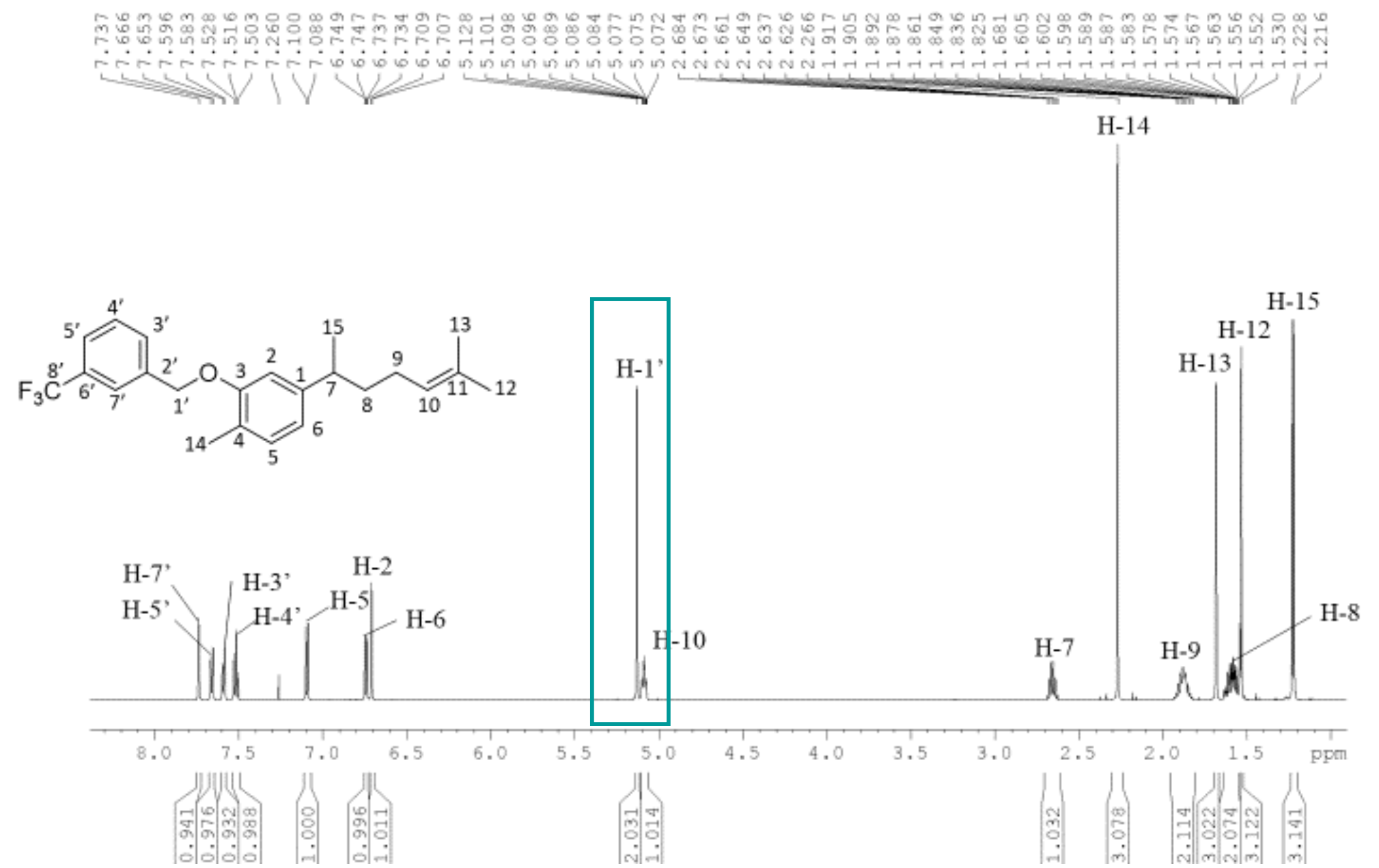
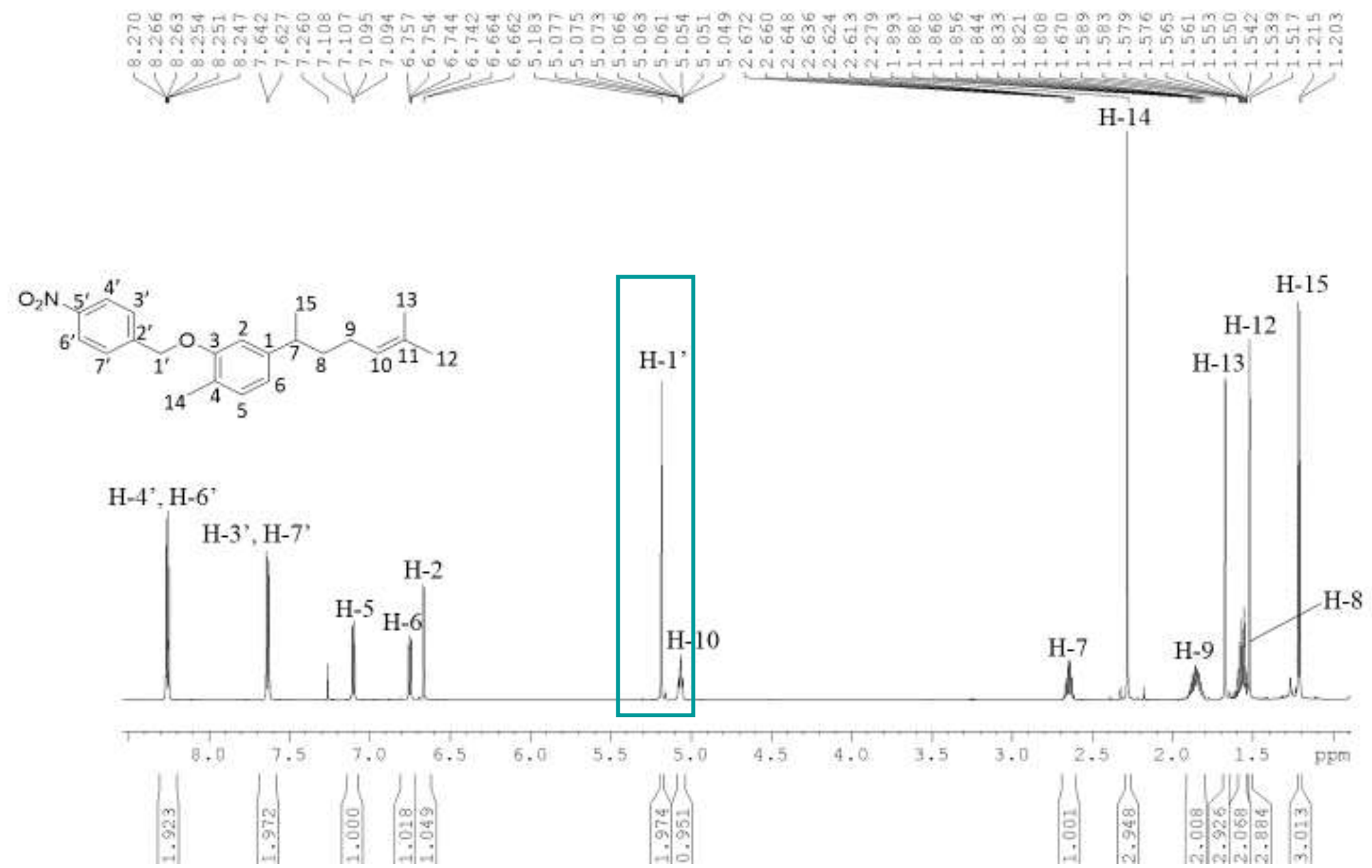
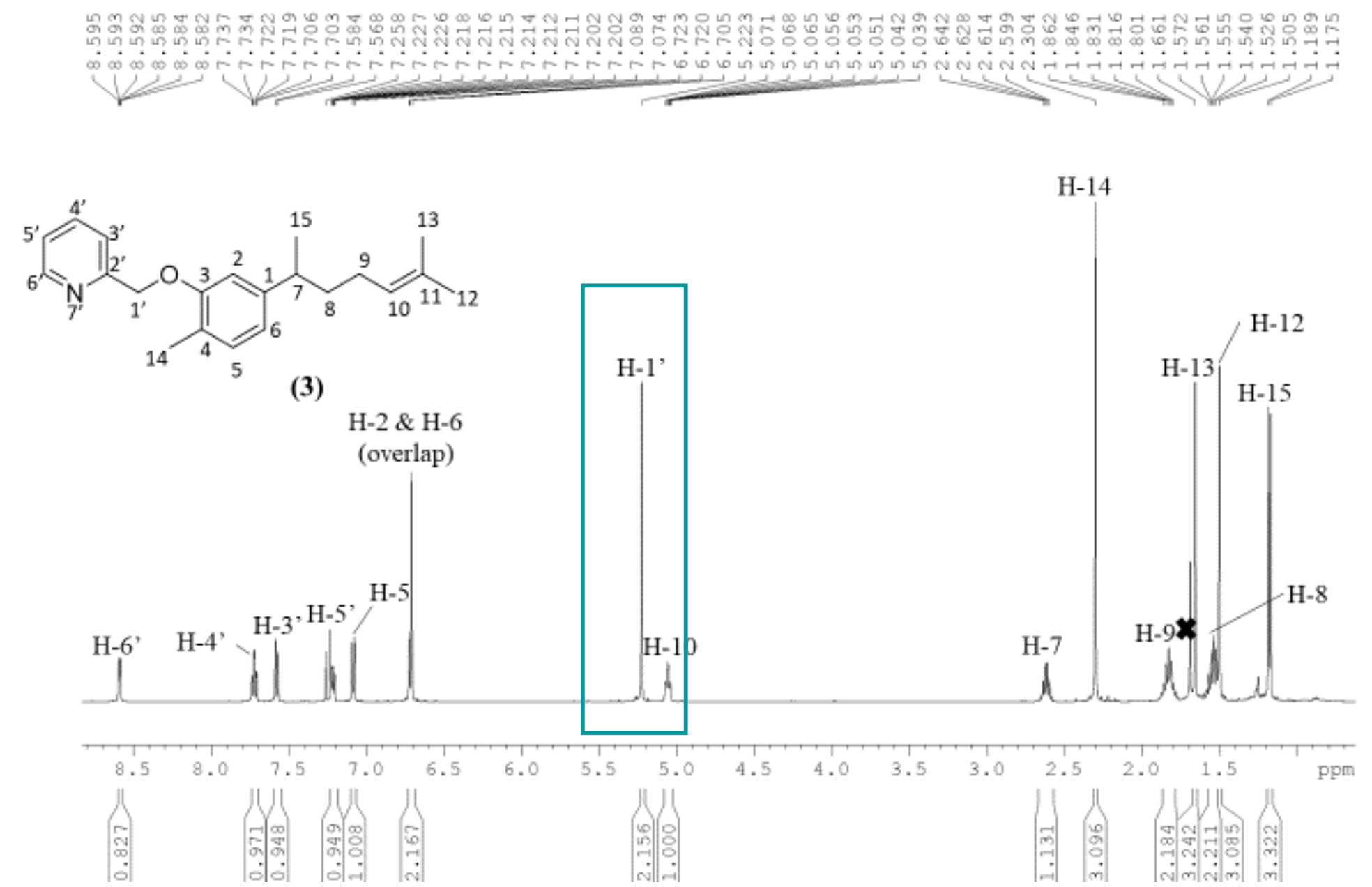
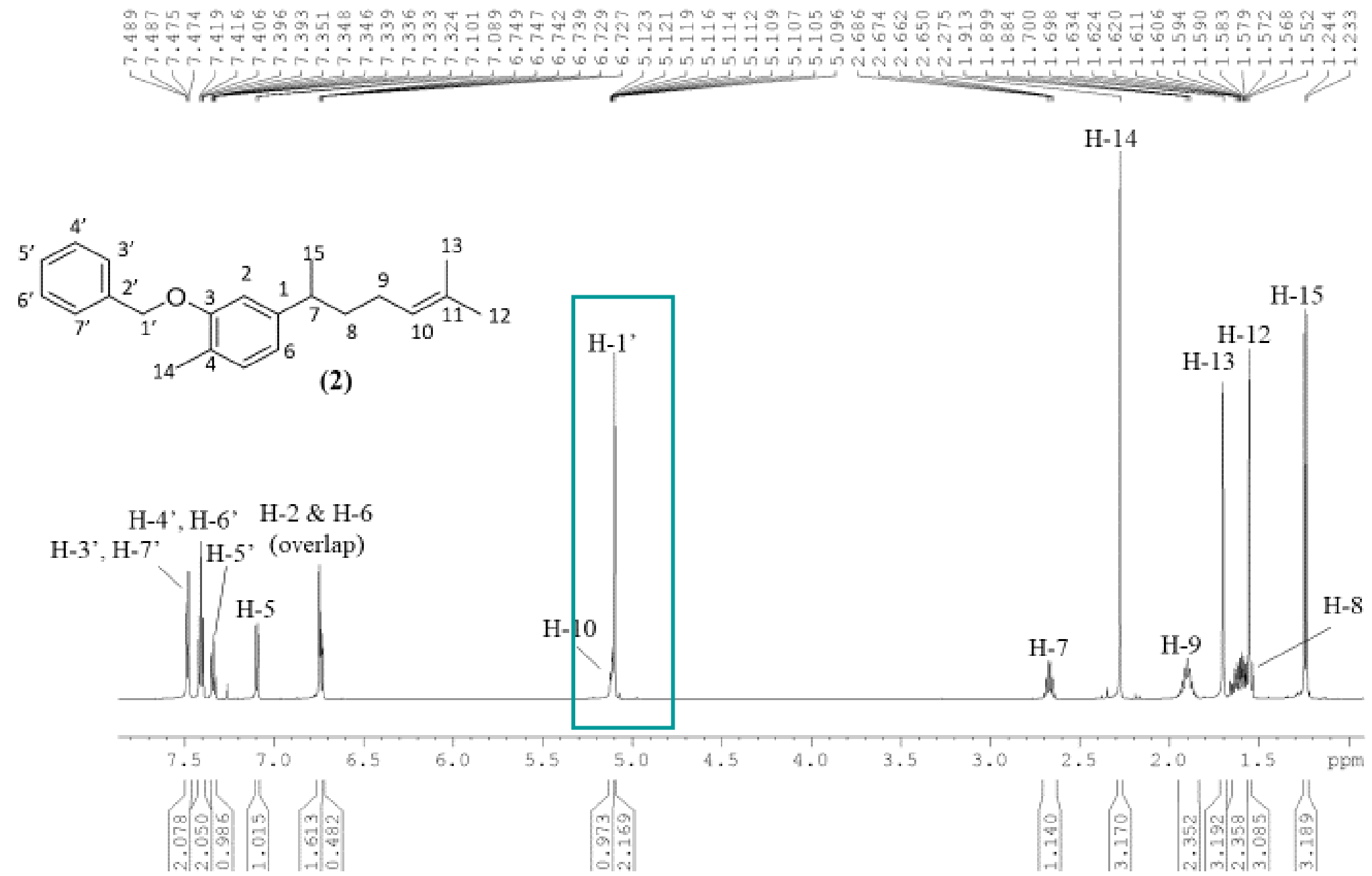
yellow oil
(103.20 mg, 63.74 %);



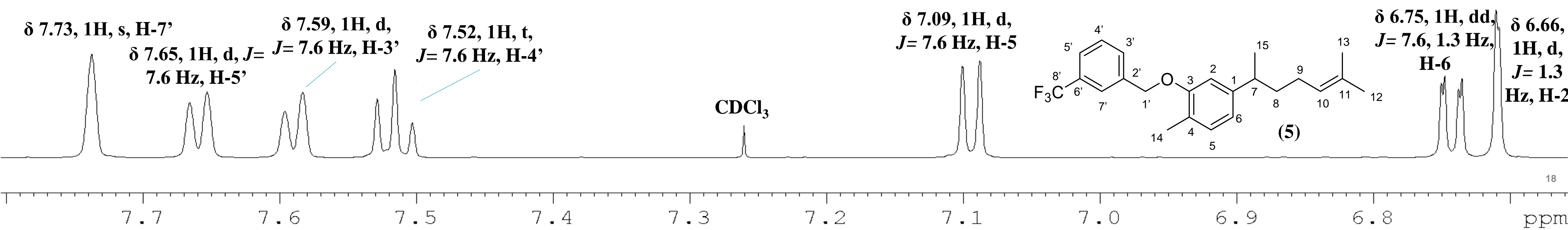
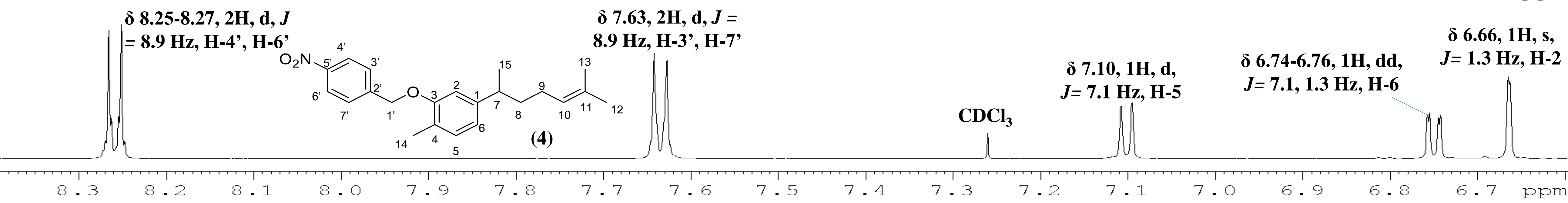
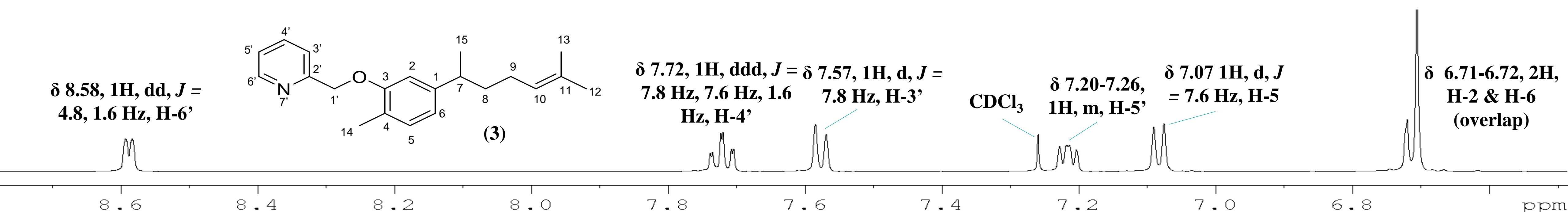
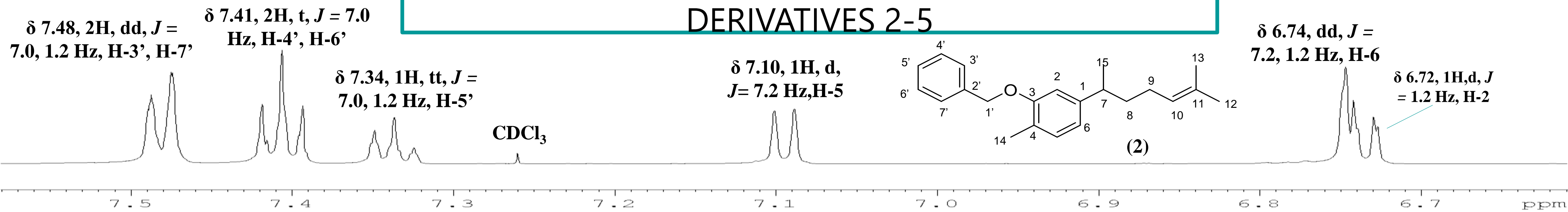
5

colourless oil
(98.40 mg, 57.07 %)

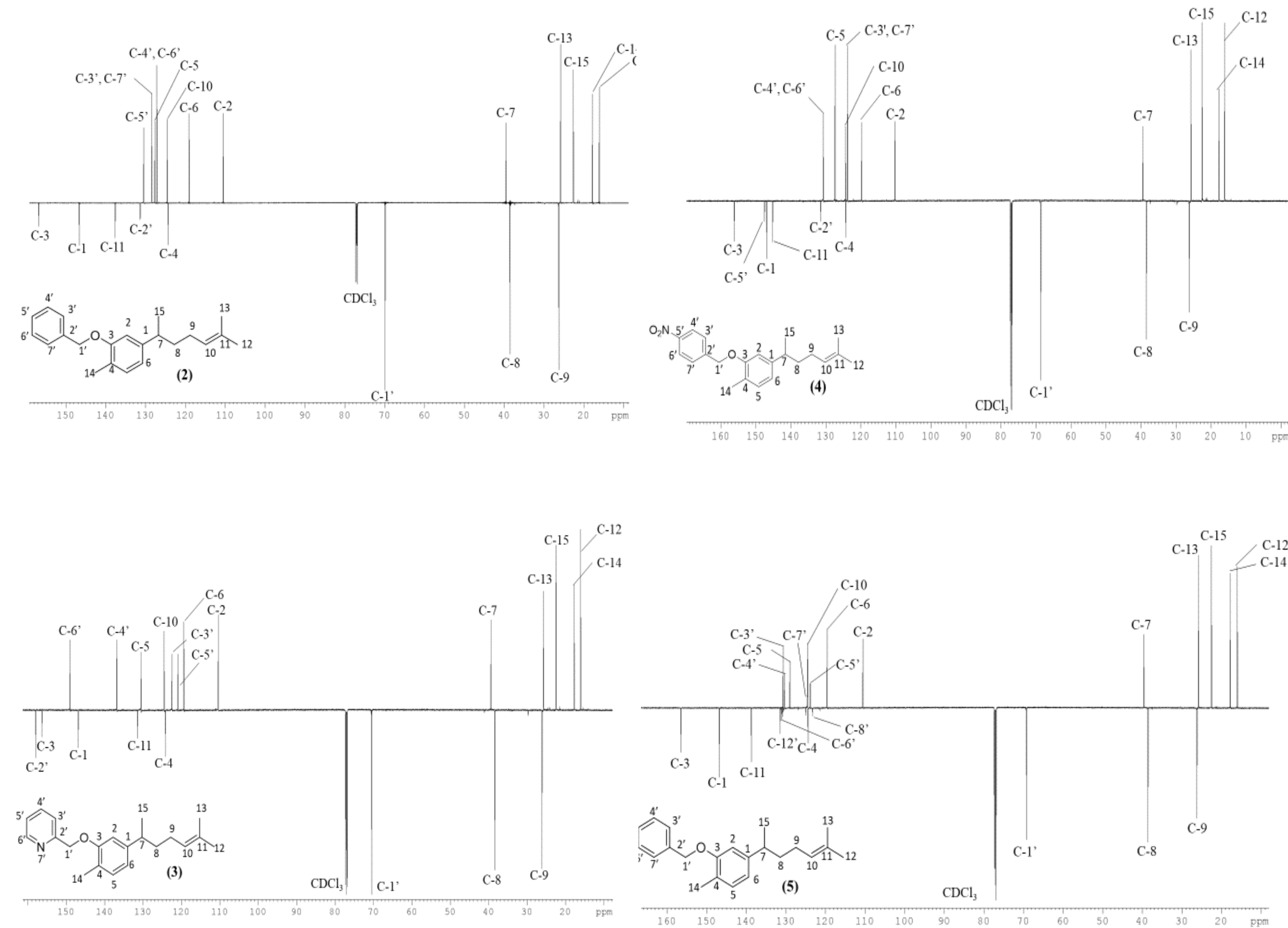
RESULT AND DISCUSSION: ¹H NMR OF XNT DERIVATIVES 2-5



RESULT AND DISCUSSION: ¹H NMR OF XNT DERIVATIVES 2-5

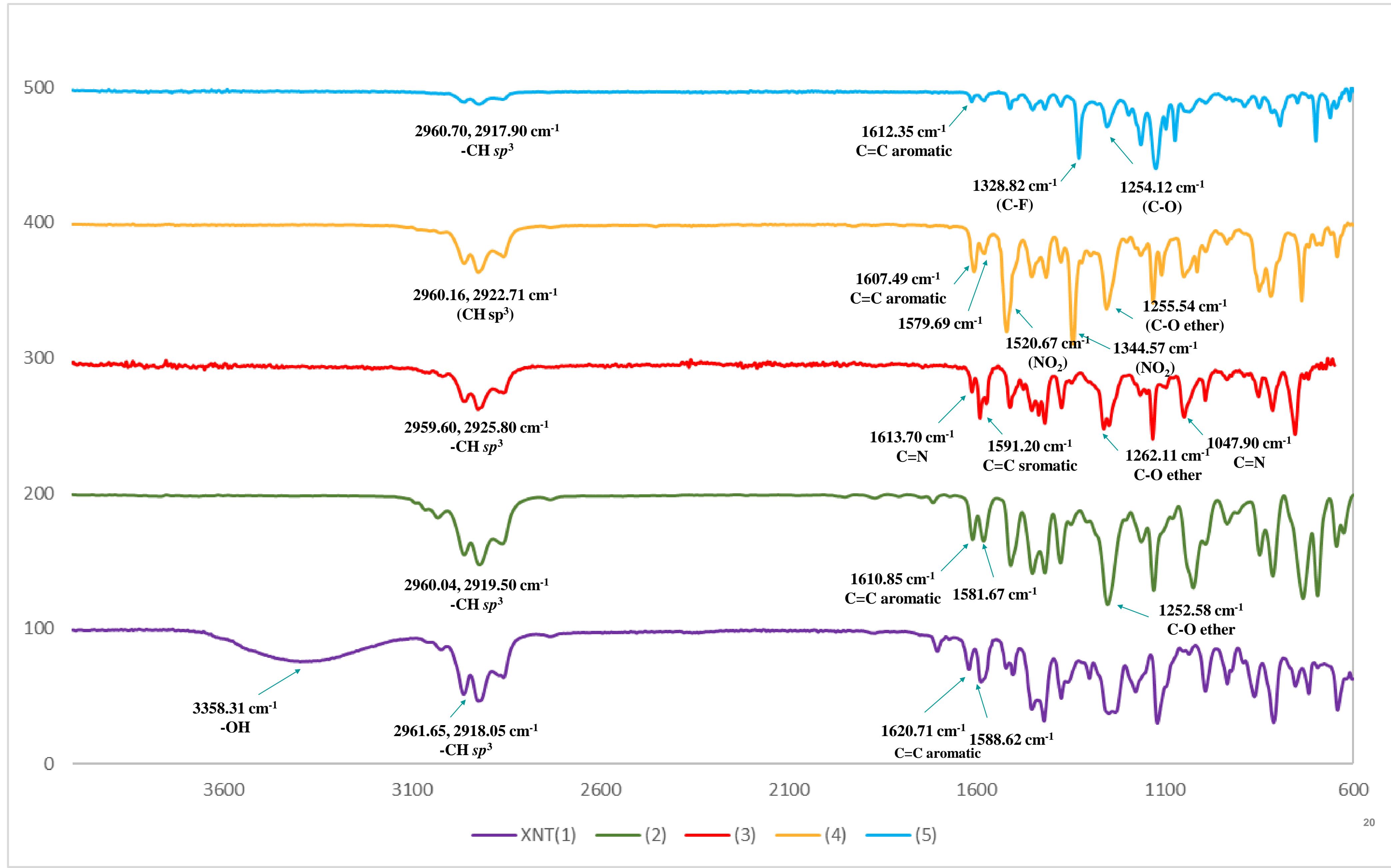
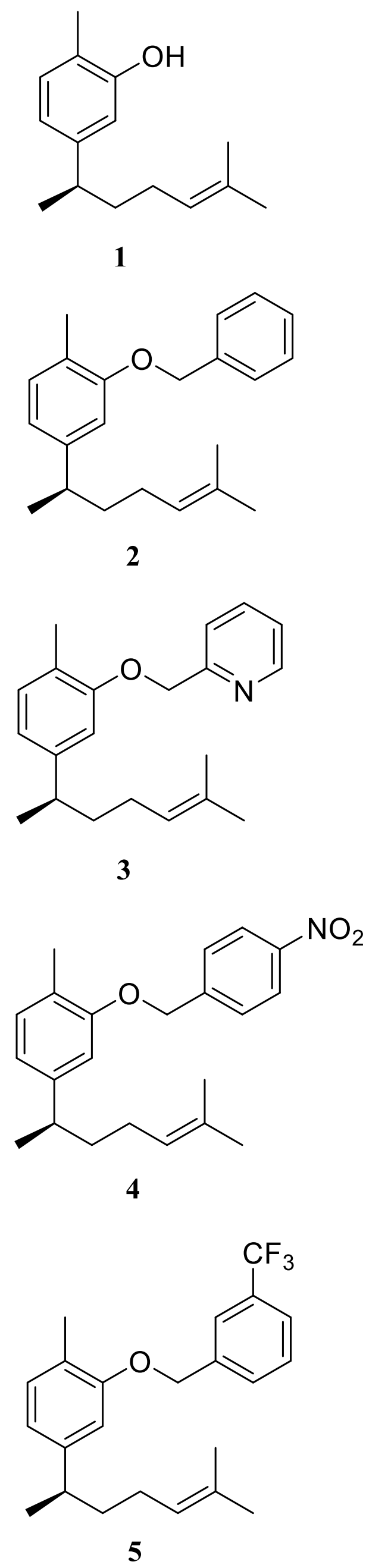


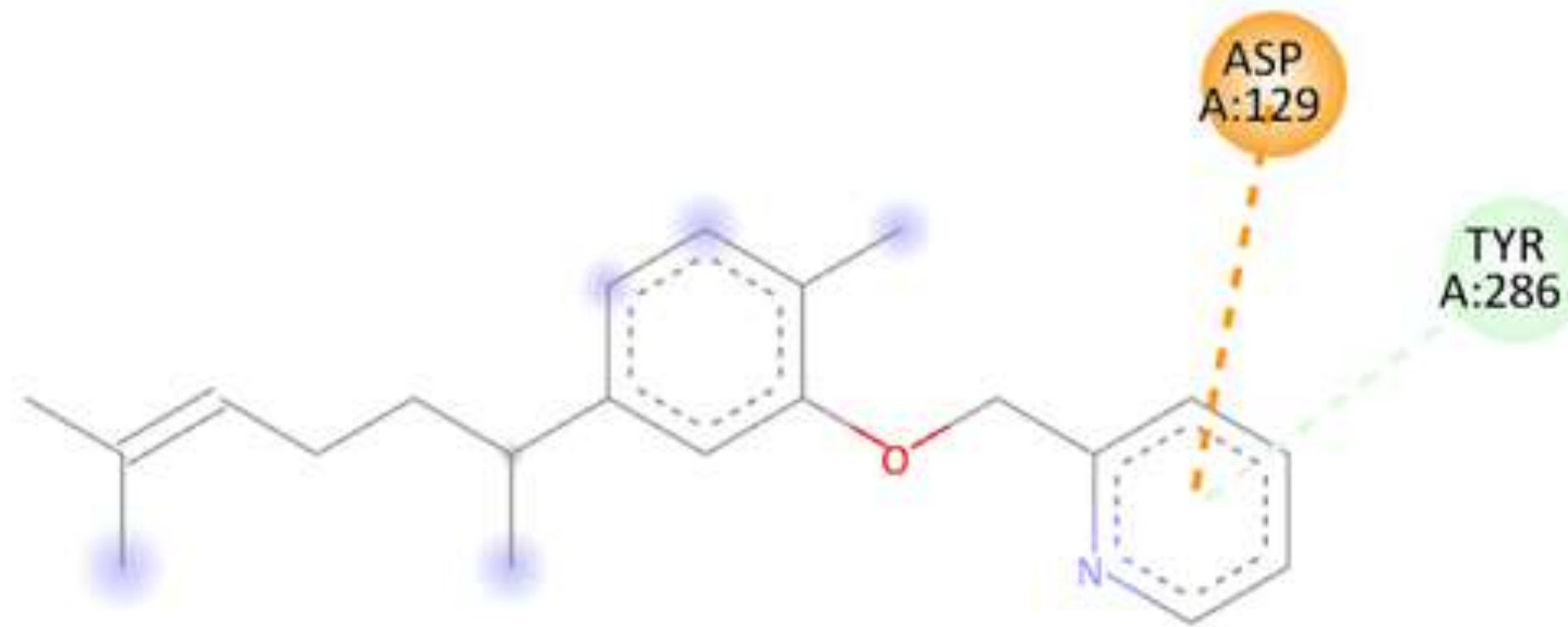
RESULT AND DISCUSSION: ^{13}C DEPTQ NMR OF XNT DERIVATIVES 2-5



<i>Derivatives</i>	-CH_3	-CH_2	-CH	-C_q
(2)	5	10	3	4
(3)	4	3	9	5
(4)	6	9	3	4
(5)	7	9	3	4

RESULT AND DISCUSSION: ATR-IR SPECTRA OF COMPOUND 1-5



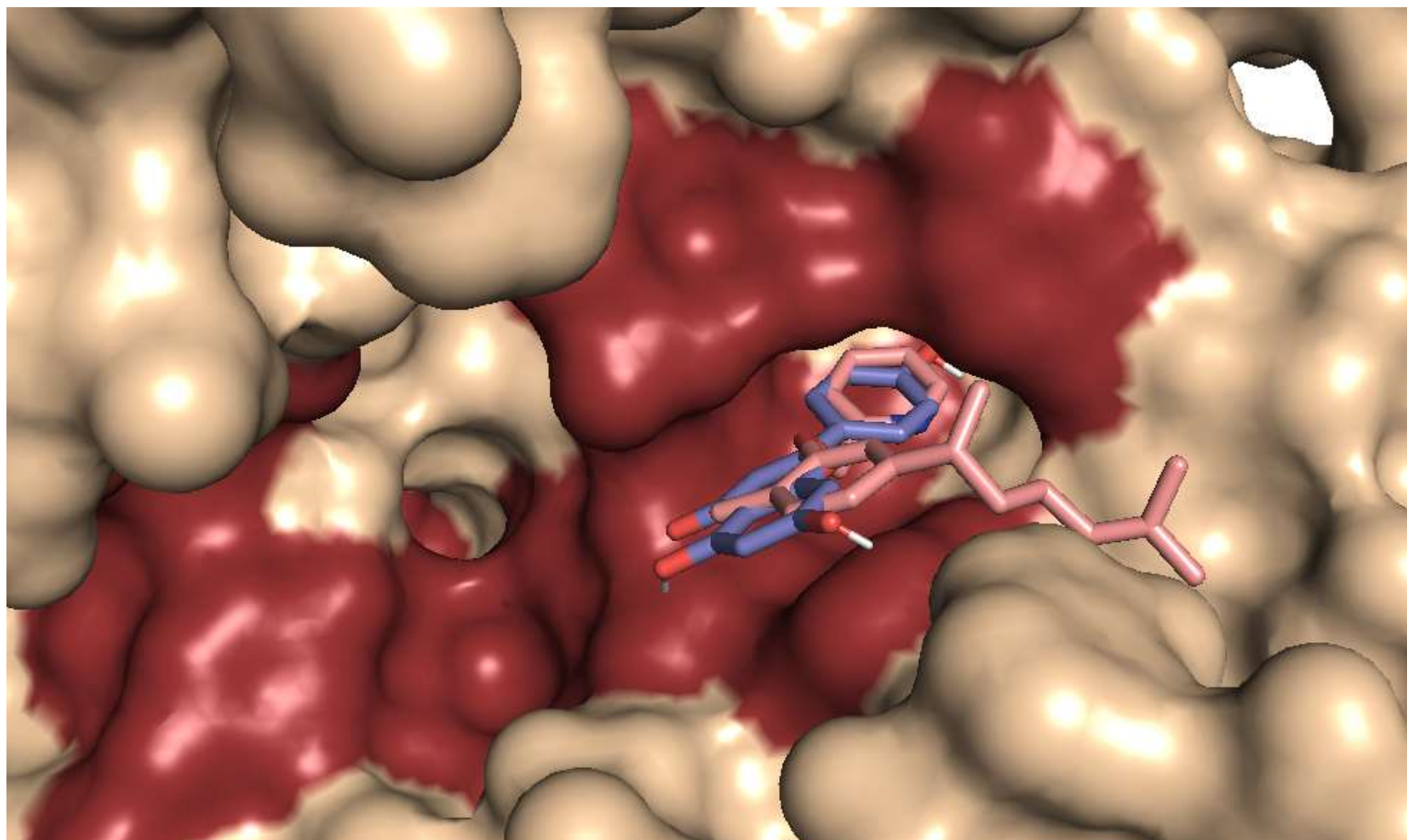


(3)

Binding energy = -7.8 kcal/mol

Compound 3 (pink) bound to hyaluronidase active site with similar conformation to apigenin (purple)

Pyridine ring interacted with Asp129 *via* pi-anion interaction





XNT derivatives were successfully synthesized

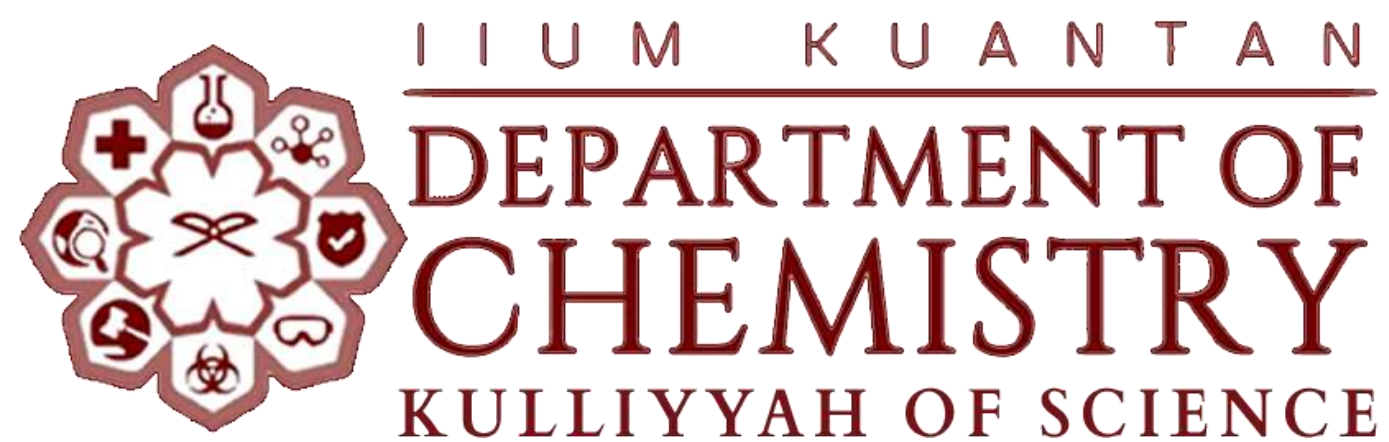


All synthesized derivatives exhibited improved activity against hyaluronidase enzyme



Combination of computational techniques helps give insights for important functionalities to improve XNT activity

THANK YOU!



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Dr. Nurul Iman Aminudin
nuruliman @iium.edu.my

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MALAYSIAN
NATURAL PRODUCTS
SOCIETY

INTERNATIONAL CONFERENCE ON NATURAL PRODUCTS
Seminar Tahunan Sebatian Semulajadi Malaysia ke-38

ICNP2023

PROGRAM BOOK

11-13 September 2023 | ALOFT Kuala Lumpur Sentral, Malaysia





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FORWARDS



VICE CHANCELLOR UiTM



Assalamualaikum and Good Morning.

Alhamdulillah, all praise to Allah, the Merciful and the All-beneficent for His grace and blessings that led to this momentous occasion. It is with great pleasure and utmost honour that I address you all today as Vice-Chancellor to officiate the prestigious International Conference on Natural Products (ICNP) 2023. I extend a warm welcome to all esteemed guests and participants gathered here at the Aloft Hotel in Kuala Lumpur. My heartfelt gratitude to everyone in attendance for gracing us with your presence. Your participation in this conference is proof of your untiring commitment to advancing knowledge and exploration in the fascinating field of natural products.

I am truly humbled by the dedication and hard work put forth by the organising committee, helmed by Prof. ChM. Dr. Nor Hadiani Ismail as the chairperson of ICNP, in making this conference a reality.

Today we gather here in Kuala Lumpur, united by a common purpose to explore the intricate world of natural products and their diverse applications in various fields, including healthcare, agriculture, and environmental sustainability. Our collective efforts in understanding and harnessing the power of nature can pave the way for innovative solutions and contribute to the well-being of our society. The theme for ICNP 2023 "Changing the Landscape for a Sustainable Future" resonates deeply with the current global landscape.

Natural products have long been regarded as a source of inspiration for healing, environmental restoration, and sustainable development. As we navigate the complexities of our modern world, the significance of natural products in supporting human well-being and environmental preservation becomes ever more apparent. Hence, the theme of ICNP 2023 serves as a clarion call to collectively work towards a world where the power of nature is harnessed responsibly, and the potential of natural products is fully realised for the betterment of humanity and our planet.

This conference serves as a platform for scholars, researchers, and industry experts to converge, collaborate, and exchange cutting-edge ideas, innovations, and discoveries in the realm of natural products. It provides an invaluable opportunity to foster interdisciplinary dialogue, share research findings, and explore avenues for collaboration and partnership. I am delighted to witness the diversity and expertise represented in this gathering. Each one of you plays a pivotal role in unlocking the vast potential of natural products and shaping the future of scientific advancements in this field. Let us seize this opportunity to engage in vibrant discussions, forge meaningful collaborations, and inspire one another with new ideas and perspectives. May the outcomes of the conference spur transformative changes and the birth of innovative solutions that address global challenges.

Once again, my appreciation and thanks to everyone involved in the making of this event. My deepest gratitude to all participants and attendees who have journeyed from near and far to join us in this remarkable event. Your presence here reflects the global significance of ICNP 2023 and our shared commitment to advancing scientific knowledge for the betterment of society. Lastly, I wish you all a fruitful and inspiring experience at this conference.

Profesor Datuk Dr. Hajah Roziah Mohd Janor
Vice Chancellor
Universiti Teknologi MARA



Recent Developments in Natural Product Chemistry for Health, Agriculture, and Beyond

Natural products, derived from plants, animals, fungi, and microbes, have been a rich source of bioactive compounds with diverse applications in health, agriculture, and various other fields. Over the past few years, significant advancements have been made in natural product chemistry, uncovering new compounds, elucidating their mechanisms of action, and exploring novel applications. New natural compounds with selective anticancer activities are being identified, offering potential solutions for personalized cancer therapy. Personalized therapies utilizing natural products based on individual genetic makeup hold the potential to revolutionize healthcare. Natural products are being explored for their potential to modulate stem cell behavior, opening avenues for regenerative medicine.

Natural products rich in antioxidants and anti-inflammatory agents hold promise for chronic disease prevention. Natural products could also be crucial in developing treatments for neglected tropical diseases that affect vulnerable populations in Africa and Asia. Amid growing antibiotic resistance, natural products are being explored as alternatives to conventional antibiotics. The legalization of cannabis has led to a surge in research on its bioactive compounds, uncovering potential medical uses. The discovery of bioactive molecules produced by gut microbiota has shed light on their role in maintaining human health and preventing diseases. Genetic manipulation using CRISPR-Cas9 has enabled the engineering of microbes to produce valuable natural products more efficiently. Natural products, such as anti-CRISPR proteins, have been identified as potent inhibitors of the CRISPR-Cas gene editing system. Advances in synthetic biology have facilitated the synthesis of complex natural compounds, enabling the creation of designer molecules. Peptides from natural sources are gaining prominence as potential therapeutics for various diseases, including cancer and microbial infections. Exploring natural products for their anti-aging properties could lead to interventions for promoting healthy aging. Nanotechnology is also impacting natural product chemistry. Incorporating natural products into nanomaterials has enabled targeted drug delivery and enhanced therapeutic efficacy. Another field of great potential is that of marine natural products. Exploration of marine ecosystems has yielded a plethora of unique natural products with pharmaceutical potential. Natural products are being investigated for their potential to modulate pathways involved in neurodegenerative disorders. Natural products with neuroprotective properties could offer breakthroughs in treating neurodegenerative diseases. Our work in this fascinating field will be described.

Integration of genomics, transcriptomics, proteomics, and metabolomics has revolutionized the identification and characterization of natural products. Another area that has come to the fore is that of artificial intelligence (AI). Machine learning algorithms are now being employed to predict bioactive compounds from natural sources, accelerating drug discovery.

Studying the complex interactions between plants and microbes has led to the discovery of novel natural products with agricultural applications, such as biopesticides and growth enhancers. Natural products involved in environmental signaling are being harnessed for sustainable agriculture and pest management. Developing environmentally friendly biopesticides from natural sources could mitigate the negative impacts of chemical pesticides. Enzymes from bacteriophages are finding applications in areas such as food safety and biofilm control.

As technology continues to evolve, the synergy between natural product chemistry and other scientific disciplines is likely to yield even more exciting discoveries and applications in the years to come. I hope that some of these emerging areas are being vigorously pursued at Aurlns in UiTM. I am greatly humbled that this Center has been named in my honour.

Professor Emeritus Dr. Atta-ur-Rahman FRS

FRS, N.I., H.I., S.T., T.I., Khwarizmi Laureate | Meritorious Professor

Honorary Life Fellow, Kings College, University of Cambridge, Cambridge, UK.

Patron-in-Chief International Center for Chemical & Biological Sciences, University of Karachi, Karachi, Pakistan.

CHAIRPERSON ICNP2023



Assalamualaikum and Good morning.

On behalf of the organising committee and Malaysian Natural Products Society, I am pleased and honored to welcome all distinguished guests and delegates to the International Conference on Natural Products 2023 (ICNP2023), Kuala Lumpur.

It is a great honour and opportunity for Universiti Teknologi MARA to be the main organiser of this year's meeting. ICNP was first held as *Seminar Tahunan Sebatian Semulajadi* to promote natural product research in Malaysia and elevate it to an international setting. The meeting was formally registered as the Malaysian Natural Products Society in 1995.

Since then, the meeting has been organized annually in Malaysia to promote networking in natural products research. The conference has become an important natural products meeting in Malaysia and regional regions.

The theme for this year's meeting is '*Changing the Landscape for a Sustainable Future*', which aspires to promote a paradigm shift as to how natural product science throughout the globe is pursued and conducted to efficiently harness endemic resources towards the sustainable translation of scientific findings for human benefit.

Malaysia is blessed with a plethora of biodiversity. It is estimated that at least 15,000 species of vascular plants in Malaysia, with about 8,300 species in Peninsular Malaysia and about 12,000 species in Sabah and Sarawak. At least 3000 plants have medicinal value. There are thousands of research in natural products, and many are yet to reach the bedside.

However, the rapid development of urban areas has tremendously depleted our natural resources. It is estimated the natural forest cover in Peninsular Malaysia was depleted from 70% in the 1970s to 44% in 1997. A sustainable approach to natural product research is crucial in ensuring the preservation of our biodiversity for the next generations.

This meeting is aspired to promote sustainable scientific findings from tree to bedside and serve as a platform to foster stronger research collaborations.

I would like to express appreciation to our strategic partners including industry players, research institutes, and universities who have all gracefully accepted our invitations to be part of this scientific gathering.

Wishing all delegates an enjoyable and fruitful meeting.

Professor Dr. Nor Hadiani Ismail FASc.

Chairperson International Conference on Natural Products 2023 (ICNP2023)

President Malaysian Natural Products Society (MNPS)

Director Atta-ur-Rahman Institute for Natural Product Discovery (AuRIns), UiTM



MNPS was formed as a spin-off from the ASOMPS VIII activity, which was successfully held in Melaka in 1994. It was first announced during the Symposium, and Dr. J. R. Cannon was the first and only recipient of its Gold Medal Award, as a gesture of recognition for his enormous contribution to the development of natural products research in Southeast Asia. It was anticipated that it is through this society that the voice of the members can be brought forth as one, to the center stage and to be heard by the policymakers for the sake of the advancement of its members as well as the science and technology status in the country. Science, and particularly Chemistry in Malaysia then was at its infancy. The main reason for forming the society (MNPS) was to create interest and awareness in natural product research among the local scientists and use it as the foundation to developing other research areas such as organic synthesis, analytical methodology, and medicinal chemistry as well as other associated sciences. At the same time, MNPS encouraged multidisciplinary collaborative research among the local scientists utilizing its Annual Meetings as the platform to initiate interaction between them.

The society was formally registered in 1995 with the main intentions as follows:

- To promote research in NP and elevate it to the international standing.
- To be used it as the platform for forum, dialogue, and interaction between fellow chemists, between chemists and other scientists as well as with relevant government agencies.
- To promote/enhance integrated research.
- To contribute in policy making (when requested) on matters related to NP research and development.

Prior to its formation efforts to build up research enthusiasm and capacity in NP were through the following initiatives (in chronological order)

- UNESCO Regional Network for the Chemistry of Natural Products in Southeast Asia – 1975. [through the National Point of Contact Representative (NPCR's) of the network.
- Network for the Chemistry of Biologically Important Natural Products [an initiative funded by Australia International Development Bureau (ADAB)] – 1987 to 1995.
- Jawatankuasa Kebangsaan bagi Rangkaian Serantau UNESCO dalam Bidang Kimia Sebatian Hasil Semulajadi (Suruhanjaya Kebangsaan UNESCO Malaysia) – 1987 to 1995.
- Sometime during 1980's and 90's initiatives by the Japanese Government were also established including JICA and JSPS, which have also contributed in one way or another to the growth of NP research in Malaysia.

The field of natural products has now advanced tremendously and the boundary of natural products as an exclusive field of study has become blurred due to overlap with other fields of science. NP chemists are no longer able to work in isolation for the sake of pursuing his (or her) own personal enthusiasm. One needs to explore a new approach to doing NP so that the benefits can be realized and shared. The challenge to stride forward and progress is always there, perhaps only in different forms at different times.





**Remembering Professor Jack
Richard Cannon
01.10.1927 – 08.08.2014**

Jack Richard Cannon or better known as Jack Cannon was born in Sydney, NSW in October 1927 and received his early education in Sydney. He graduated with first-class honours in Chemistry from the University of Sydney in 1948 and later with M.Sc from the same university. In 1951 he sailed to Cambridge to continue his study in Chemistry under the supervision of Sir Richard Todd and obtained his PhD, in 1954. He became a Visiting Research Fellow of the California Institute of Technology after the completion of his Ph.D. and later served as a Research Officer at CSIRO, Australia. He joined the Department of Chemistry, University of Western Australia (UWA) as a Senior Lecturer in 1959. He ended his career as the academic staff of UWA in 1992. During his tenure at UWA, he became a Fellow of the Royal Australian Chemical Institute (RACI) and a Research Associate at Rensselaer Polytechnic Institute, USA (1967), a Member of the Society of the Sigma Chi, the Scientific Research Society of North America (1967) and Acting Head of the Chemistry Department, UWA (1970-71).

His persistence to the service of his fellow scientists and to the public in general was recognized in many different ways. These include the Honorary D.Sc. from Prince of Songkhla University, the Einstein Gold Mode Award by UNESCO (1989), the Federation of Asian Chemical Societies Citation (1989), Honorary Professor of Chemistry at the University of Santo Tomas (1990), Honorary Research Fellow of the University of Western Australia (1992), Elected Fellow of Asian Chemical Society (1992), Gold Medal Award of the Malaysian Chemical Society (1994), Honorary D.Sc. from the University of Western Australia (1994), Member of the Order of Australia (1996), appointed Honorary Fellow of RACI (1996), and Appointed Honorary Member of the Natural Products Society of the Philippines (1996).

What made Jack special to the Chemistry of Natural Products in this region? There has not been a clear answer to this, but many of the earlier chemists in this region could only appreciate the benefits from his consistent advice and encouragement to indulge in research and his continuous assistance in carrying out research under a very limited capacity and discouraging environment. Indeed Jack has become a friend, a teacher, and a mentor to many of us.

How did he contribute? It began when he had a student from Thailand who told him (before the completion of his Ph.D. programme) about the near impossibility of doing research in his country. This remark triggered his sympathetic impulse to pursue ways to help this potentially good chemist and in the process, he also discovered the similar pathetic conditions (to do research) in other countries in the region including ours. He began his efforts in this direction by becoming the Advisor in Natural Products Chemistry under the Short-term Technical Assistance Programme at Prince of Sonkla University. His efforts were expanded through his involvement among others, as a Member of UNESCO Working Group to Plan the Federation of Asian Chemical Societies (1978), the Australian Representative to the Regional Network for the Chemistry of Natural Products in Southeast Asia (1979-82), a Member of the Australian National Commission for UNESCO (1980-82), a Member and Chairman of the Development Assistance Committee (1980-85), an Honorary Chairman of the Network for the Chemistry of Biologically Important Natural Products (1982-95), a Member of the Asian Coordinating Group for Chemistry (1983 - present), the

Consultant to International Development Program of Australian Universities and Colleges (1984), the Consultant for UNESCO Mission to Ethiopia on the Establishment of the National Science Center (1987), the AIDAB Consultant and Team Leader for the Tertiary Science Education Upgrading Programme in Burma (1988), the International Project Coordinator for the UNDP Project for Upgrading the Universities' Research Center in Myanmar (1991-93), and the Chairman of the International Relation Committee of the Royal Australian Chemical Institute. As the result of his efforts, directly or indirectly, publications of international standards began to appear from the laboratories of this science-deprived region. His tireless efforts in searching for ways to help the chemists and the field of chemistry in this region should become an inspiration to us in enhancing our efforts in promoting research in this country. His sincerity and honesty in helping other fellow chemists and people in general must be exemplary to all of us.

Naming this lecture after Prof. Jack Richard Cannon is our small way of showing our appreciation to this man's contribution to us and the field of chemistry in this country.

Professor Emeritus Dr. Md. Nordin Bin HJ. Lajis
Malaysian Natural Product Society

SCIENTIFIC PROGRAM

10 SEPTEMBER 2023													
6.00 - 8.00 pm	Early Registration Aloft Kuala Lumpur Sentral												
DAY 1 11 SEPTEMBER 2023													
8.00 - 8.20 am	Registration												
8.20 – 8.25 am	Quran Recital Ustaz Mohd Norhisyam Azman Academic Affairs, Universiti Teknologi MARA Cawangan Selangor.												
8.25 – 8.30 am	Welcome Remark from MNPS President & ICNP2023 Chairperson YBhg. Professor Dr. Nor Hadiani Ismail FASc.												
8.30 – 8.45 am	Opening Address Ybhg. Professor Datuk Dr. Hajah Roziah Mohd Janor Vice Chancellor, Universiti Teknologi MARA												
8.45 – 9.30 am	Keynote lecture Professor Emeritus Dr. Atta-ur-Rahman FRS, N.I., H.I., S.T., T.I., Khwarizmi Laureate Meritorious Professor International Centre for Chemical and Biological Sciences (ICCBS) Chairperson: Professor Dr. Nor Hadiani Ismail FASc.												
9.30 - 10.15 am	Jack Cannon lecture Professor Dr. Jean-Luc Wolfender University of Geneva Chairperson: Professor Emeritus Dr. Md Nordin Lajis												
10.15-11.00 am	Coffee break & poster presentation												
	Invited lectures												
	<table border="1"> <thead> <tr> <th>Ballroom A</th> <th>Ballroom B</th> </tr> </thead> <tbody> <tr> <td> Chairperson: Professor Dr. Doralyn S. Dalisay (USA) Moderator: Dr. Fatimah Salim (UiTM) </td> <td> Chairperson: Professor Dr. Mohamad Rafi (IPB, Indonesia) Moderator: Dr. Syahrul Imran Abu Bakar (UiTM) </td> </tr> <tr> <td> A1-1 Dr. Prathapa S. Jagannatha Product Manager and Application Scientist Bruker India Scientific Pvt. Ltd. </td> <td> B1-1 Professor Dr. Lalith Jayasinge National Institute of Fundamental Studies, Sri Lanka </td> </tr> <tr> <td> A1-2 Assistant Professor Dr. Rawiwan Charoensup Mae Fah Luang University, Thailand </td> <td> B1-2 Dr. Annie George Biotropics Malaysia Sdn Bhd </td> </tr> <tr> <td> A1-3 Mr. Manish Thakur Business Development Manager Purification-Asia BUCHI Laboratory Equipment </td> <td> B1-3 Professor Dr. Syarul Nataqain Baharum Universiti Kebangsaan Malaysia </td> </tr> <tr> <td> A1-4 Dr. Moses K. Langat Royal Botanic Gardens, UK </td> <td> B1-4 Associate Professor Dr. Premrutai Thitilertdecha Mahidol University, Thailand </td> </tr> </tbody> </table>	Ballroom A	Ballroom B	Chairperson: Professor Dr. Doralyn S. Dalisay (USA) Moderator: Dr. Fatimah Salim (UiTM)	Chairperson: Professor Dr. Mohamad Rafi (IPB, Indonesia) Moderator: Dr. Syahrul Imran Abu Bakar (UiTM)	A1-1 Dr. Prathapa S. Jagannatha Product Manager and Application Scientist Bruker India Scientific Pvt. Ltd.	B1-1 Professor Dr. Lalith Jayasinge National Institute of Fundamental Studies, Sri Lanka	A1-2 Assistant Professor Dr. Rawiwan Charoensup Mae Fah Luang University, Thailand	B1-2 Dr. Annie George Biotropics Malaysia Sdn Bhd	A1-3 Mr. Manish Thakur Business Development Manager Purification-Asia BUCHI Laboratory Equipment	B1-3 Professor Dr. Syarul Nataqain Baharum Universiti Kebangsaan Malaysia	A1-4 Dr. Moses K. Langat Royal Botanic Gardens, UK	B1-4 Associate Professor Dr. Premrutai Thitilertdecha Mahidol University, Thailand
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12.00 – 12.30 pm													
12.30 - 1.00 am													
1.00 – 2.15 pm	Lunch												

	Oral presentations (parallel sessions)			
	Ballroom A Chairperson: Professor Dr. Sukardiman (UNAIR) Co-Chairperson: Dr. Mohd Shukri Baba (IIUM)	Ballroom B Chairperson: Professor Dato' Dr. Ibrahim Jantan (MNPS) Co-Chairperson: Associate Professor Dr. Juriyati Jalil (UKM)	Tactic 3 Chairperson: Associate Professor Dr. Lam Kok Wai (UKM) Co-Chairperson: Associate Professor Dr. Najihah binti Mohd Hashim (UM)	Tactic 2 Chairperson: Dr. Nor Azah Binti Mohamad Ali (MNPS) Co-Chairperson: Associate Professor Dr. Monica Suleiman (UMS)
2.15 – 2.30 pm	O1-1 Associate Professor Dr. Wan Mohd Nuzul Hakimi Wan Salleh (UPSI)	O2-1 Dr. Lau Hui Jin (Sunway Medical Centre)	O3-1 Dr. Murni Nazira Sarian (UKM)	O4-1 Professor Ts. Dr. Asmah Awal (UiTM)
2.30 – 2.45 pm	O1-2 Nor Syaidatul Akmal Mohd Yousof (IMR)	O2-2 Dr. Nurul Yuziana Mohd Yusof (UKM)	O3-2 Dr. Mohamad Nurul Azmi Mohamad Taib (USM)	O4-2 Dr. Fauziah Abdullah (FRIM)
2.45 – 3.00 pm	O1-3 Ahmad Alif Danial Zailan (USM)	O2-3 Dr. Chia Shir Reen (UNITEN)	O3-3 Nurul Alam Inayatsyah Saifuddin (UiTM)	O4-3 Anis Hazirah Izzati Hasnu Al Hadi (UiTM)
3.00 – 3.15 pm	O1-4 Dr. Muhammad Safwan bin Ahamad Bustamam (UPM)	O2-4 Dr. Nur 'Izzati Mansur (UKM)	O3-4 Tengku Kamilah binti Tengku Nazmi (IIUM)	O4-4 Nurul Najwa Binti Rusmadi (USM)
3.15 - 3.30 pm	O1-5 Dr. Tutik Sri Wahyuni (UNAIR)	O2-5 Dr. Retno Widyowati (UNAIR)	O3-5 Abubakar Siddiq Salihu (UPSI)	O4-5 Dr. Zunoliza Abdullah (FRIM)
3.30 – 3.45 pm	O1-6 Associate Professor Dr. Siow-Ping Tan (TARC)	O2-6 Nur Raihan Aqilah Binti Mohammad Azmin (UiTM)	O3-6 Dr. Natale Badalamenti (Italy)	O4-6 Muhammad Idham Bin Shukor (IIUM)
3.45 – 4.00 pm	O1-7 Professor Dr. Velazhahan Rethinasamy (Oman)	O2-7 Dr. Mohamad Shazeli Che Zain (USM)	O3-7 Mohd Faris Osman (UPM)	O4-7 Norhaliza Ahad (UNIMAS)
4.00 – 4.15 pm	O1-8 Nurin Syamimi binti Ahmad Izuren Shah (IIUM)	O2-8 Professor Dr. Sukardiman (UNAIR)	O3-8 Dr. Nisha Thopla Govender (UKM)	O4-8 Siti Mariatul Hazwa Mohd Huzir (UiTM)
4.15 – 4.30 pm	O1-9 Dr. Maulidiani (UMT)	O2-9 Dr. Getha Krishnasamy (FRIM)	O3-9 Dr. Relicardo M. Coloso (USA)	O4-9 Dr. Mohd Fazlin Rezali (National Metrology Institute of Malaysia)
4.30 – 4.45 pm	O1-10 Dr. Fadzureena Jamaludin (FRIM)	O2-10 Dr. Noorhaslina Binti Hashim (Aafiyat Group)	O3-10 Subhan Rullyansyah (UNAIR)	O4-10 Dr. Idha Kusumawati (UNAIR)
4.45 – 5.00 pm	Coffee break & poster presentation			
8.00 – 11.00 pm	Conference reception			

DAY 2	12 SEPTEMBER 2023			
8.30 – 9.15 am	Plenary lecture 1 Professor Dr. Dulcie Mulholland University of Surrey Chairperson: Professor Dr. Mukram McKeen			
9.15 – 10.00 am	Plenary lecture 2 Professor Datuk Wira Dr. Raha Abdul Rahim FASc. CEO, National Institute of Biotechnology Malaysia Chairperson: Professor Emeritus Dato' Dr. Ikram M. Said			
10.00-10.45 am	Coffee break & poster presentation			
	Invited lectures			
	Ballroom A Chairperson: Professor Dr. Hasnah Mohd Sirat (MNPS) Moderator: Dr. Roza Dianita (USM)		Ballroom B Chairperson: Professor Dr. Khozirah Shaari (MNPS) Moderator: Dr. Nurliana Abd Mutalib (UiTM)	
10.45 – 11.15 am	A2-1 Professor Dr. Doralyn S. Dalisay University of San Agustin		B2-1 Professor Dr. Mohamad Rafi, Ssi., Msi Institut Pertanian Bogor	
11.15 – 11.45 am	A2-2 Dr. Teh Chin Hoe NMR Application Scientist, Bruker Malaysia		B2-2 Mr. Khongwattananon Kwanchai Director of MRS Sales SEA, Taiwan & Oceania, Bruker	
11.45 – 12.15 pm	A2-3 Dr. K. B. Rameshkumar Jawaharlal Nehru Tropical Botanic Garden and Research Institute, India		B2-3 Professor Dr. Faridah Abas FRSC Universiti Putra Malaysia	
12.15 – 12.45 pm	A2-4 Professor Mario A. Tan, Ph.D. University of Santo Thomas, Philippines		B2-4 Mr. Mohamad Faisal Ahmad Fadzil Founder and Managing Director FA Herbs & Tanamera Tropical Spa Personal Care	
12.45 – 1.15 pm	A2-5 Professor Dr. A. Ganesan University of East Anglia, UK		B2-5 Dr. Mohd Ridzuan Mohd Abdul Razak Institute of Medical Research, Ministry of Health	
1.15 - 2.15 pm	Lunch			
	Oral presentations (parallel sessions)			
	Ballroom A Chairperson: Professor Dr. Faridah Abas (UPM) Co-Chairperson: Dr. Thiruventhan Karunakaran (USM)	Ballroom B Chairperson: Professor Dr. Syarul Nataqain Baharum (UKM Bangi) Co-Chairperson: Dr. Rozaini Mohd Zohdi (UiTM)	Tactic 3 Chairperson: Professor Dr. Jonel P. Saludes (Philippines) Co-Chairperson: Associate Professor Dr. Wan Mohd Nuzul Hakimi Wan Salleh (UPSI)	Tactic 2 Chairperson: Professor Dr. Intan Safinar Ismail (UPM) Co-Chairperson: Dr. Mohamad Nurul Azmi Mohamad Taib (USM)
2.15 – 2.30 pm	O1-11 Professor Dr. Aty Widyawaruyanti (UNAIR)	O2-11 Noor Izzah Abd Rahman (UPM)	O2-20 Dr. Nurliana Abd Mutalib (UiTM)	O1-22 Mailina Jamil (FRIM)

2.30 – 2.45 pm	O1-12 Hidayatul Atiqah binti Abd Karim (UiTM)	O2-12 Dr. Fauziahanim Zakaria (USM)	O2-21 Dr. Hamizah Shahirah Binti Hamezah (UKM)	O1-23 Dr. Fatimah Salim (UiTM)
2.45 – 3.00 pm	O1-13 Kamsirah Binti Jim Shamsudin (UiTM)	O2-13 Anita binti Kamaruddin (UM)	O2-22 Muhammad Nor Farhan Saat (IKN)	O1-24 Nor Amalia Nazri (USM)
3.00 – 3.15 pm	O1-14 Professor Dr. Norizan Ahmat (UiTM)	O2-14 Dr. Salfarina Ramli (UiTM)	O2-23 Dr. Roza Dianita (USM)	O1-25 Dr. Melissa June Paderog (USA)
3.15 - 3.30 pm	O1-15 Nurul Shahira Zakaria (UiTM)	O2-15 Dr. Nurul Shafiqah Hashim (Aafiyat Group)	O2-24 Siti Norliyana binti Che Mat Zubaidi (UPM)	O1-26 Adiana Mohamed Adib (UiTM)
3.30 – 3.45 pm	O1-16 Isna Athirah Othman (UiTM)	O2-16 Nur Khaleeda Zulaikha Zolkeflee (UPM)	O2-25 Iman Nabilah Abd Rahim (UiTM)	O1-27 Dr. Siti Zuraidah Mohd Zobir (NIBM)
3.45 – 4.00 pm	O1-17 Dr. Ahmad Nazif bin Aziz (UMT)	O2-17 Dr. Norfahana binti Abd Talib (Aafiyat Group)	O2-26 Wong Pei Lou (UPM)	O3-11 Yasothaa Ramaiyah (UKM)
4.00 – 4.15 pm	O1-18 Nursabrina Najwa binti Salmin (UiTM)	O2-18 Dr. Nurhanan Murni Yunos (FRIM)	O1-20 Ainur Awanis binti Mohd Badiazaman (UNISZA)	O3-12 Alim Alsukor Aznirulhisham (UiTM)
4.15 – 4.30 pm	O1-19 Nur Syahidah Shahrudin (NIBM)	O2-19 Chen Chee Shien (TARUC)	O1-21- Siti Zakirah Azahar (UiTM)	O3-13 Dr. Abubaker Mustafa Abdelaal Elsayed (UPSI)
4.30 – 5.00 pm	Coffee break & Poster presentation			
5.00 - 6.00 pm	MNPS annual meeting			
8.00 – 10.00 pm	Kuala Lumpur City Tour			

DAY 3		13 SEPTEMBER 2023		
8.30-10.30 am	Ballroom A Special Workshop on Herbal Medicine Research Guidelines Speakers: Dr. Siti Hajar Muhamad Rosli Dr. Khadijah Mustapha Kamal Dr. Ami Fazlin Syed Mohamed Dr. Puspawati Krishnan	Ballroom B Bruker NMR Workshop Speakers: Dr. Teh Chin Hoe Mr. Khongwattananon Kwanchai Bruker Malaysia	Tactic 2 Commercialisation of a Natural Product: Larixyne, a Case Study. Speakers: Professor Dr. Dulcie Mulholland University of Surrey	8.30-11.30 Tactic 3 LCMS: Introduction to metabolomics and compound annotation Speakers: Professor Dr. Jean-Luc Wolfender (University of Geneva) Dr. Dhaval Patel (Thermo Fischer Scientific)
	10.30-11.15 am	Coffee Break		
11.15 – 1.15 pm	The Future of Natural Products in Regional Development. Chairperson: Professor Dr. Nor Hadiani Ismail FASc. Host: Professor Emeritus Dr. Geoffrey A. Cordell Guests Professor Dato' Dr. Ibrahim Jantan (Malaysia) Professor Dr. Jonel P. Saludes (Philippines) Associate Professor Dr. Premrutai Thitilertdecha (Thailand) Professor Dr. Mohamad Rafi Msi. Ssi. (Indonesia) Mr. Mohamad Faisal Ahmad Fadzil (Malaysia)			
1.15 – 2.30 pm	Lunch			
2.30 – 3.15 pm	Plenary Lecture 3 Professor Emeritus Dr. Geoffrey A. Cordell Natural Products Inc. USA Chairperson: Professor Emeritus Dato' Dr. Laily Din			
3.15 - 4.15 pm	Prize-Giving Ceremony Closing remarks			
4.15 - 5.00 pm	Coffee and Farewell			



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O3-4

Design and Synthesis of Xanthorrhizol Derivatives Using *in Silico* Fragment-Based Drug Design (FBDD) Approach as Hyaluronidase Inhibitors

Tengku Kamilah Tengku Nazmi¹, Nurul Iman Aminudin^{1,*}, Nurasyikin Hamzah¹, Mazura Md Pizar², Siti Nur Aisyah Mohd Hashim²,

¹ Department of Chemistry, Kulliyah of Science, International Islamic University Malaysia (IIUM), 25200, Kuantan, Pahang, Malaysia.

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Abstract: Xanthorrhizol (XNT), a sesquiterpene found in *Curcuma xanthorrhiza*, possesses anti-inflammatory properties *via* the inhibition of pro-inflammatory enzymes such as cyclooxygenase (COX), and inducible nitric oxide synthase (iNOS) and lipoxygenase (LOX). With its small molecular weight (281.33 g/mol) and biological activity, XNT is a promising active compound to be further enhanced as a more potent anti-inflammatory agent. An Initial *in vitro* screening study demonstrated low activity (IC₅₀ value = 103.21 µg/mL) of XNT against hyaluronidase (Hyal), another pro-inflammatory enzyme responsible for the generation of small hyaluronic acid fragments that can induce inflammation in the human body. With its small molecular weight (281.33 g/mol) and ? biological activity, XNT is a promising compound to be further optimised as a more potent anti-inflammatory agent, due to its small molecular weight (281.33 g/mol) and good biological activity. Hence, our objective of this study was to optimise and enhance the XNT's activity against Hyal by designing its derivatives and modifying its hydroxyl functionality *via in silico* fragment-based drug design approach using a combination of *in silico* computational techniques, namely molecular docking and fragment-based drug design (FBDD). In this study, we employed a fragment of software called LigBuilder software was employed to generate a total of 1195 novel XNT derivatives of XNT as potential Hyal inhibitors. From these derivatives, The top 100 compounds exhibiting binding energies ranging from -7.8 to -8.5 kcal/mol were assessed *via* molecular docking studies using AutoDock Vina were selected. These derivatives featured diverse cyclic ring systems as the new fragments in the XNT structure. Subsequently, these generated derivatives underwent further evaluation and modification based on their ADME (absorption, distribution, metabolism, and excretion) properties, druglikeness as well as synthetic accessibility of these derivatives, resulting in the generation identification of the final five structures of XNT derivatives. promising XNT derivatives. These derivatives were synthesised and their activity against Hyal enzyme was evaluated through *in vitro* enzyme inhibition assay. All derivatives exhibited improved activity against Hyal enzyme, ranging from 44.45 to 93.71 µg/mL. Among them, the 3-methylenoxypyridine derivative, exhibited the best activity against Hyal with an IC₅₀ value of 44.54 µg/mL. This research demonstrated the efficiency of *in silico* computation methods in facilitating drug design and modification to produce novel compounds with enhanced potency.

Keywords: Xanthorrhizol; hyaluronidase; *in silico* fragment-based drug design; molecular docking; ADME profile; anti-inflammatory activity

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