

〔大学院総合医薬学研究科総合医薬学専攻博士前期課程〕

〔Graduate School of Medicine and Pharmaceutical Sciences (Master's Course)〕

先端薬科学プログラム (Pharmaceutical Sciences)

受験番号 (Examinee's No.)

科目名 (Subject)

小論文・適性検査 (Short Essay and Aptitude Test)

氏 名 (Name)

(裏面にわたる場合は、この線より下に解答すること。)

(If your answer is longer than the space provided, you can write on the back of this page, but please write below this line.)

- (1) 近年、人工知能 (AI) 技術が創薬研究に活用されるようになってきている。これにより薬学研究者の役割にどのような変化が求められるか、あなたの意見を述べなさい。

In recent years, artificial intelligence (AI) technologies have increasingly been applied to drug discovery research. Please discuss how this development is changing the roles and responsibilities of pharmaceutical researchers, and present your perspective on the matter.

- (2) 大学院で取り組みたい研究について、これまでの学修・研究経験との関連を踏まえつつ、倫理・多様性への配慮、国内外への波及効果および将来のキャリア形成への活用について、薬学的視点から論理的かつ具体的に述べなさい。

Please discuss the research you wish to conduct in graduate school, drawing on your previous academic and research experiences. Address ethical considerations, respect for diversity, potential impact of your research both domestically and internationally, and how it may contribute to your future career development. Provide a logical and concrete discussion from a pharmaceutical viewpoint.

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In recent years, artificial intelligence (AI) technologies have increasingly been applied to drug discovery research. Please discuss how this development is changing the roles and responsibilities of pharmaceutical researchers, and present your perspective on the matter.

【出題の意図】

近年急速に進展している AI 技術の導入により、創薬研究の在り方は大きく変化しつつある。このような状況において、受験者が AI とどのように向き合い、薬学研究者としての視点からその役割や課題をどのように捉えているかを論じさせることで、論理的思考力および文章構成力を評価するとともに、AI に対する基礎的理解や応用力を測ることを目的とする。

【解答例】

定型的な解答は求めておらず、AI 技術に対する理解と、それに伴う薬学研究者の役割についての見解が、論理的かつ一貫性をもって述べられていれば評価に値する。

【Purpose of the Question】

With the rapid advancement of artificial intelligence (AI) technologies, the landscape of drug discovery research is undergoing significant transformation. This question aims to assess how applicants engage with AI from the perspective of pharmaceutical research, and to evaluate their ability to construct logical arguments in writing, as well as their understanding and application of AI-related knowledge.

【Sample Answer】 There is no single correct answer. Responses will be positively evaluated if the applicant demonstrates a clear and logical understanding of AI technologies and articulates a well-reasoned view on the evolving role of pharmaceutical researchers in this context.

- (2) 大学院で取り組みたい研究について、これまでの学修・研究経験との関連を踏まえつつ、倫理・多様性への配慮、国内外への波及効果および将来のキャリア形成への活用について、薬学的視点から論理的かつ具体的に述べなさい。

Please discuss the research you wish to conduct in graduate school, drawing on your previous academic and research experiences. Address ethical considerations, respect for diversity, potential impact of your research both domestically and internationally, and how it may contribute to your future career development. Provide a logical and concrete discussion from a pharmaceutical viewpoint.

【出題の意図】

大学院で取り組もうとする研究について、これまでの学修および研究経験との関連性を踏まえつつ、倫理的配慮、多様性の尊重、社会的責任への意識を含めた視点から論じさせることにより、薬学研究に対する理解と姿勢を確認する。また、研究成果の波及効果や将来のキャリア形成への展望についての考察を通じて、薬学的視野とグローバルな感覚が備わっているかを評価する。

【解答例】

定型的な解答を求めるものではなく、受験者自身の研究への関心や計画が、過去の経験と結びつけて論理的かつ具体的に述べられており、加えて倫理・多様性への配慮、社会への貢献、将来のキャリア形成との関連性が的確に示されていれば望ましい。

【Purpose of the Question】

This question invites applicants to discuss the research they intend to pursue in graduate school, while reflecting on the relevance of their prior academic and research experiences. It also aims to evaluate their awareness of ethical considerations, respect for diversity, and sense of social responsibility. Furthermore, by addressing the potential societal impact of their research and its role in future career development, the question assesses whether the applicant possesses both a solid pharmaceutical perspective and a globally informed outlook.

【Sample Answer】

There is no single model answer. Ideal responses should present the applicant's research interests in a logical and concrete manner, drawing clear connections to their previous academic and research background. In addition, thoughtful consideration of ethics, diversity, societal impact, and future career relevance will be regarded favorably.

先端薬科学プログラム (Pharmaceutical Sciences)

受験番号 (Examinee' s No.)

科目名 (Subject) 外国語 (英語) (Foreign Language (English)) 氏 名 (Name)  
(全 / 枚中の / 枚目)

(裏面にわたる場合は、この線より下に解答すること。)

(If your answer is longer than the space provided, you can write on the back of this page, but please write below this line.)

Read the following sentences and answer each question.

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Please note that the text in this section cannot be published due to copyright laws.

(authority: Dong Dong et. al., Biochemical Pharmacology 178, 114045, 2020, partially modified)

Question 1. What is responsible for the cycles of physiology and behavior in mammals and other species?  
( )

Question 2. If a human being is placed in an environment where time is unknowable, and is made to live with an intrinsic rhythm, how many hours per day does he/she live?  
( )

Question 3. In mammals, where is the central clock localized?  
( )

Question 4. What are the mechanisms by which the central clock synchronizes the peripheral clocks?  
( )

Question 5. What are the four major pharmacokinetic processes?  
( ), ( ), ( ), ( )

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Read the following sentences and answer each question.

(authority: Dong Dong et. al., Biochemical Pharmacology 178, 114045, 2020, partially modified)

Question 1. What is responsible for the cycles of physiology and behavior in mammals and other species?

( planet's rotation )

Question 2. If a human being is placed in an environment where time is unknowable, and is made to live with an intrinsic rhythm, how many hours per day does he/she live?

( 25 h )

Question 3. In mammals, where is the central clock localized?

( suprachiasmatic nuclei (SCN) )

Question 4. What are the mechanisms by which the central clock synchronizes the peripheral clocks?

( nervous and hormonal signals )

Question 5. What are the four major pharmacokinetic processes?

( absorption ), ( distribution ), ( metabolism ), ( excretion )

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科目名(Subject) 外国語(英語)(Foreign Language(English)) 氏名(Name)

(全1枚中の1枚目)

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(1) Read the following text and answer the questions.

(著作権処理のため省略)

(Cited from Y. Matsuya, *et al.*, HETEROCYCLES 65 (2005) 1741–1749, the Japan Institute for Heterocyclic Chemistry, partially modified)

a) Summarize the biological activities of macrospinelides in English or Japanese.

b) Describe the importance of synthetic studies of macrospinelides including your own ideas in English.

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(Cited from Y. Matsuya, *et al.*, HETEROCYCLES 65 (2005) 1741–1749, the Japan Institute for Heterocyclic Chemistry, partially modified)

a) Summarize the biological activities of macrosphelides in English or Japanese.

【出題の意図 (Intention of the question)】

英文読解力と情報整理能力を確認する。

【解答例 (Sample Answer)】

天然物であるマクロスフェライド類は、これまでに A-L の 12 種類が単離されており、それぞれ生物活性を示すことが知られている。最初に報告されたのは、マクロスフェライド A と B の強力な細胞接着阻害活性である。ヒト Leukemia HL-60 細胞と HUVEC との接着阻害が、投与量依存的に起こることが確認されている。その他のマクロスフェライド類においても、同様の活性が確認されている。その他、免疫抑制作用や抗真菌作用も報告されている。

b) Describe the importance of synthetic studies of macrosphelides including your own ideas in English.

【出題の意図 (Intention of the question)】

英文読解力および英作文力を確認する。

【解答例 (Sample Answer)】

個々人により記載内容は異なる。

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The following column is the first paragraph of “Preface: To the Student” of the text book titled “The Art of Writing Reasonable Organic Reaction Mechanisms (Third Edition)” written by Robert B. Grossman (Springer Nature Switzerland AG 2019).  
Read it and answer the following question in English.

著作権処理のため省略

#### Question

The author said that to draw reasonable mechanisms is similar to drawing the travel. You have traveled from your home town to Toyama when you came here.

Explain your travel from your home town to Toyama like as describing a reaction mechanism.

For example,

(the mechanism): This conversion includes 3 steps. The first step is from New York to Pennsylvania through New Jersey. The second step is .....

You should point out (an overall reaction), (the mechanism), (reaction conditions), (intermediates), (side reactions), and also the speed at various points and more than one way (alternative route) in your travel.

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## 【出題の意図 (Intention of the question)】

英文読解力、想像力、英文作成力を問う。

## 【解答例 (Sample Answer)】

I am from Osaka. So I travel from Osaka to Toyama.

(an overall reaction): The starting Osaka is converted into Toyama.

(the mechanism): This reaction is two step conversion, and firstly it produces Tsuruga which is converted into Toyama.

(reaction conditions): The first reaction proceeds under the express “Thunderbird” conditions then the second reaction is carried out under the super-express “Kagayaki” conditions.

(intermediates): In the first step, Kyoto is formed as an intermediate, and the second reaction goes through Kanazawa.

(side reactions): When the second reaction proceeds under “Tsurugi” conditions, Fukui and the other compounds can be formed as intermediates. These intermediates can cause the side reactions to give complex mixture.

the speed at various point: The first reaction is slower than the second one. This means the first step would be the rate-determining step.

an alternative route: As an alternative route to Toyama, we can go to Nagoya first under “Shinkansen” conditions then to Toyama though Takayama under “Hida” conditions. But the second Hida conditions needs very long reaction time, so usually we would not select this route.



〔大学院総合医薬学研究科総合医薬学専攻博士前期課程〕(外国人留学生特別入試)

先端薬科学プログラム (Pharmaceutical Sciences)

科目名 (Subject)

受験番号 (Examinee's No.)

小論文・適性検査 (Short Essay and Aptitude Test)

分野名 (Educational Area) Synthetic and Medicinal Chemistry 氏 名 (Name)

(裏面にわたる場合は、この線より下に解答すること。)

(If your answer is longer than the space provided, you can write on the back of this page, but please write below this line.)

(1) Explain the following reactions and stereoselectivities using suitable examples in English or Japanese.

(a) Diels-Alder reaction and *endo* rule

(b) Wittig reaction and *E/Z* selectivity

(2) Describe your research plan during the 2-year master's course in English or Japanese.

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(a) Diels-Alder reaction and *endo* rule(b) Wittig reaction and *E/Z* selectivity

【出題の意図 (Intention of the question)】

有機化学における基礎知識のレベルと説明表現力を確認する。

【解答例 (Sample Answer)】

- (a) Diels-Alder 反応は、1,3-ブタジエン誘導体（ジエン）とアルケン誘導体（ジエノフィル）との間での環化付加反応の1種で、シクロヘキセン誘導体が生成物となる。反応機構は、 $6\pi$ 電子による協奏的な環化であり、一般的な形では、ジエンの HOMO とジエノフィルの LUMO との相互作用（逆の場合もある）により反応が進行する。置換様式によっては、2種のジアステレオマーが生成する場合があります。置換基が内向きの遷移状態を経ると *endo* 付加体が、置換基が外向きの遷移状態を経ると *exo* 付加体が生成する。前者の遷移状態では、ジエノフィルの置換基の二次軌道相互作用が働いて安定化され、*endo* 付加体が優先的に生成することがあり、これをエンド則とよぶ。
- (b) Wittig 反応は、ホスホラン（ホスホニウムイリド）と、アルデヒドまたはケトンとの間で結合の組み換えが起こる反応で、アルケン類とホスフィンオキシドを与え、アルケン類の合成法として有用である。生成するアルケンに幾何異性体（*E* 体と *Z* 体）がある場合は、その立体選択性が問題となる。一般に、ホスホニウムイリドにカルボニル基のような電子求引性置換基がある場合（安定イリド）は *E* 体が優先し、そのような置換基がない場合（不安定イリド）は *Z* 体が優先して生成するが多い。

(2) Describe your research plan during the 2-year master's course in English or Japanese.

【出題の意図 (Intention of the question)】

有機化学研究に対するビジョンと説明表現力を確認する。

【解答例 (Sample Answer)】

個々人により記載内容は異なる。

先端薬科学プログラム (Pharmaceutical Sciences)

科目名 (Subject)

受験番号 (Examinee's No.)

小論文・適性検査 (Short Essay and Aptitude Test)

分野名 (Educational Area)

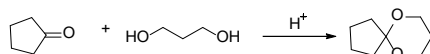
氏名 (Name)

分子合成化学 (Synthetic and Biomolecular Organic Chemistry)

(裏面にわたる場合は、この線より下に解答すること。)

(If your answer is longer than the space provided, you can write on the back of this page, but please write below this line.)

Q1 Draw a reasonable mechanism for the following organic reaction.



Q2 Aromatic compounds such as substituted benzenes can react with acyl chlorides or acid anhydrides to give acylated aromatic products.

1) This reaction is well known as a name reaction.

What is the name of this reaction?

reaction name:

2) This reaction needs an additive to proceed the desired reaction.

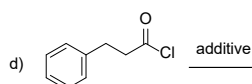
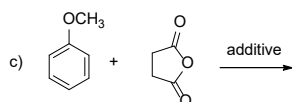
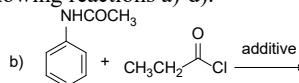
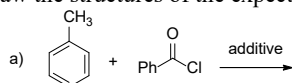
What is the most common additive for this reaction?

additive:

3) Draw a reasonable mechanism for the reaction of benzene with acetyl chloride in the presence of an additive.

4) The electronic nature of the substituents on an aromatic ring has a strong effect on the regioselectivity of the reaction.

Draw the structures of the expected major products in the following reactions a)-d).



5) This acylation reaction of benzene gives only mono-acylated product without any di- and tri-acylated compounds, while the similar alkylation of benzene affords poly-alkylated products as by-products. Explain the reason why this difference is observed, in English.

6) This reaction needs the excess amount of the additive, while the similar alkylation requires the only catalytic amount of the additive. Explain the reason why this difference is observed, in English.

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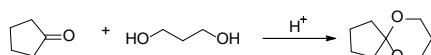
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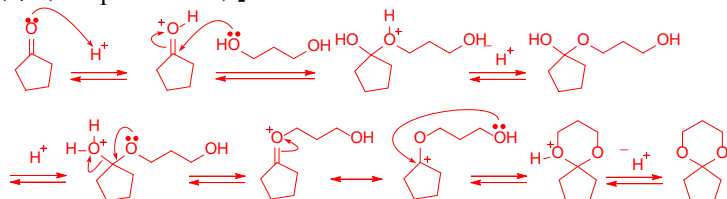
Q1 Draw a reasonable mechanism for the following organic reaction.



【出題の意図 (Intention of the question)】

基本的な酸触媒有機化学反応の反応機構の理解度を問う。

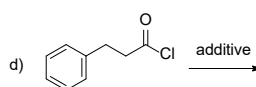
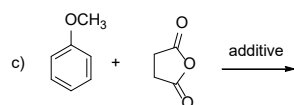
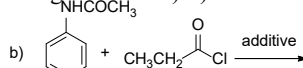
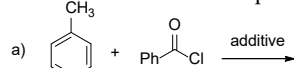
【解答例 (Sample Answer)】



Q2 Aromatic compounds such as substituted benzenes can react with acyl chlorides or anhydrides to give acylated aromatic products.

- 1) This reaction is well known as a name reaction. What is the name of this reaction?
- 2) This reaction needs an additive to proceed the desired reaction. What is the most common additive for this reaction?
- 3) Draw a reasonable mechanism for the reaction of benzene with acetyl chloride in the presence of an additive.
- 4) The electronic nature of the substituents on an aromatic ring has a strong effect on the regiochemistry of the reaction.

Draw the structures of the expected major products in the following reactions a)-d).



- 5) This acylation reaction of benzene gives only mono-acylated product without any di- and tri-acylated compounds, while the similar alkylation of benzene affords poly-alkylated products as by-products. Explain the reason why this difference is observed, in English.
- 6) This reaction needs the excess amount of the additive, while the similar alkylation requires the only catalytic amount of additive. Explain the reason why this difference is observed, in English.

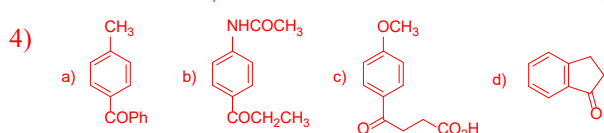
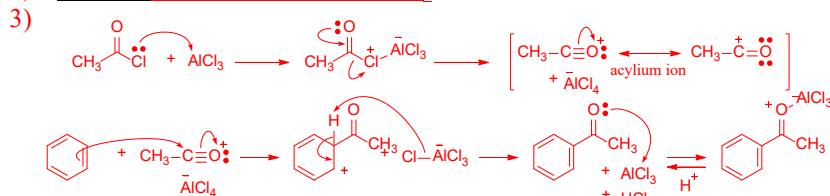
【出題の意図 (Intention of the question)】

基本的な炭素炭素結合反応の理解度を問う。

【解答例 (Sample Answer)】

1) reaction name: Friedel-Crafts (acylation) reaction ○○

2) additive: aluminum chloride, AlCl<sub>3</sub>



- 5) An acyl group in the product, acylbenzene, is electron withdrawing group that can deactivate the Friedel-Crafts reaction. Therefore, acylbenzene does not react any more.
- 6) In alkylation reaction, <sup>-</sup>AlCl<sub>4</sub> abstracts the proton from arenium ion to regenerate AlCl<sub>3</sub> and HCl. The resultant AlCl<sub>3</sub> can react with another starting material. However, in acylation, regenerated AlCl<sub>3</sub> forms the complex with the product and it cannot react any more.