

Before you begin:

A brief comment: Some of the schemes had russian words in the actual scheme images. Some of these have been translated into english, however some are still in russian. If you feel it is necessary to translate these words (I no longer remember if the untranslated words were necessary), it may interest you to pass a screenshot of the russian words in question through Yandex image translation.

Solutions to all problems can be found at
<http://www.chem.msu.ru/rus/olimp/welcome.html>

The russian national olympiads are on the right column titled Всероссийские олимпиады школьников по химии (or All-Russian Chemistry Olympiads in english). Simply go to the year that you're looking for and find the solutions link (for some years this might take some digging)

Lastly, I tried to rate some of the questions with difficulty ratings since I find such things amusing. My advice however is to not pay too much attention to the numerical ranking and just try the problem if it looks interesting.

Difficulty Rating

- 1: Generic USNCO style extremely short scheme
- 2: Older ICHO/older UKCHO (lots of intermediates, hints etc.)
- 3: Legitimate scheme with beginner reagents (1987 ICHO #4)
- 4: Some more intermediate reagents (2016 ICHO #6, harder UKCHOs)
- 5: Advanced reagents, but the problem isn't that hard overall (2014 ICHO #7)
- 6: Problem solving required, but not too long (2016 ICHO #7, second half)*
- 7: Very nontrivial, but doable given enough time and trial & error
- 8: Extreme Cleverness required, difficult-impossible for 80-90% of campers (2015 ICHO #6)
- 9: Impossible. (Tetracycline, Russian Camp)

*5 & 6 are roughly interchangeable. Hard reagents are intimidating if you've never seen them before. Problem solving is always difficult. I ranked 6 above 5 because advanced reagents can be fixed by experience, but problem solving is something you need to work for.

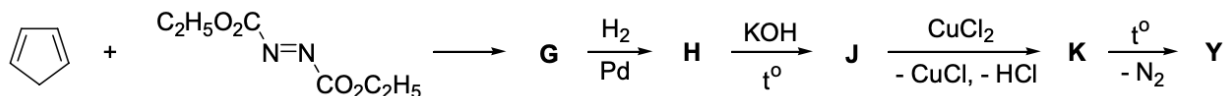
On some questions I've left hints that are highlighted in black in case you don't want to see them. For example:

HINT: XXXXXXXXXX

If you want to view the hint, simply highlight the text and the highlighting will make it viewable (or you can copy paste it without formatting into a word doc etc).

2011 Russia Tour 1 Class 11 Task 4 Abridged

Substance **Y** has formula C_5H_8 . For a long time, this compound was considered the champion in the length of one of the C – C bonds (1.62 Å). It is known that **Y** also does not interact with a solution of $KMnO_4$ at $0^\circ C$. One of the syntheses of **Y** was carried out from cyclopentadiene and DEAD according to the scheme

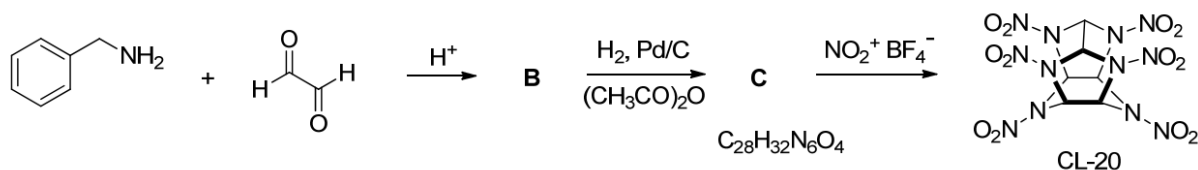


4. Write the structural formulas of compounds **G** - **K**, **Y**.

5. Write the formulas of the three other C_5H_8 isomers that do not discolor the potassium permanganate solution.

2012 Russia Tour 2 Organic Task 1 Abridged (pt 1)

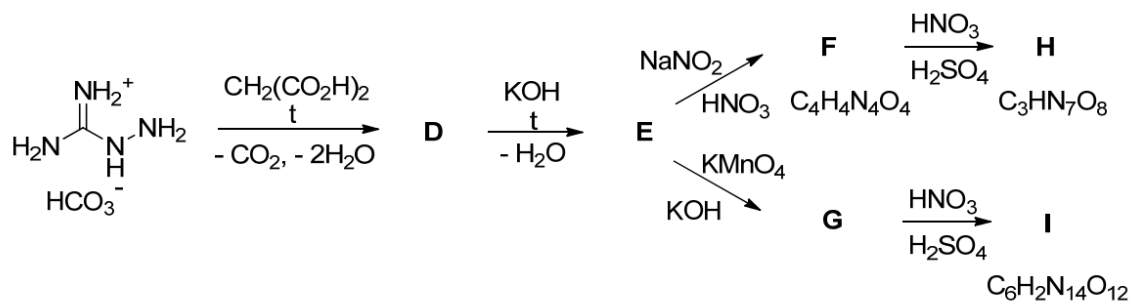
CL-20 is prepared as follows:



Draw **B** and **C**.

2012 Russia Tour 2 Organic Task 1 Abridged (pt 2)

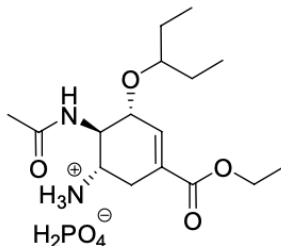
Recently, American scientists have described a series of high-energy substances based on nitro-containing heteroaromatic compounds:



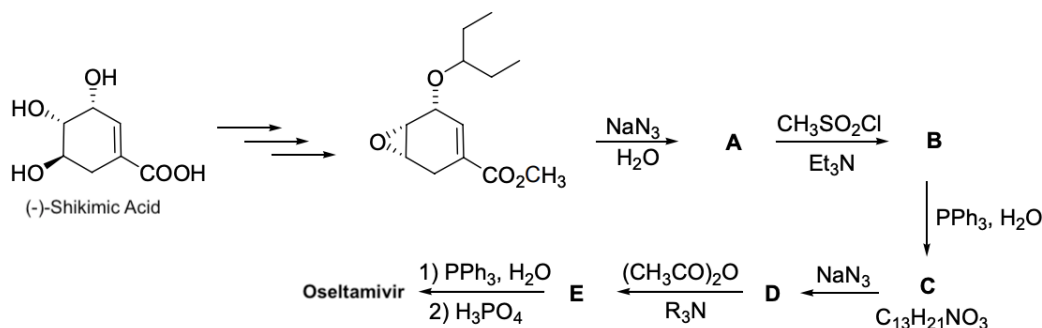
Draw **D**-**I**

2011 Russia Tour 2 Organic Task 1

In 2009, a swine flu pandemic swamped the world, the virus of which was resistant to exposure to commonly used M2 protein inhibitors such as rimantadine and amantadine in the treatment of conventional flu. Effective against swine flu are only compounds which inhibit the enzyme neuraminidase. The most popular drug of this type is Oseltamivir (trade name Tamiflu):

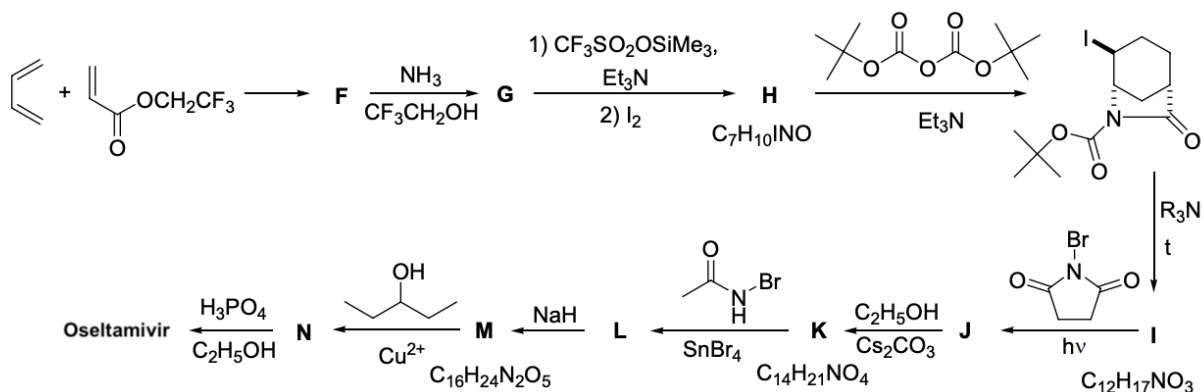


This drug was developed by Gilead Sciences Inc. Scientists of this company used natural (-)-shikimic acid as the starting material (a simplified synthesis scheme is given below):



1. Write the structural formulas of compounds **A** – **D**, taking into account that the opening of the three-membered ring by nucleophiles can be considered as an example of the S_N2 reaction, that is, the attack by the nucleophile proceeds at the less hindered carbon atom, leading to inversion of configuration.

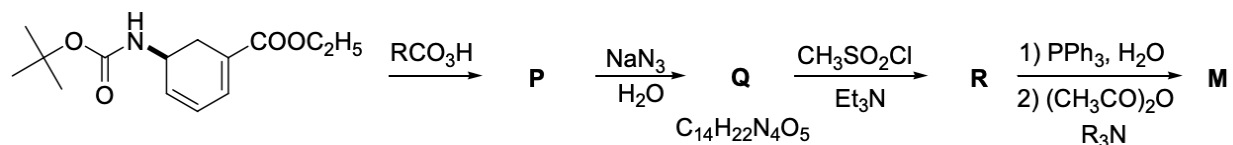
Subsequently, several other routes for the synthesis of oseltamivir were proposed. One of the most effective methods for producing racemic oseltamivir from simple starting compounds was proposed by a group of scientists led by Nobel laureate E.J. Corey:



In **L** the bromine atom is located at the same carbon atom as in **J**.

2. Write the structural formulas of compounds **F** – **N**.

AstraZeneca (a British-Swedish pharmaceutical company) used a different approach to prepare Compound **M** as described in the following scheme:



3. Write the structural formulas of compounds **P** – **R**.

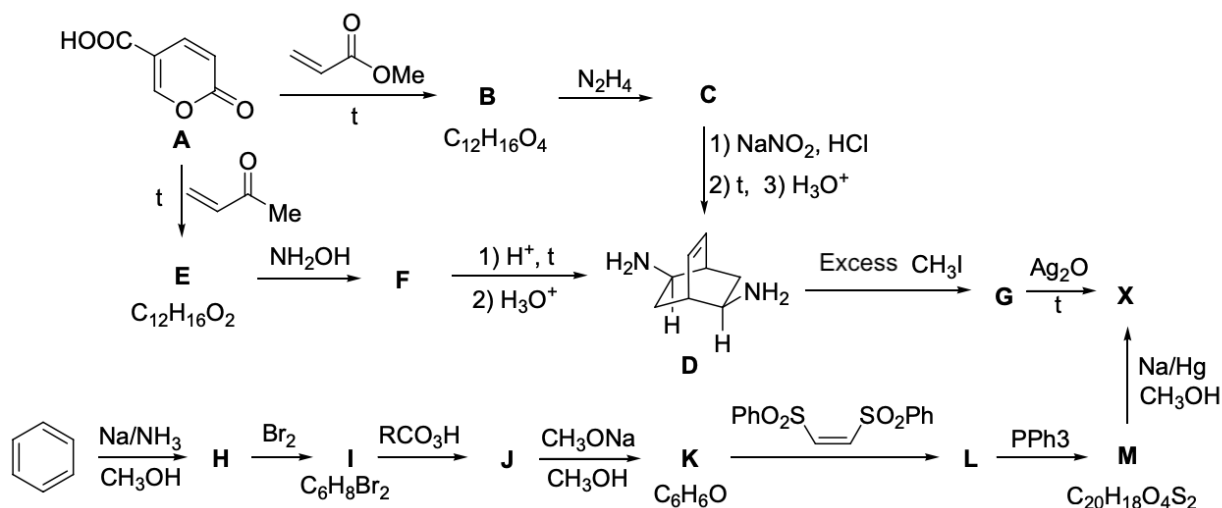
Oseltamivir is a prodrug. In the human body, under the action of the enzyme carboxyl esterase, it is hydrolyzed to an active form.

4. Draw the structural formula of the hydrolysis product.

The enantiomer of oseltamivir pictured in the beginning of the question is bioactive (of course the other enantiomer exists, but it is probably not bioactive). Indicate the absolute configuration of each chiral center of the enantiomer shown at the beginning of the question.

2011 Russia Tour 1 Organic Task 2

Below is a diagram describing some methods for the synthesis of barrelene C_8H_8 (**X**), which has long been of interest to theoretical chemists. The synthesis of **X** was first carried out by Zimmerman and Puffler in 1960, with Coumalic acid (**A**) being taken as the starting compound. In 1997, a group of Italian chemists proposed a more efficient synthesis of **X**, starting from benzene.



Hydrocarbon **X** contains two types of hydrogen atoms and two types of carbon atoms. Substances **B** – **F** have a second-order axis of symmetry (that is, they coincide with their image when they rotate $360^\circ / 2 = 180^\circ$ around a certain axis). Upon ozonolysis of **B** followed by treatment with an alkaline solution of hydrogen peroxide, compound **N** is formed, which has two planes of symmetry.

1. Write the structural formulas of compounds **B**, **C**, **E** – **N**, and **X**, taking into account that in none of the stages shown in this diagram does the configuration invert at reacting carbon atoms.
2. How many chiral centers are there in molecule **B**? How many stereoisomers are there for compound **B**?

Upon bromination of **X**, two isomers with the molecular formula $C_8H_8Br_2$ are formed. One the isomer (**O**) contains 6 types of hydrogen atoms; in the other (**P**), all hydrogens are nonequivalent. When kept in an atmosphere of hydrogen in the presence of a catalyst at a moderately elevated temperature and pressure, both isomers give a mixture of isomeric hydrocarbons **Q** and **R** of composition C_8H_{14} . In compound **Q**, there are only two types of hydrogen atoms in a 6: 1 ratio, and in compound **R** there are 5 types of carbon atoms.

3. Write the structural formulas of compounds **O** – **R**.

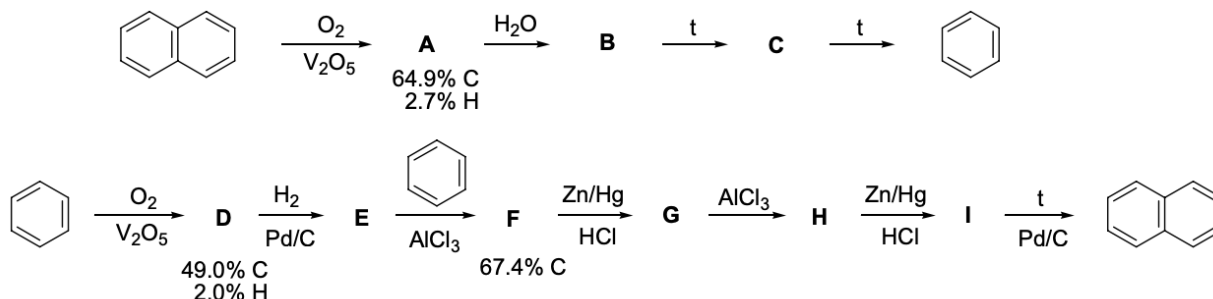
Upon irradiation, **X** turns into an isomeric compound **Y**, in which there are only CH groups, and in the molecule there are 5 types of carbon atoms. Hydrogenation of **Y** at moderate elevated temperature and pressure leads to the formation of a mixture of **R** and isomeric product **S** containing three types of carbon atoms.

4. Write the structural formulas of compound **Y** and **S**.

(comment: Part 4 of this question is actually very interesting, and was the idea behind a very long question we had at camp 2020 about the photoisomerization to **Y** which I got <50% on because I had not seen a relevant preparatory problem, or maybe I'm just bad who knows lol)

2011 Russia Tour 1 Organic Task 3

The simplest aromatic hydrocarbon - benzene - was isolated by M. Faraday in 1825 from an oily film that deposited from the gas used for lighting. A few years earlier, a sharp-smelling white substance was isolated from coal tar. In 1821, J. Kidd called it naphthalene, and in 1826 Faraday established its composition as $(C_5H_4)_x$. However, the structure of naphthalene was first proposed only in 1866. Following is a pair of synthetic schemes interconverting benzene to naphthalene which were used to prove the proposed structure was correct.

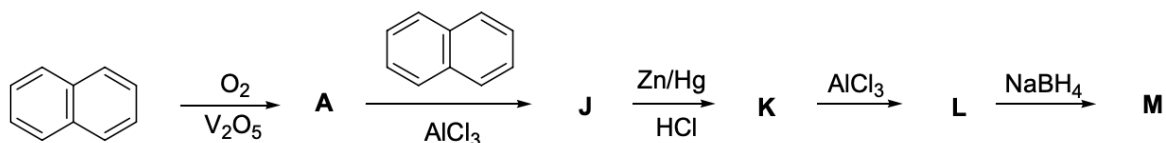


My comment: The O_2/V_2O_5 reaction is a molar mass bash which I usually find tiresome. I recommend you at least try it, but if you get held up figuring it out then you might want to just use my hint for what that specific step does before you look at the answer key. To view the hint simply highlight the text below and you should be able to read it

Hint:

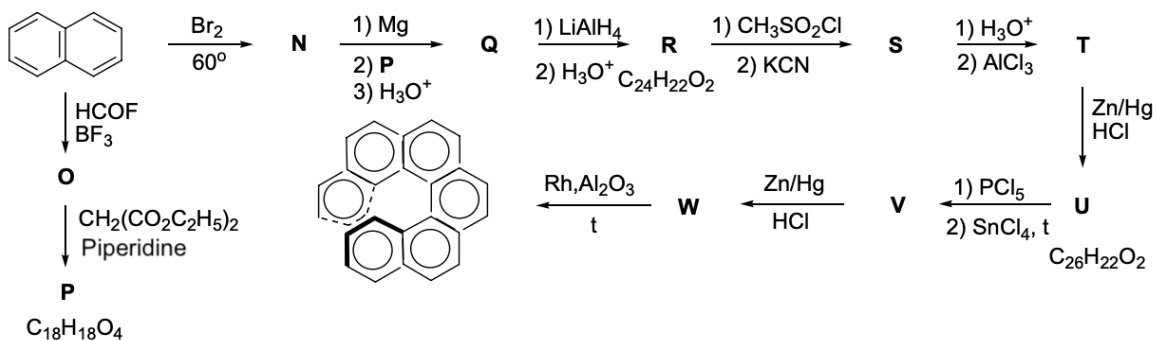
1. Write the structural formulas of compounds **A – I**.

So naphthalene can be converted into benzene, and also obtained from two benzene molecules. Using a reaction sequence similar to that used to convert benzene to naphthalene, naphthalene itself can be converted into a tetracyclic aromatic hydrocarbon **M**:



2. Write the structural formulas of compounds **J-M**.

The synthesis of complex polyaromatic hydrocarbons has attracted the attention of chemists for many years. In 1956, [6]helicene was first synthesized:



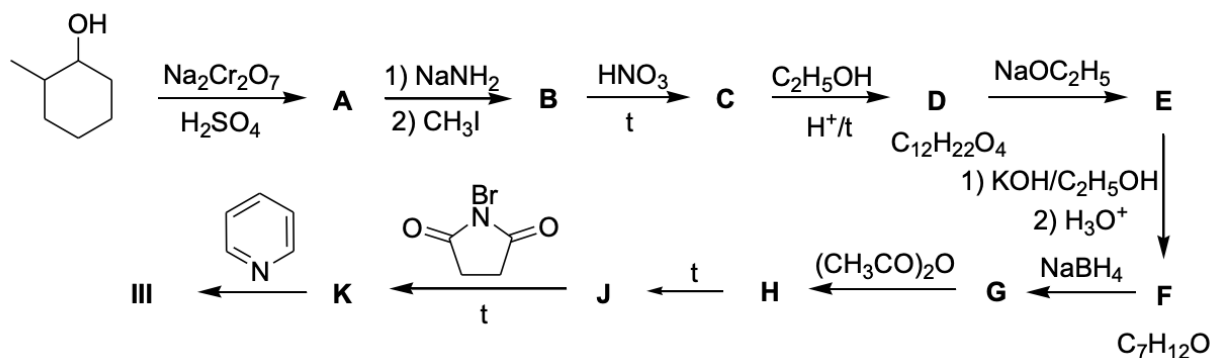
3. Draw the structural formulas of compounds **N** – **W**. Note that in the ^1H NMR spectrum of compound **Q** there is a doublet in the aliphatic region.

By the synthetic scheme shown above, [6]helicene is obtained in the form of a racemic mixture, which can be divided into two enantiomers.

4. Explain why the [6]helicene molecule is chiral, although it does not contain asymmetric carbon atoms.

2013 Russia Tour 2 Organic Task 2 Abridged

The low boiling fractions of the pyrolysis of petroleum feed and coking of coal contain hydrocarbon **I**, from where it is extracted by distillation ($t_{\text{boil}}=40.8\text{ }^{\circ}\text{C}$). When standing, **I** slowly dimerizes to form the only product **II**, which, when heated, again turns into **I**. Homologous to **I**, compound **III** (bp $71.3\text{ }^{\circ}\text{C}$), was first obtained by Wilcox in 1960 as a result of multistep synthesis from 2-methylcyclohexanol:



HINT (for scheme):

(Identities of **I** and **II**):

1. Draw **A-K** and **I-III**

An attempt to obtain **J** by one-stage acid dehydration of **G** instead of **G** leads to the formation of product **L**.

2. Draw the structural formula **L**.

In a benzene solution at $20\text{ }^{\circ}\text{C}$, **I** enters an exothermic reaction with the geometric isomers **M** and **N**, in the first case, two compounds **O** (85%) and **P** (15%) are formed, and in the second, the only product **Q**.

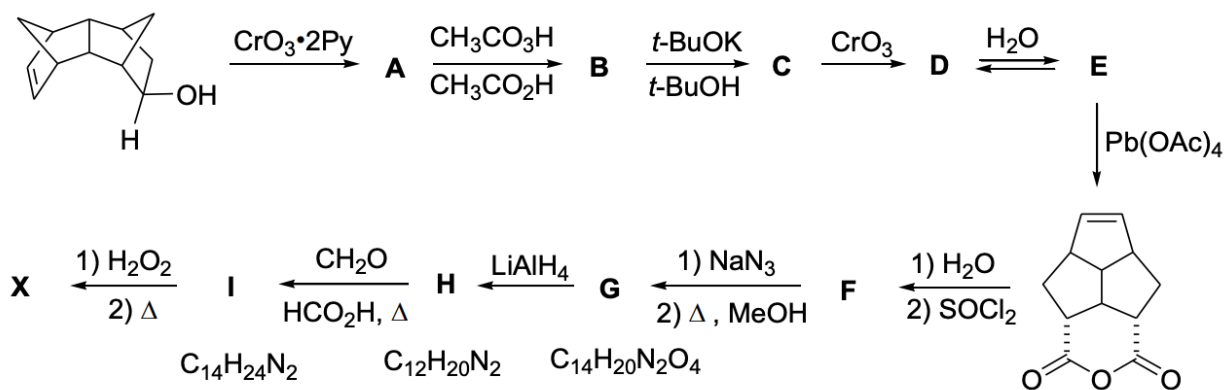
3. Write the structural formulas **M – Q**, given that **O**, **P** and **Q** have the molecular formula $\text{C}_9\text{H}_{10}\text{O}_4$.

4. Draw a (qualitative) energy diagram of the reaction of **I** with **M**, given that **O** is thermodynamically less stable than **P**.

2013 Russia Tour 2 Organic Task 3

The synthesis of polyhedranes whose carbon skeleton has the shape of regular polyhedra is a difficult task even for modern organic chemistry. So, dodecahedrane has the empirical formula CH and is a molecular analog of the regular polyhedron of the dodecahedron.

The first attempt to synthesize this compound was made in 1964 by R. Woodward, who proposed to use for this purpose the elegant, but unfortunately impossible, dimerization of hydrocarbon **X**. This hydrocarbon is interesting in itself, primarily because of its high symmetry. **X** was synthesized by Woodward as follows:



1. Write the structural formulas of compounds **A** – **I** and hydrocarbon **X**, if it is known that:
- **B** and **C** are isomers, and they contain the same number of cycles and do not contain C=C bonds
 - **E** belongs to the class of cyclic hemiacetals
 - In the ^1H NMR spectrum of compound **X** there are only three signals (doublet, doublet of triplets and quadruplet with relative integral intensities of 6: 3: 1).

(1st half is before the Pb(OAc)_4 product intermediate, 2nd half is after)

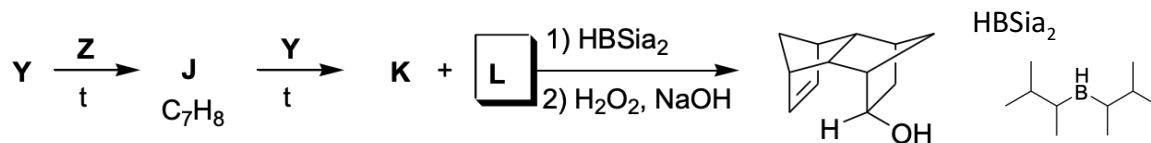
HINT (1st half): [REDACTED]

HINT (2nd half): [REDACTED]

HINT (2nd half): [REDACTED]

HINT (2nd half): [REDACTED]

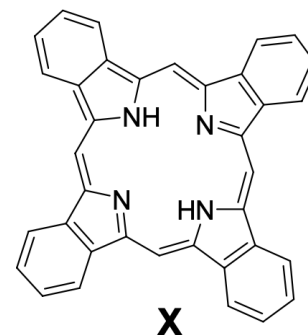
The starting compound was synthesized from available hydrocarbons **Y** and **Z**:



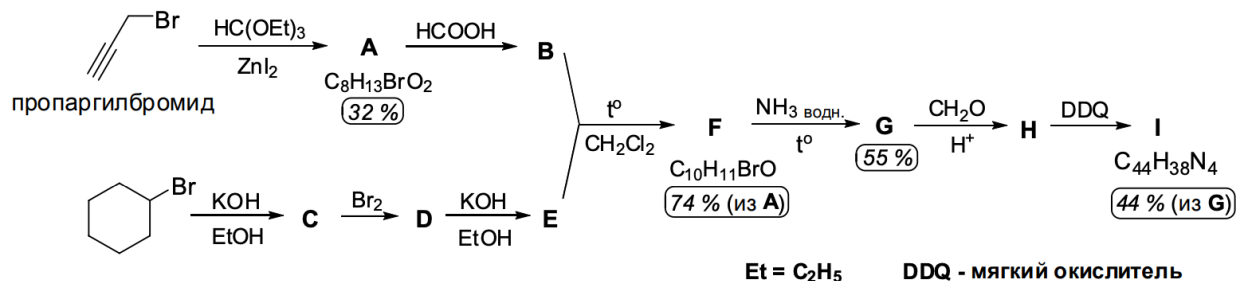
2. Write the structural formulas of compounds **Y**, **Z**, **J** – **L**. Note that **K** and **L** are stereoisomers.

2014 Russia Tour 2 Organic Task 1

Tetrabenzoporphyrin X, its derivatives and their complexes with metals attract the great attention of chemists in connection with their useful properties. For example, they are used to create field-effect transistors, photoelectric elements, and other electronic devices. This use is connected, among other things, with the ability of tetrabenzoporphyrins to form peculiar stacks due to the overlapping of π -orbitals of neighboring molecules (π - π stacking). But the same effect causes the low solubility of these compounds, which not only complicates their synthesis, but also complicates the manufacture of the corresponding electronic device.



In 2012, Korean scientists offered their own method to avoid these difficulties. For this, they synthesized substance I (see diagram below). Their idea is that a relatively highly soluble substance I can be effectively applied to the desired surface, and the subsequent heating will lead to the formation of X as a result of the elimination of four molecules of gaseous substance Y from each molecule I.



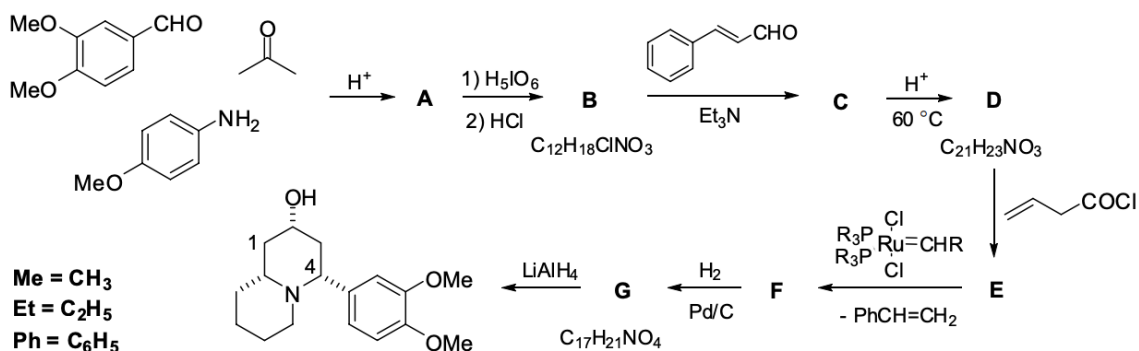
Пропаргилбромид = propargyl bromide

DDQ - мягкий окислитель = DDQ is a mild oxidant.

1. Name one natural substance containing porphyrin cycle.
2. Write the structural formulas of compounds A-I and Y.
3. Given the given yields, determine how much propargyl bromide (in g) is required to produce 1 g of compound I.
4. Compound D exists in a solution in the form of two main conformations, D1 and D2, with the D1 conformation prevailing in polar solvents, and D2 predominating in non-polar solvents. Draw these conformations.

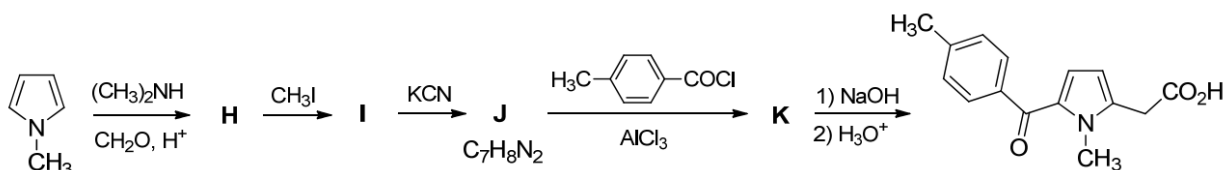
2014 Russia Tour 2 Organic Task 3 Abridged

The Mannich reaction was used, for example, to obtain the alkaloid Lasubini II. The synthesis scheme (for the racemic mixture) of its epimer at position 2 is shown below.



2. Write the structural formulas A - G, taking into account that C, unlike its isomer D, is capable of entering into the haloform reaction, but does not give the reaction of a silver mirror, B is a salt, and compound F contains a non-conjugated double bond.

The Mannich reaction is used for aminoalkylation and other types of compounds that can act as nucleophiles. For example, the synthesis of tolmetin, an anti-inflammatory agent used in the treatment of arthritis, arthrosis and the like, includes aminoalkylation of N-methylpyrrole.



3. Write the structural formulas of compounds N-K.

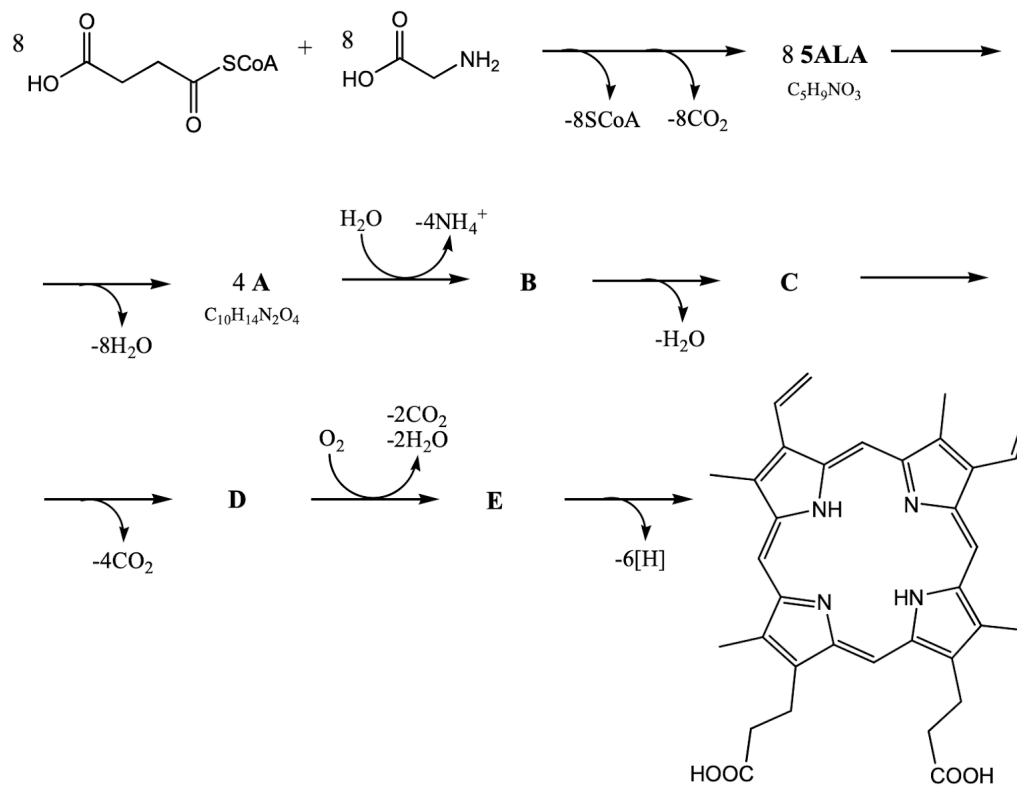
4. During acylation of J, along with K, an isomeric product of acylation of L is formed in a small amount. Write down its structure, taking into account that 4 signals are present in the aromatic region of its ^1H NMR spectrum: two doublets and two singlets.

2014 Russia Tour 2 Biochemistry Task 1

While this is a biochemistry task, the second half of it is a good quality scheme, and I quite enjoyed the first half of it even though it isn't conventional organic.

One of the biggest problems for mankind in the XXI century is cancer. The main therapy of these diseases is surgery, which often prolongs a person's life for some time. There is such a form of cancer as glioblastoma of the human brain. In surgery of this tumor, the main problem is the visualization of its borders. One of the imaging methods is intraoperative fluorescent navigation. 2 hours before surgery, a patient is administered a large dose of 5-aminolevulinic acid (5ALA or 5ALK), which is a precursor of protoporphyrin IX containing 4 pyrrole rings and having an intense fluorescence, intravenously. This product selectively accumulates in abnormal cells. Thus, the surgeon can clearly mark the border of the tumor and carry out its more complete removal.

In the human body, 5ALA is obtained by condensation of succinyl-SCoA and glycine with the formation of a C – C bond. The resulting acid is then converted to protoporphyrin IX as follows:



Hints:

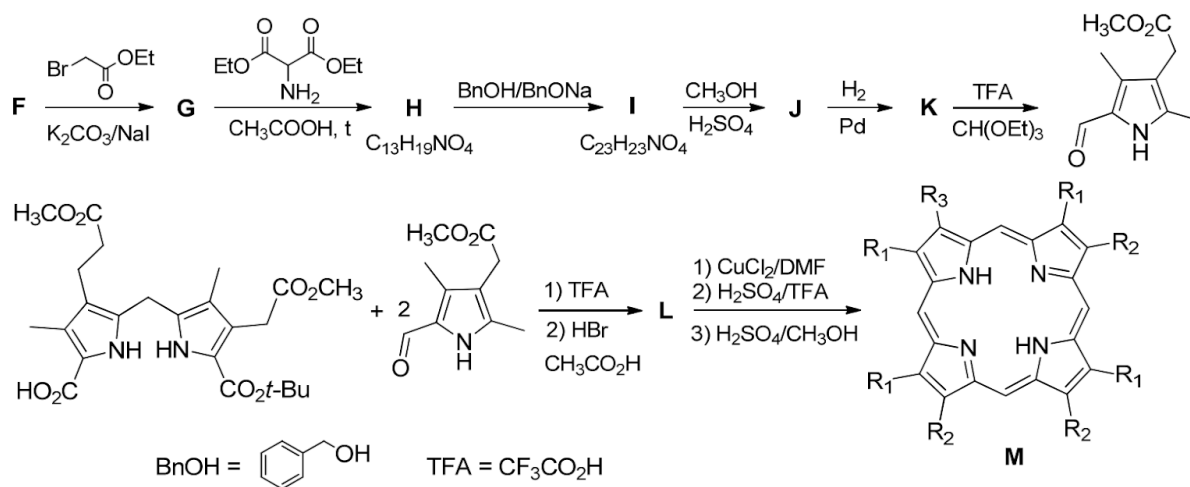
A contains a pyrrole ring

A => B involves an isomerization step

B is tetracyclic and made up of four fragments, three of which are connected "head to tail", and the last one is "tail to tail"

1. Give the structural formulas of substances A-E and 5ALA.

In 2011, a group of scientists from the United States developed a method for the synthesis of porphyrins from 2,4-pentanedione (F) for a detailed study of the mechanisms of some enzymes of the protoporphyrin IX biosynthesis pathway.



2. Give the structural formulas of the substances F-M. When converting G to H, one ester group is split off. The conversion of I to J affects only one group, and trifluoroacetic acid decarboxylates a single carboxyl group directly at the heterocycle. Note also that in the connection $L = 0.0583$. L in its structure resembles compound B. In compound M, it is necessary to specify substituents (identical substitutes are equally marked).

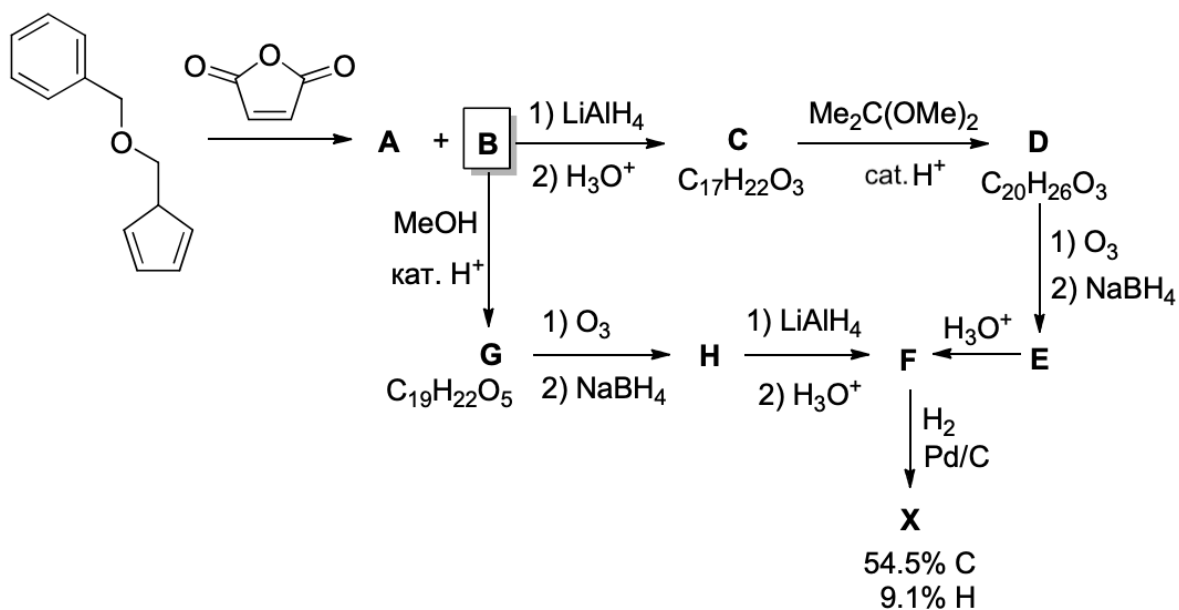
Fluorescence - the ability of some compounds to emit a quantum of light when going from an excited state to the ground state. This process is successful if the structure is rigid (practically does not change when the molecule is excited) and has a system of conjugated bonds. It is still not known why protoporphyrin IX selectively accumulates in cancer cells; however, in normal cells, this compound is transformed into heme, a complex compound, where the iron atom is coordinated by four nitrogen atoms of the pyrrole rings, and the other two free orbital water.

3. Based on the foregoing, predict whether heme will show fluorescent activity.

2015 Russia Tour 1 Class 11 Task 3

In 1985, American scientists described the highly symmetric compound **X** having only two types of carbon atoms and three types of hydrogen atoms. This compound was synthesized according to the scheme below. The main isomer of the Diels – Alder reaction product was converted to compound **G** by reaction with methanol in the presence of an acid catalyst. The ozonation of **G**, according to the authors, gave compound **H** after treatment with sodium borohydride, which was further converted to **F**, and the target product **X** was obtained from it. Since no physicochemical characteristics of **F-H** and **X** were given in this work, in 2013 French scientists studied this synthesis more thoroughly and found that under the described conditions, instead of **H**, a tricyclic compound (**I**, $C_{17}H_{18}O_5$) is obtained, which, however, upon reduction with $LiAlH_4$ (and subsequent neutralization) gives the same compound **F**, which under the previously described conditions turns into **X**.

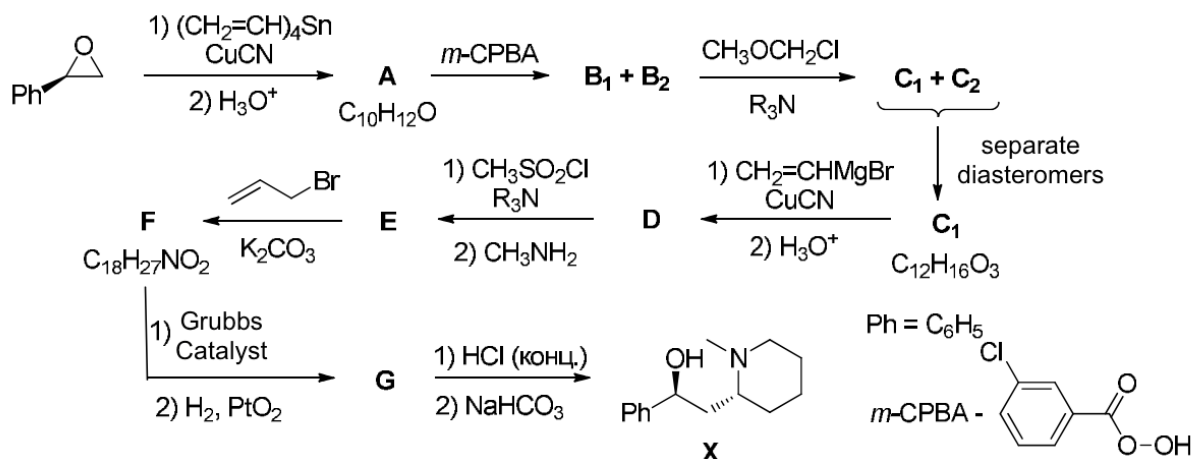
French scientists have proposed a modified synthesis scheme **X**, according to which **B** is first reduced with lithium aluminum hydride to compound **C**. The following steps are shown in the scheme below.



Draw the structural formulas of compounds **A – I** and **X**.

2015 Russia Tour 1 Class 11 Task 4 Abridged

In 2004, Korean scientists used the metathesis reaction to form a cycle for the stereoselective synthesis of the alkaloid (+)-allosedamine (**X**).

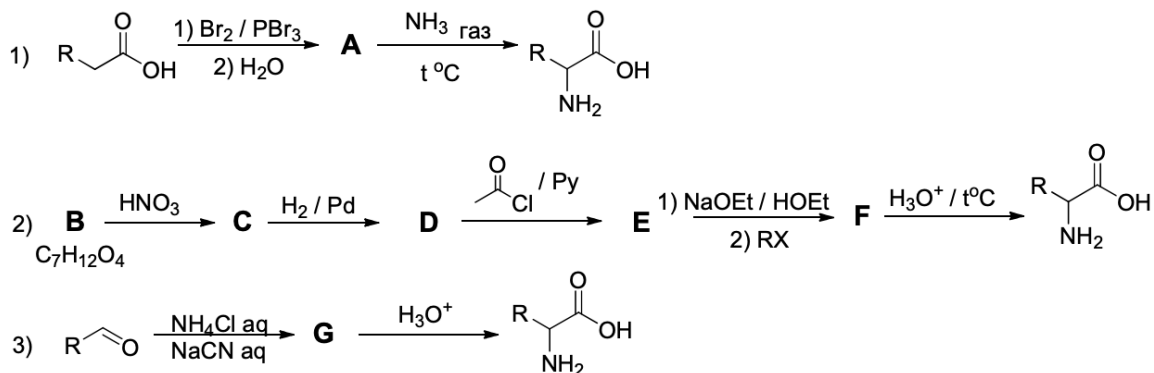


3. Give the structural formulas of compounds A, B₁, B₂, C₁, C₂, D – G. Note that B₁ / B₂ and C₁ / C₂ are pairs of diastereomers, while in the molecules B₁ and C₁ one chiral center has an R configuration and the other an S configuration.

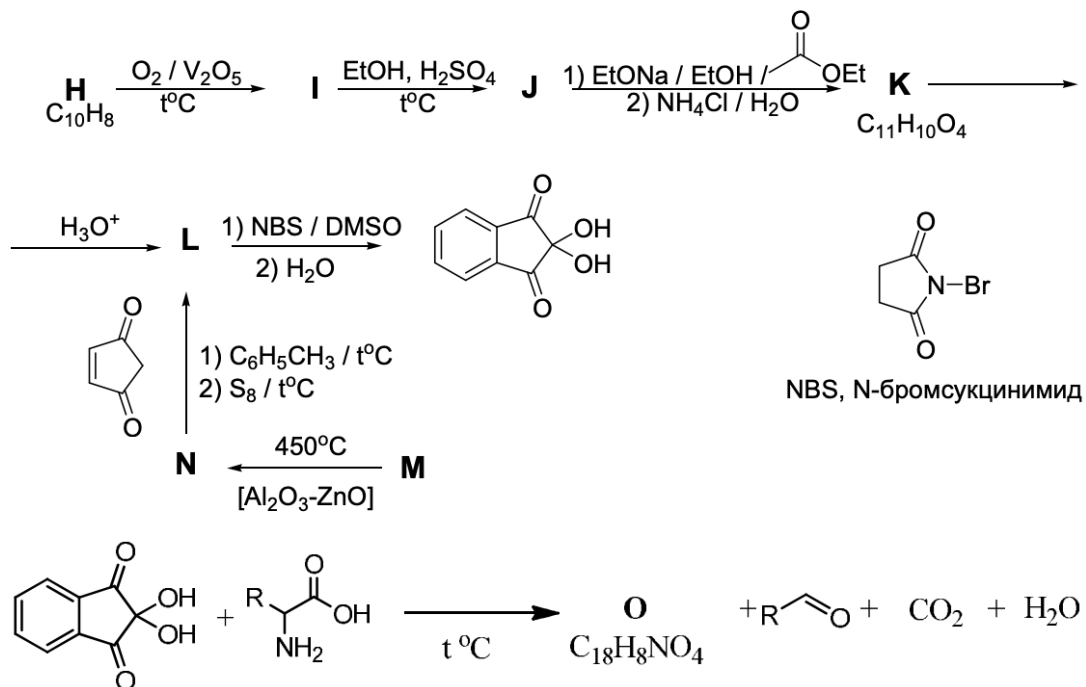
Attention! A full score is given for structures with correctly specified stereochemistry. If the stereochemistry is absent or incorrect, the structure is assessed by an incomplete score.

2015 Russia Tour 2 Biochem Task 3

Fingerprints are the result of secretions from the surfaces of the fingers. By themselves, these precipitates are 99% water, the rest are sodium chloride and organic compounds, among which are a mixture of different amino acids. The following synthetic pathways for amino acids are proposed:



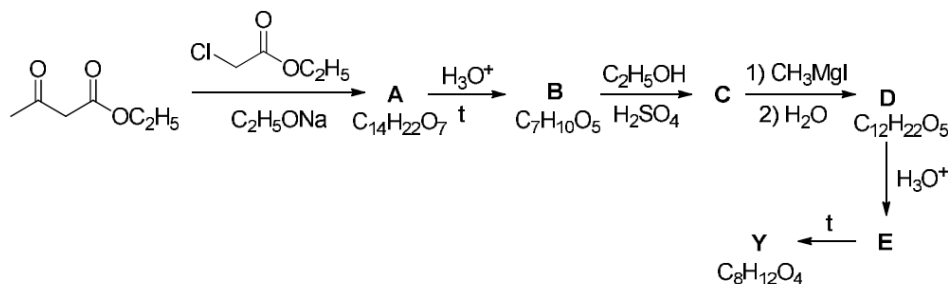
1. Decipher the synthesis schemes. B is a very reactive substance, easily forms metal derivatives. Assume which of the synthesis paths is the most convenient to execute. Justify your answer. Ninhydrin reacts with amino acids. The synthesis of Ninhydrin and its reaction with amino acids are depicted in schemes below.



The forensic chemist, suspecting something was wrong, isolated the resulting aldehyde and analyzed it according to the following scheme:

2015 Russia Tour 2 Organic Task 1

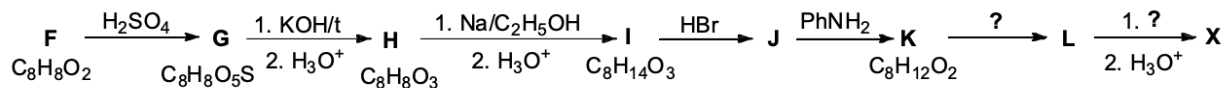
Structure of **X** ($C_{10}H_{17}OH$) was first established by the Russian organic chemist E.E. Wagner, who used oxidation for this reaction. When **X** is treated with an acidified $KMnO_4$ solution, when heated, a mainly equimolar mixture of acetic acid and acid **Y** is formed. The structure of the latter was confirmed by its counter synthesis:



2. Write the structural formulas of compounds **A – E, Y**.

3. Establish structure **X** if its conversion to **Y** involves the formation of a ketone, which oxidizes to form **E**. Note that the oxidation of asymmetric ketones proceeds predominantly from the side of a less hydrogenated carbon atom.

One of the first syntheses of **X** was carried out according to the following scheme:



4. Write the structural formulas of compounds **F – L**.

In an acidic medium, **X** isomerizes into a bicyclic compound **Z**, the molecule of which contains a plane of symmetry. In the form of a drug called "Eucalyptol," this compound, which has antimicrobial and anti-inflammatory properties, is used for topical use in ENT practice.

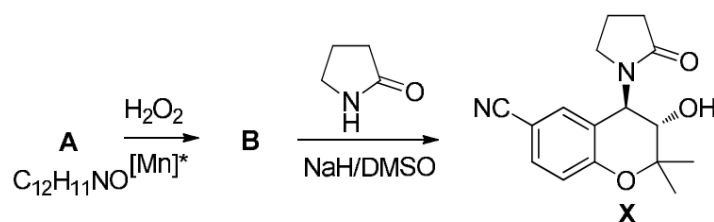
5. Write the structural formula of compound **Z**.

2015 Russia Tour 2 Organic Task 2

Potassium channel activators

ATP-sensitive potassium channels are present in endocrine cells, smooth muscle cells and skeletal muscle tissue, etc. These channels are involved in important physiological processes: hormone secretion, smooth muscle contraction, and neurotransmitter secretion. The work of potassium channels can be regulated with the help of special substances - activators. Such substances are actively used in medicine for the treatment of hypertension and angina pectoris, as well as bronchodilators.

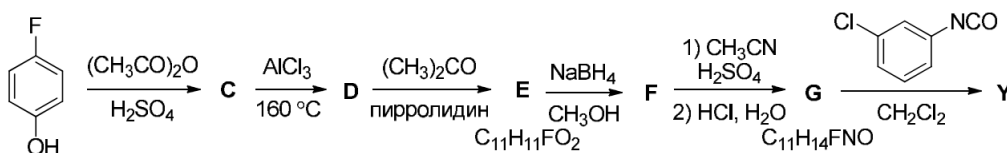
One of the most common potassium channel activators is cromakalim (**X**). This compound can be obtained as follows from compound **A**.



[Mn*] = Chiral Manganese Complex

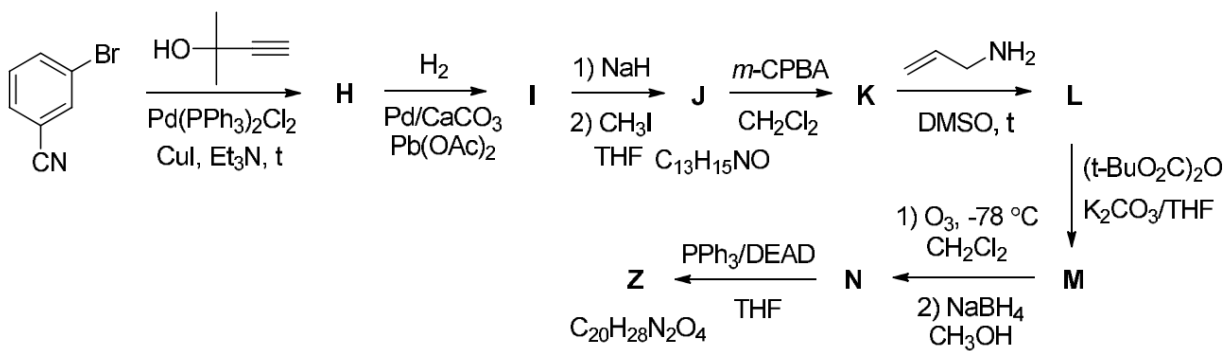
1. Give the structural formulas of compounds **A – B**.
2. Why is the chiral complex used in the first stage of synthesis?

In order to obtain a drug that lowers the secretion of insulin in the β -cells of the pancreas, but at the same time minimally affects smooth muscle cells, in 2006, Belgian scientists synthesized a number of substances of similar structure, which, like cromakalim, contain a chromane (dihydrobenzopyran) heterocyclic system. Compound **Y** turned out to be the most effective and selective, the synthesis scheme of which is given below.



3. Give the structural formulas of compounds **C-G** and **Y**, given that:
 - In the aromatic region of the ^1H NMR spectrum of compound **D** contains one signal more than for compound **C**.
 - In the aliphatic region of the ^1H NMR spectrum of compound **E**, there are only two signals with an intensity ratio of 3:1.

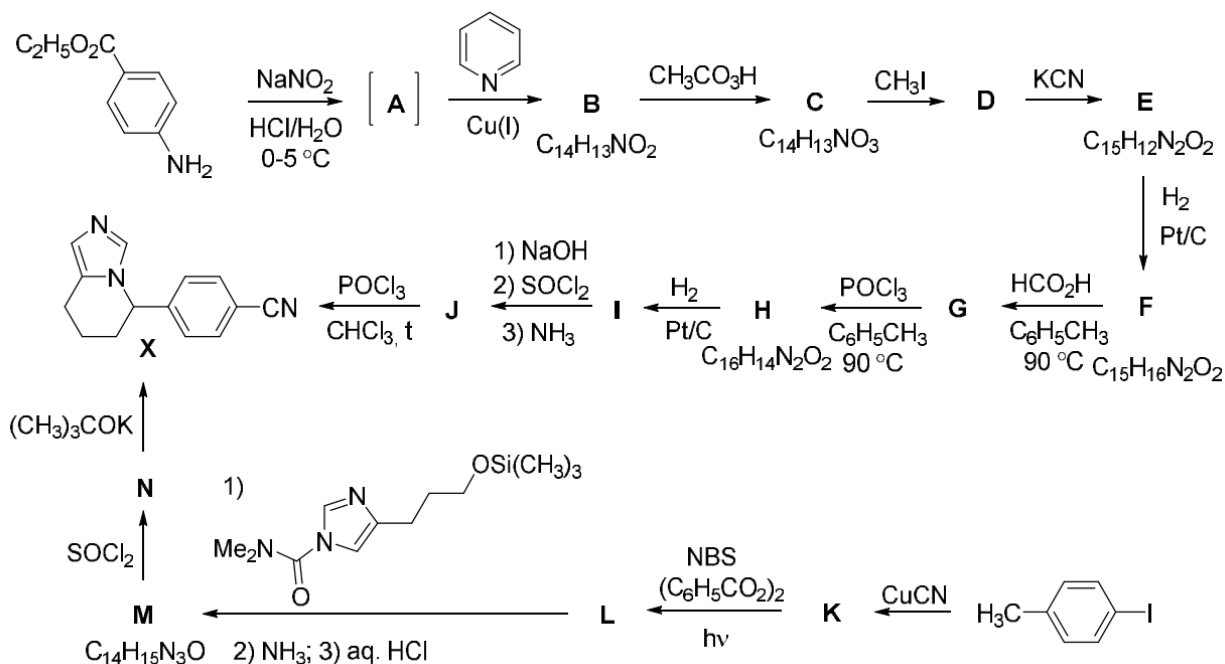
In 2004, Taiwanese scientists synthesized substance **Z**, the structure of which is also quite similar to that of cromakalim, although **Z** does not contain a chroman system. Note that compound **Z** contains two six-membered rings.



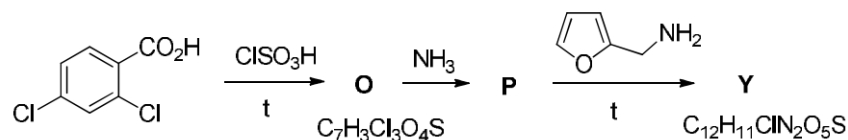
4. Give the structural formulas of compounds **H-N** and **Z**.

2015 Russia Tour 2 Organic Task 3

Inhibitors of the aromatase enzyme, which plays an important role in the synthesis of estrogen, are used to treat a number of diseases, primarily breast cancer. However, these compounds may not be used for good purposes. Dishonest athletes use them as doping because they increase testosterone levels. One of the anti-cancer drugs of this type used by doping enthusiasts was Fadrozole (X), two synthesis methods of which are shown in the diagram.



Dishonest athletes also take furoseamide (Y), which in itself cannot improve results, but, being a diuretic, helps to hide the use of doping. The synthesis of furoseamide is presented below.

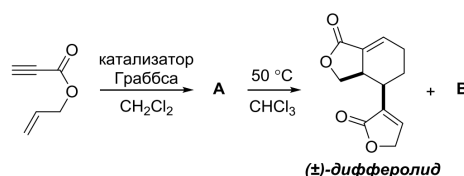


Decrypt these schemes. Write the structural formulas of compounds **A – P** and **Y**. Note that:

- **A** is an unstable intermediate that decomposes slowly at low temperatures and quickly when heated
- in the aromatic region of the ^1H NMR spectrum of compound **B**, taken on a device with a not very high resolution, there are 6 signals: two doublets, two broadened doublets and two multiplets with a ratio of integrated intensities of 2: 2: 1: 1: 1: 1
- in the absence of catalysts, peracids are not able to oxidize the aromatic cycle
- the data of IR spectroscopy show the presence in **Y** of a strong intramolecular hydrogen bond.

2016 Russia Tour 2 Organic Task 1

The alkenes metathesis reaction was discovered in 1967, and in 1985 the first example of metathesis with the participation of alkenes and alkynes, proceeding by a similar mechanism, appeared. This reaction was used, for example, in the synthesis of (\pm)-diferolide isolated from a culture of *Streptomyces aurantiogriseus* actinomycetes. Compound A slowly dimerizes with the formation of (\pm)-diferolide and its structural isomer B even when standing at room temperature, which suggests that the differentiate is not actually present in this culture, but is an artifact of excretion:

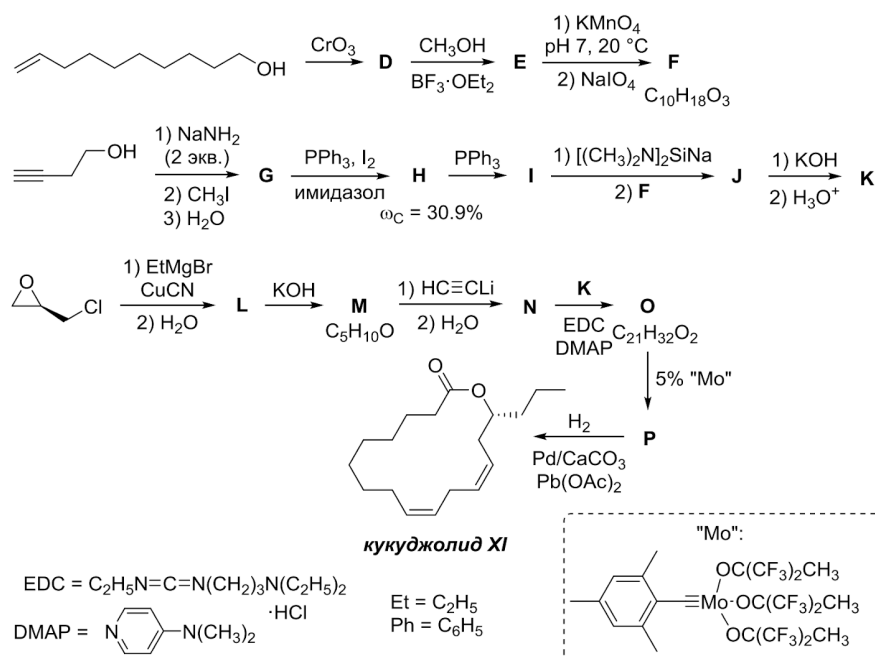


1. Write the structural formulas **A** and **B**.

It was later found that other types of compounds also enter into similar metathesis reactions. So, iron compounds catalyze the metathesis reaction with the participation of alkynes and aldehydes.

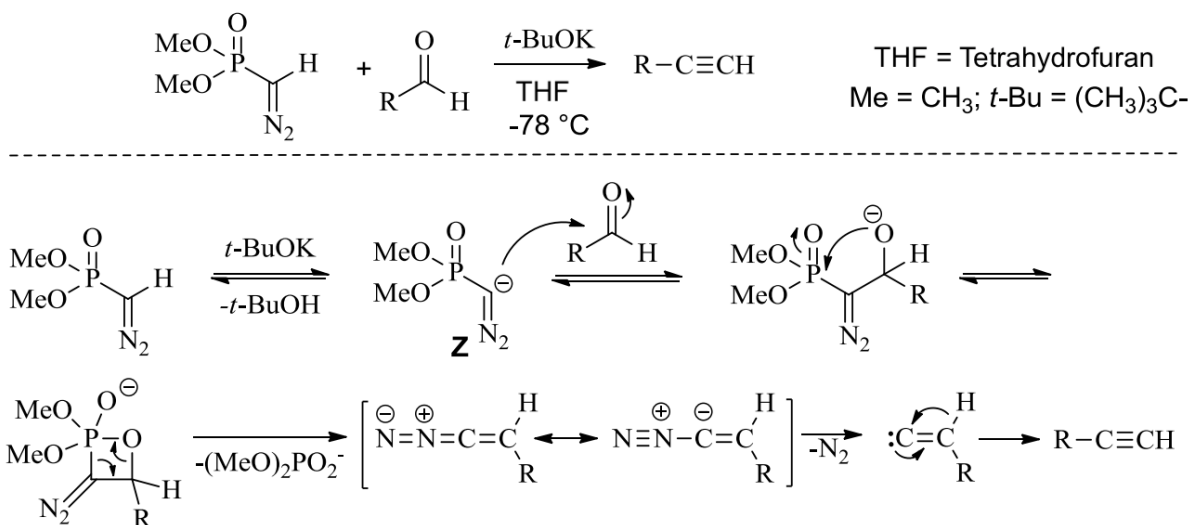
2. Write the structural formula of the product (C) of the intramolecular metathesis reaction of 2 - [(but-2-yn-1-yl) oxy] benzaldehyde.

Despite all the advantages of the alkenes metathesis reaction, it also has a drawback: in many cases mixtures of cis and trans alkenes are formed. Obviously, the metathesis reaction of alkynes is devoid of this drawback. The alkynes metathesis product can be further selectively reduced to either cis or trans alkene. This approach was recently used in the synthesis of Kukuljolid XI, the pheromone of the Surinamese mukoed *Oryzaephilus surinamensis*.



2016 Russia Tour 2 Organic Task 2

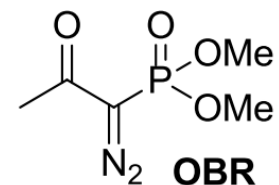
In modern organic chemistry, one of the main methods for the synthesis of terminal alkynes is the Seyfert – Gilbert reaction, the scheme and mechanism of which are given below.



A drawback of the Seyfert – Gilbert reaction is the use of a strong potassium tert-butoxide base, which often leads to side reactions.

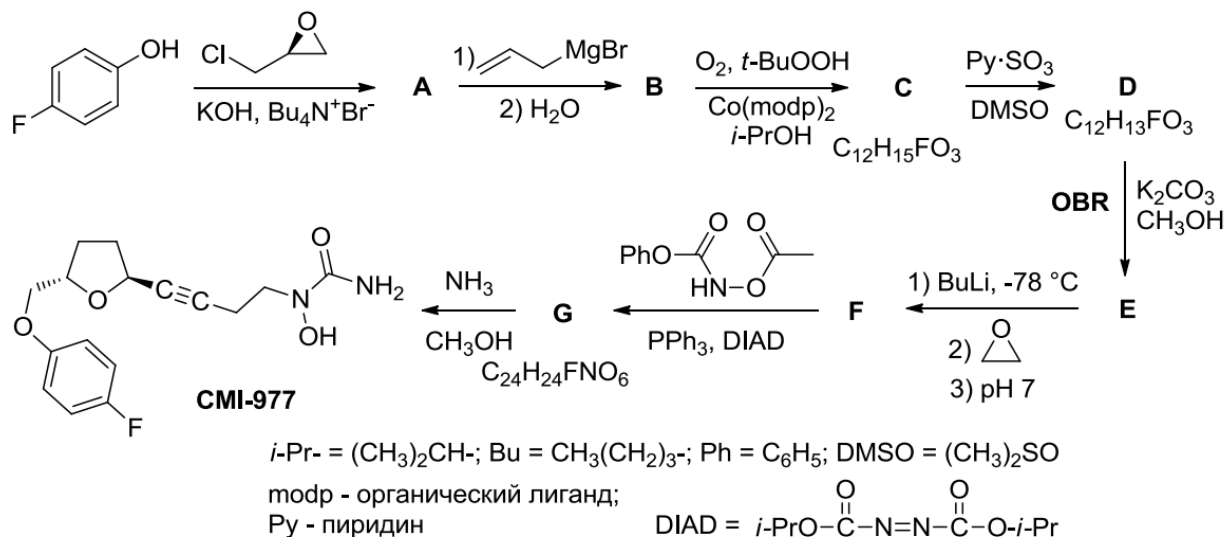
1. Suggest the structure of a possible by-product formed from phenylacetaldehyde under the conditions of the Seyfert – Gilbert reaction.

Side processes can be avoided if the Seyfert – Hilbert reaction is carried out with the Ohira – Bestmann modification, when the **Z** anion (in the above figure) is generated in situ from the so-called Ohira-Bestmann Reagent (hereinafter denoted as **OBR**) upon reaction with potassium carbonate in methanol. This minimizes side processes and achieves high yields of the desired alkyne. In addition, under such conditions, the reaction can be carried out at room temperature, and not at -78°C .

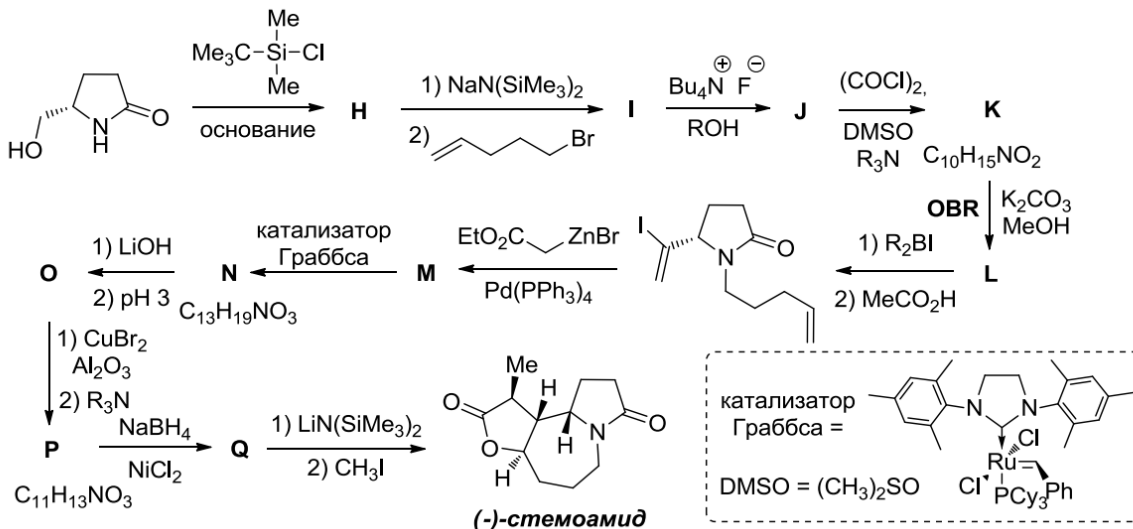


2. Suggest a mechanism for the formation of anion **Z** from Ohira Bestmann's reagent under reaction conditions

In 2013, Brazilian scientists used the Seyfert-Hilbert reaction in the Ohira-Bestmann modification to synthesize the substance CMI-977, a promising drug for the treatment of chronic asthma. The following is an encrypted diagram of this synthesis.

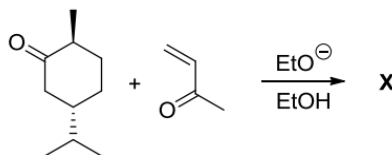


3. Give the structural formulas of compounds A - G. Note that compound C is not reduced by lithium aluminum hydride. Another example of the use of the Seyfert – Gilbert reaction in the Ohira – Bestmann modification is the stereoselective synthesis of the alkaloid (-) - stemoamide contained in the plant *Stemona tuberosa* used in traditional Chinese medicine.



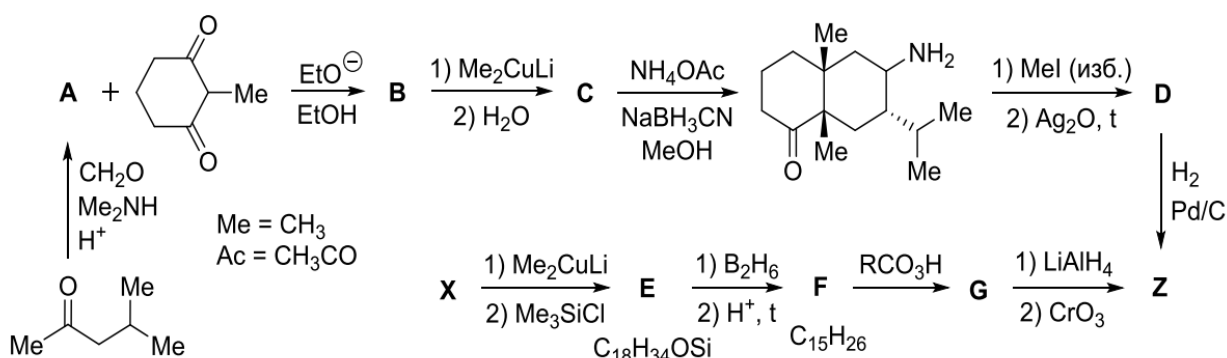
4. Give the structural formulas of compounds H - Q, given that O is a bicyclic compound and P is a tricyclic

2016 Russia Tour 2 Organic Task 3



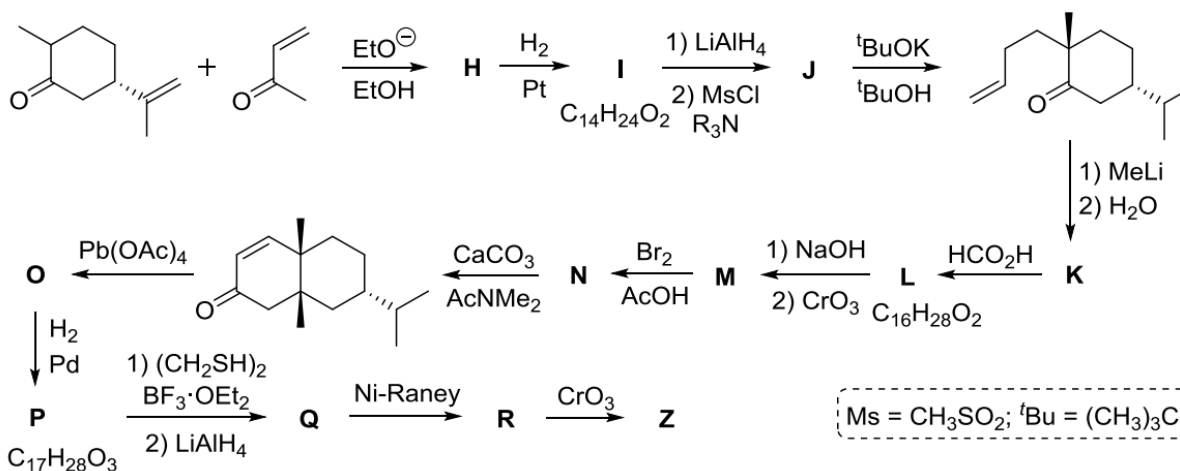
1. Write the structure of **X** given that it contains a quaternary carbon.

Instead of an enone, you can also use its synthetic equivalent - an ammonium salt of the type $R_3N^+CH_2CH_2C(O)R'$, which in turn can be easily obtained from ketone, amine and formaldehyde by the Mannich reaction. An example of the application of Robinson annelation is the synthesis of sesquiterpene valeranone (**Z**), an important constituent of fragrant valerian oil, shown in the diagram.



2. Write the structural formulas **A - G** and **Z**, given that **Z** has three chiral carbon atoms.

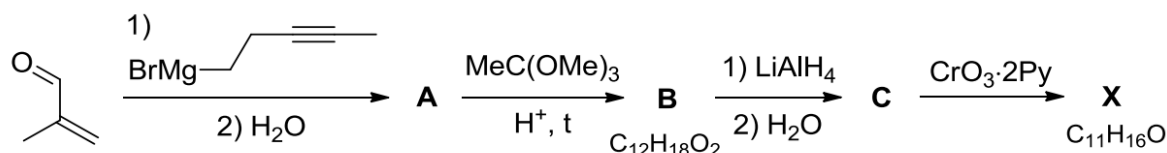
The diagram below shows one of the first syntheses of valeranone created in 1986.



5. Write the structural formulas of compounds **H - R**, taking into account that compound **L** contains 2 six-membered rings, **Q** - 3 cycles, **O** is the product of acetoxylation, and **J** contains one sulfur atom.

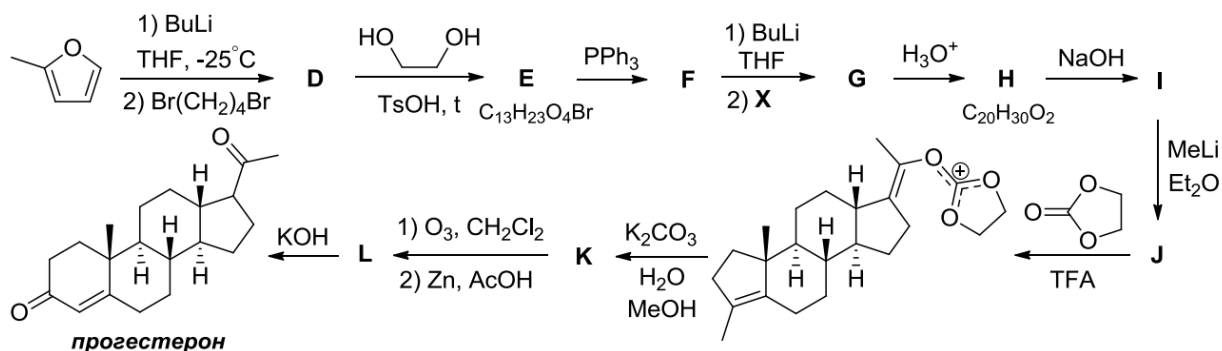
2017 Russia Tour 2 Organic Task 1

Steroid hormones regulate the vital processes in animals and humans. A common feature of all steroids is the presence of a system of four condensed cycles, three of which are six-membered, and one five-membered, as shown in the figure. For example, one of the most important female sex hormones is progesterone (Z), which plays an important role in pregnancy. The first complete synthesis, which includes 15 stages, of progesterone was published by W. Johnson in 1971. This synthesis can be divided into two parts. The product of the first is (E) -4-methyldec-3-en-8-inal (X), which is further used in the synthesis of progesterone.

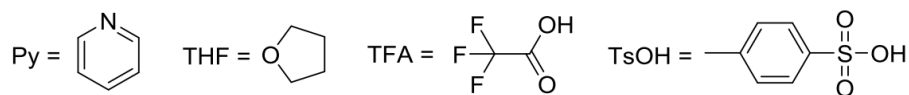


1. Give the structural formulas of compounds A – C, taking into account that the conversion of A to B is a stepwise process, including the Kleisen rearrangement (the so-called Johnson-Kleisen rearrangement).

The second part of the synthesis is shown in the diagram below:

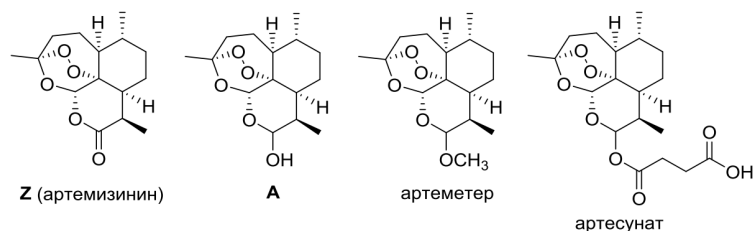


2. Give the structural formulas of compounds D – L, taking into account that G contains two double bonds of the trans configuration.

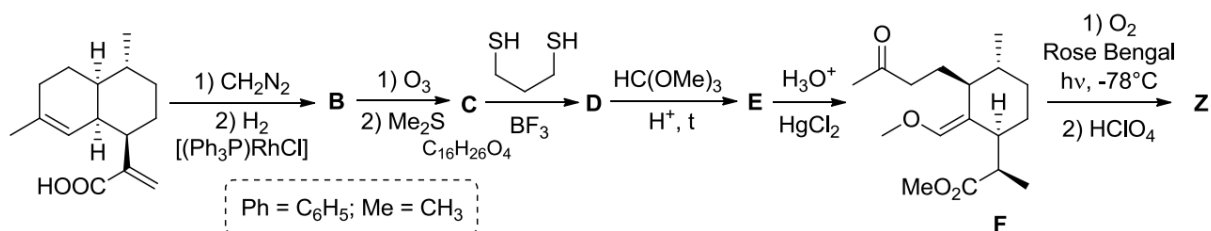


2017 Russia Tour 2 Organic Task 2

Artemisinin (Z) was discovered in 1971 by Chinese pharmacologist Tu Yuyu during a search for cures for malaria during the Vietnam War. Based on the recipe described in a book written in 340 AD e., she isolated Z from wormwood annually. In 1973, she received dihydroartemisinin (A), which has a higher antimalarial activity than Z, and then other active derivatives. For these studies, in 2015 she was awarded the Nobel Prize in medicine or physiology. Currently, artemisinin and its derivatives (artemether, artesunate) are the standard for the treatment of malaria worldwide. The antitumor activity of compound Z has been discovered in the past few years, and is now being tested as a cancer drug.

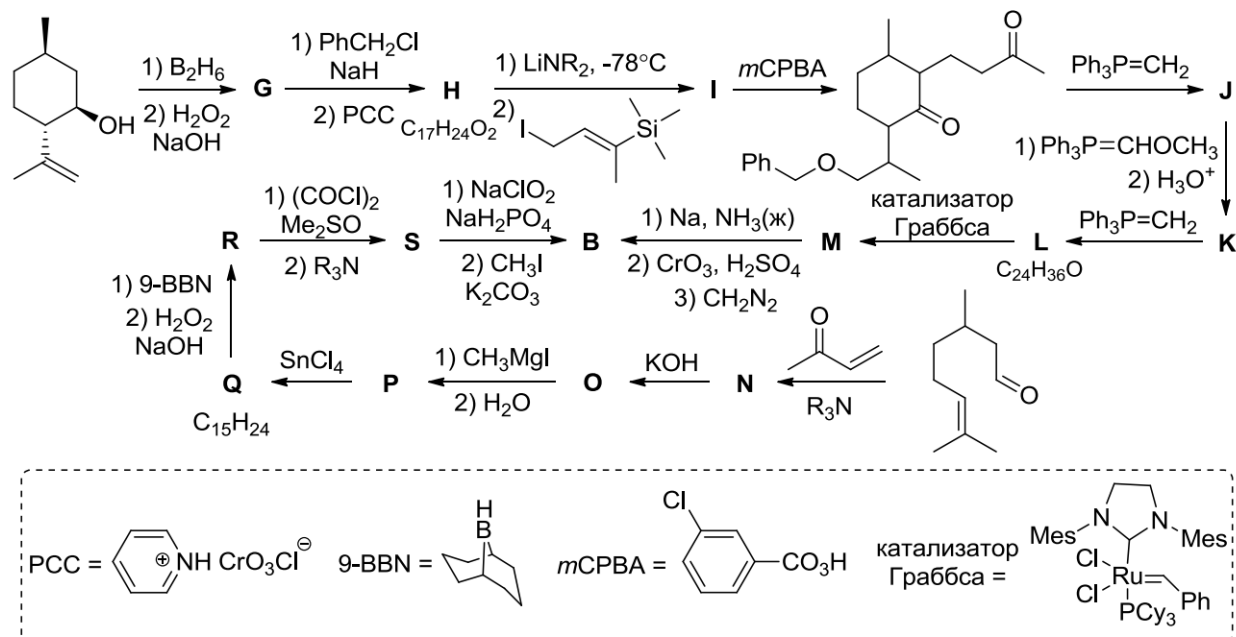


The high cost and limited bioavailability of Z led to the need to search for synthetic methods for its preparation, allowing to increase the production volume of the drug. Below is a scheme for producing Z from artemisininic acid, the content of which in wormwood is an order of magnitude higher than the amount of artemisinin itself.



1. Decipher the transformation scheme and write the product formulas B – E.

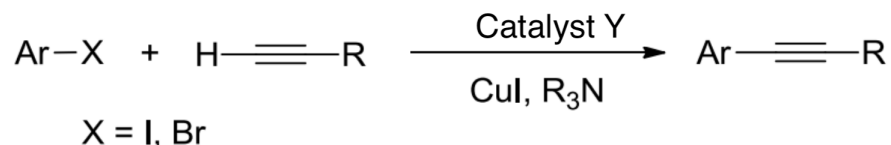
Compound B can also be obtained from available natural substances - isopulegol and citronellal, which are found in essential oils.



2. Decipher the transformation scheme and write the product formulas G – S.

2017 Russia Tour 2 Organic Task 3

In October 2016 was the 85th anniversary of the birth of Kenkichi Sonogashira, who in 1975 discovered the cross coupling reaction between aryl halides and alkynes under very mild conditions in the presence of a transition metal complex **Y**.

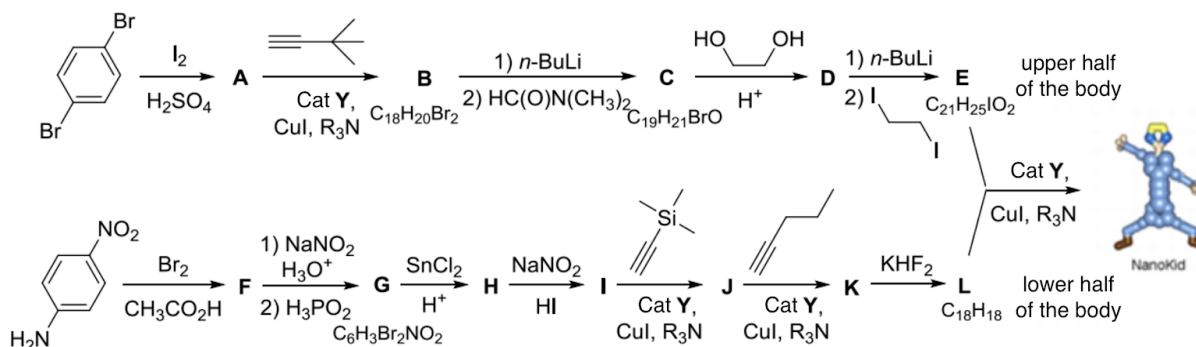


Complex **Y** can be obtained from a commercially available salt of **Z** and triphenylphosphine. Salt **Z** is obtained by co-crystallization from an aqueous solution of two halides **Q** and **R**. It is known that the content of the transition metal in **Q**, **Z** and **Y** is 60.01%, 36.17% and 15.16%, respectively.

Tasks:

1. Determine the formulas of halides **Q** and **R**, salt **Z** and complex **Y**. Also draw the structural formula of complex **Y**.

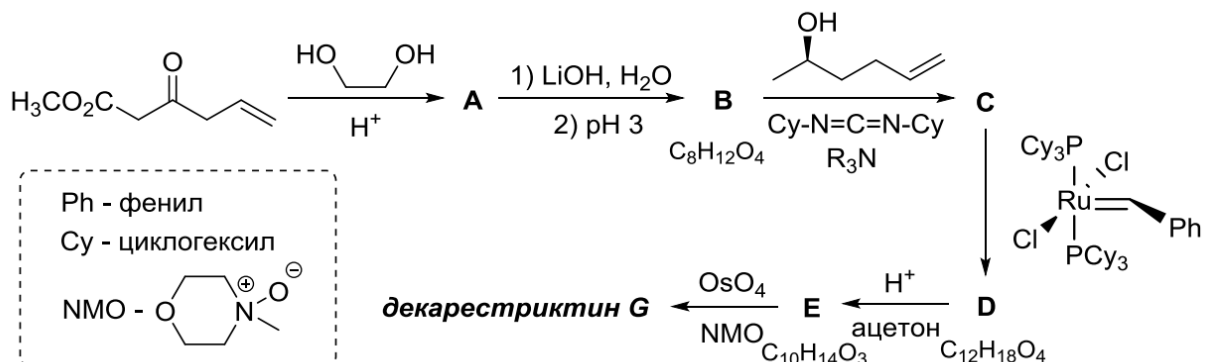
The Sonogashira reaction has firmly entered the arsenal of synthetic chemists as a reliable and general method for creating a carbon-carbon sp^2 - sp bond. In 2003, chemists from Texas published a paper describing the production of NanoPutians, human-like organic molecules with a growth of about 2 nm. In the synthesis scheme of the "nanokid" shown below, the Sonogashira reaction is used 4 times!



2. Draw the structural formulas of compounds **A** – **L** and "NanoKid" (**N**).

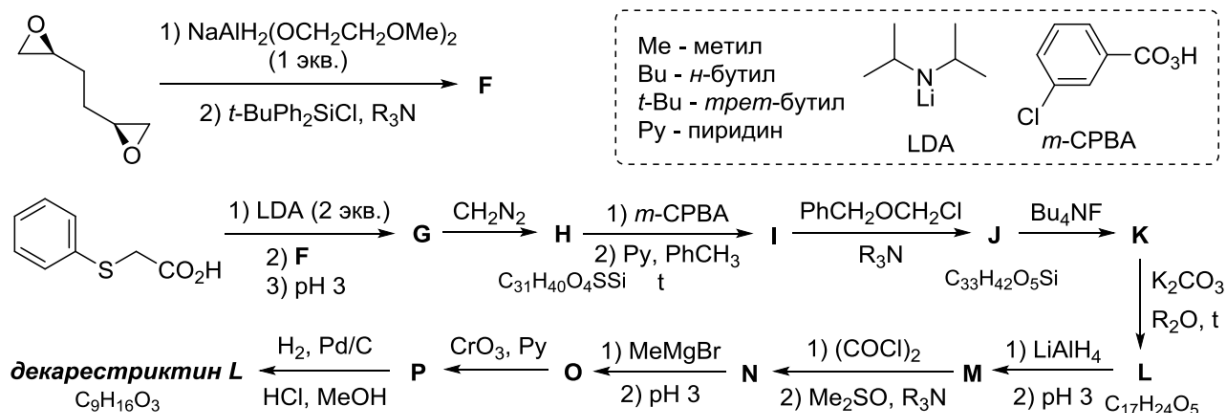
2017 Russia Tour 2 Organic Task 4

In 1992, a number of compounds of similar structure, called decarestritins, were isolated from the fungus *Penicillium Simplicissimum*. Currently, 20 decarestritins are known that have different letter designations from A to O (for example, "decarestritin A1"). Many of these compounds are of considerable interest due to their ability to inhibit cholesterol synthesis, therefore, in recent years considerable efforts have been made to develop methods for the synthesis of decarestritins. So, in 2015, according to the scheme below, the first synthesis of decarestritin G, a macrocyclic lactone with a ten-membered cycle, was carried out.



1. Give the structural formulas of compounds A – E and decarestritin G (without stereochemistry). Note that: a) the OsO₄ / NMO system is used as an effective and highly selective reagent used instead of a neutral aqueous solution of KMnO₄; b) N, N'-dicyclohexylcarbodiimide (Cy – N = C = N – Cy) facilitates the condensation reaction by binding a water molecule. Write the structure of the resulting product.

Unlike most other decarestritins, decarestritin L is not a lactone and does not contain a ten-membered cycle. However, its high biological activity led to great interest in him from synthetic chemists. The diagram shows the first synthesis of decarestritin L, carried out in 1993.

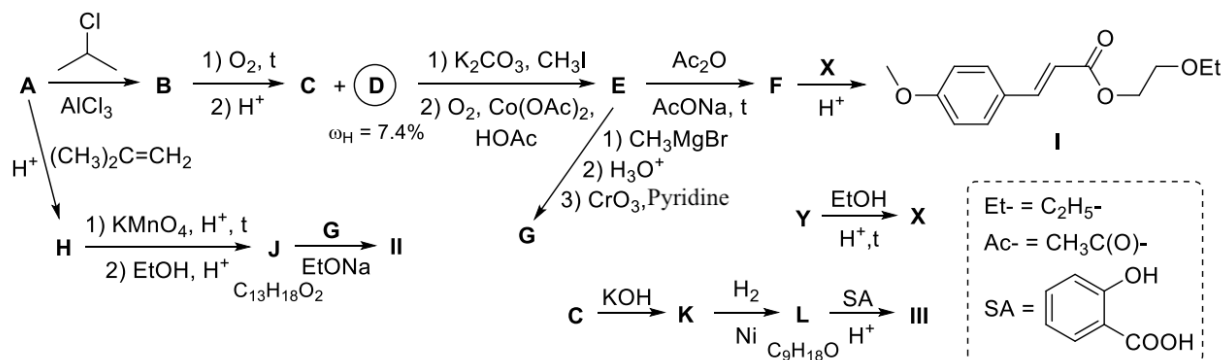


2. Write the structural formulas of compounds F – P and decarestritin L, if it is known that:

- at the first stage, only one epoxy cycle is affected, and the reaction proceeds according to a mechanism similar to the S_N2 mechanism
- compound L contains two cycles.

2018 Russia Tour 2 Organic Task 1

As far back as the end of the 19th century, it was believed that pale skin was characteristic of aristocrats, and dark skin testified to a peasant origin. In the XX century, the opinion of tanned skin changed dramatically, and tanning became popular. However, to date, it has been convincingly proven that excess ultraviolet radiation can cause premature aging and even skin cancer. To protect the skin from the effects of the sun, special creams are used - complex mixtures containing inorganic (usually titanium dioxide and zinc oxide, not more than 8%) and organic substances that can absorb either UV-A (315–400 nm) or UV -B (280-315 nm) radiation. Only some of the substances provide simultaneous protection against UV radiation in the range from 280 to 400 nm. One of these substances is zincate I, the synthesis of which is shown in the diagram below.



1. Write the structural formulas of compounds **A** – **F**, given that hydrocarbon **A** contains 91.3% by weight of carbon.

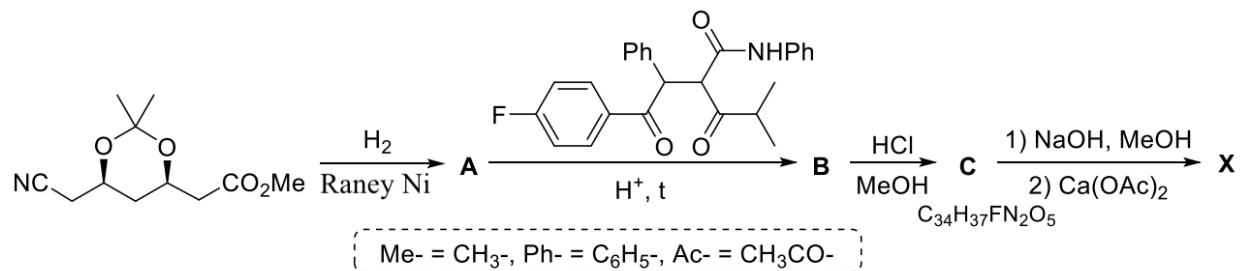
2. What substances **X** and **Y** are we talking about in the problem? Suggest their structure if it is known that **X** from **Y** is obtained selectively.

In recent years, a combination of different organic substances has replaced cyanoxate, each of which takes part of the radiation, but in total they cover the entire ultraviolet spectrum. One of the most common and stable substances is Avobenzon **II**, which absorbs the entire spectrum of UV-A radiation. The protective function of the cream can be enhanced by introducing additional substances that protect against UVB rays, for example, by adding homosalate **III**.

3. Write the structural formulas of substances **G**, **H**, **J**–**L** and components of the cream of Avobenzene **II** and homosalate **III**, if it is known that **K** has a cyclic structure.

2017 Russia Tour 2 Organic Task 2

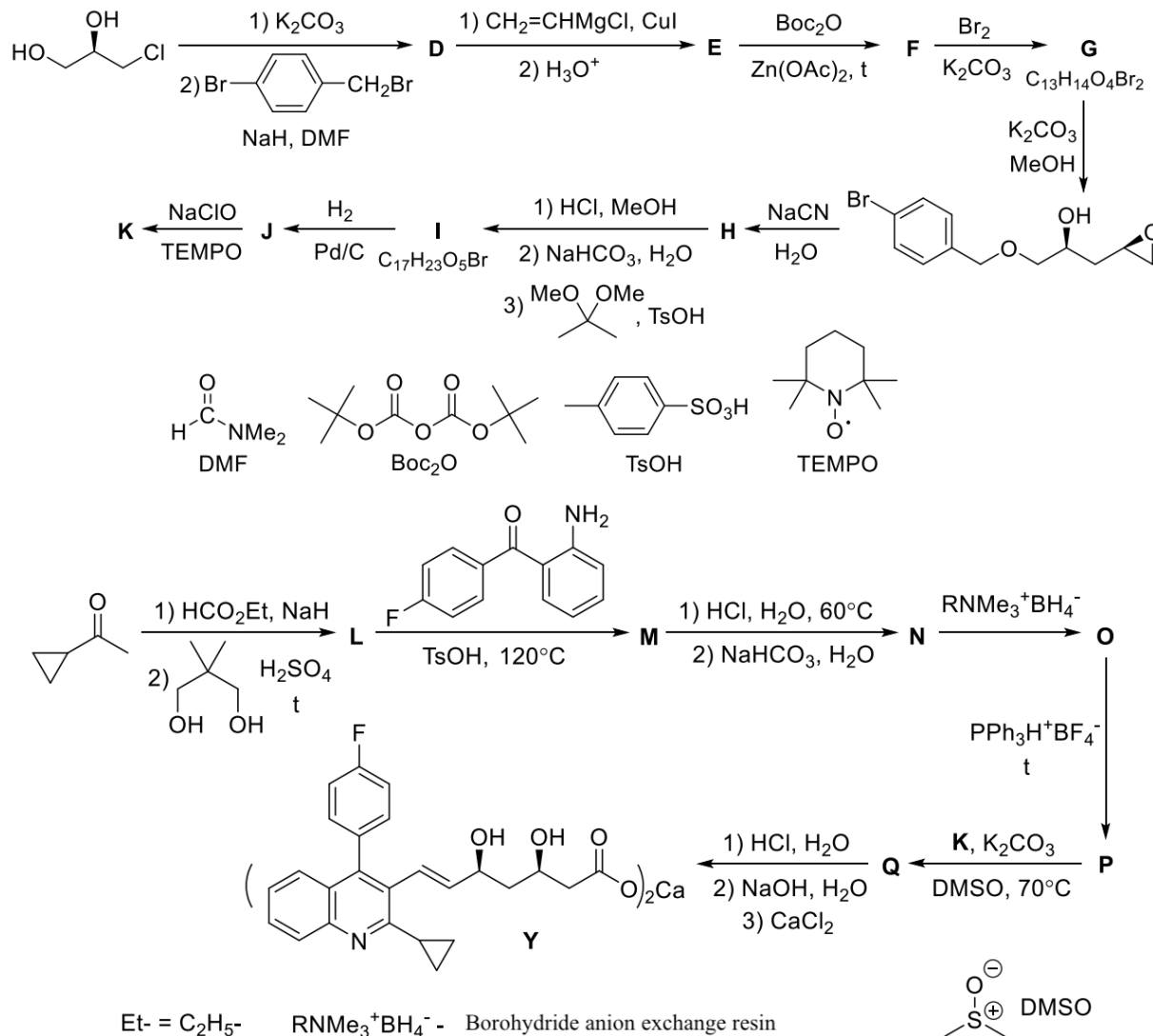
Cardiovascular disease is currently the most common cause of death in people around the world. One of the ways to prevent cardiovascular diseases is to lower blood cholesterol, for which so-called statins are actively used - inhibitors of 3-hydroxy-3-methylglutaryl-coenzyme A reductase, an enzyme that catalyzes the limiting stage of cholesterol biosynthesis. Some statins can be isolated from natural sources, others are synthetically produced, for example, atorvastatin (**X**), first obtained in 1985. It went on sale in 1996 and during this time it won first place in the world among all drugs in terms of sales. The diagram below shows the final stages of the synthesis of atorvastatin (in the form of calcium salt used in practice).



1. Give the structural formulas of compounds **A–C** and **X** if four aromatic rings are present in the structure of atorvastatin, one of which contains a heteroatom.

In 2003, an atorvastatin analog appeared on the market - pitavastatin (**Y**), also used in the form of calcium salt. Below is a diagram of the synthesis of pitavastatin, carried out in 2015 by scientists from Fudan University in Shanghai.

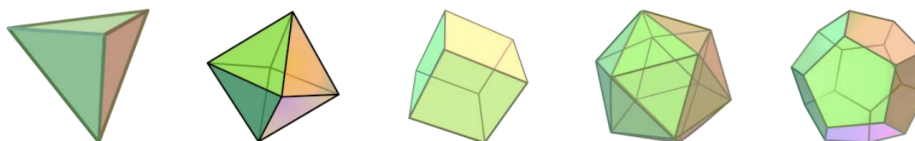
2. Give the structural formulas of compounds **D – Q**.



2018 Russia Tour 2 Organic Task 3

Platonic molecules

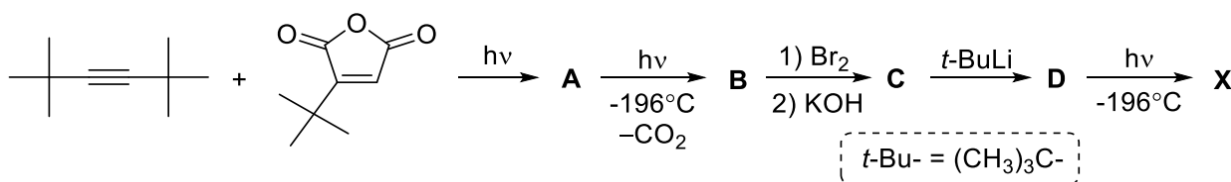
In Euclidean space, there are only five regular polyhedra, also called Platonic solids - tetrahedron, octahedron, cube (hexahedron), icosahedron and dodecahedron:



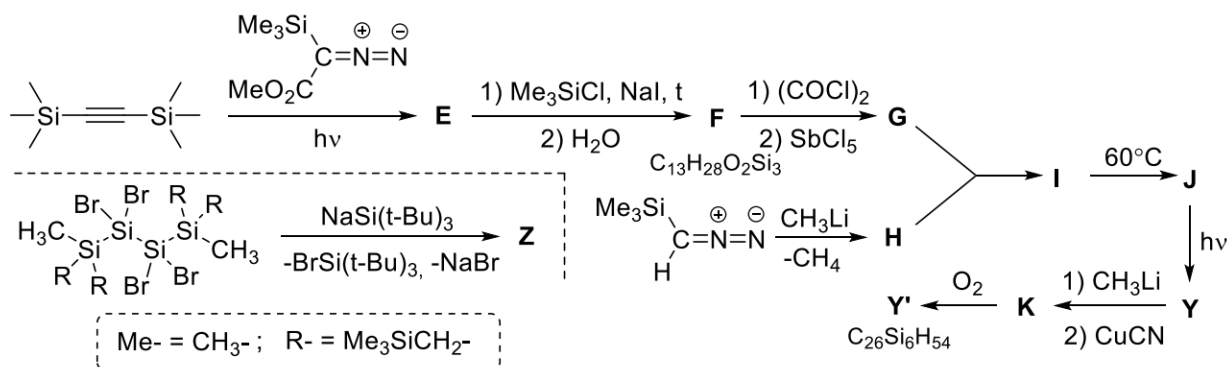
1. Which of the Platonic solids can theoretically have organic analogues with the same carbon skeleton?

Below are the synthesis schemes for compounds **X**, **Y**, **Y'**, and **Z**, the framework of which contains one of the polyhedra given above.

To obtain **X**, the product of [2 + 2] cycloaddition **A** is irradiated at liquid nitrogen temperature. In this case, compound **B** is formed, which incorporates a five-membered cycle. The bromination product **B**, substance **C**, contains three types of hydrogen atoms in a ratio of 1: 1: 1, and **D** contains two types of hydrogen atoms in a ratio of 1: 1. Upon exposure to **D**, gas evolution was detected lighter than air.



2. Give the structural formulas of compounds **A** – **D** and **X**.



3. Give the structural formulas of compounds **E** – **K**, **Y**, **Y'**, and **Z**. Note that:

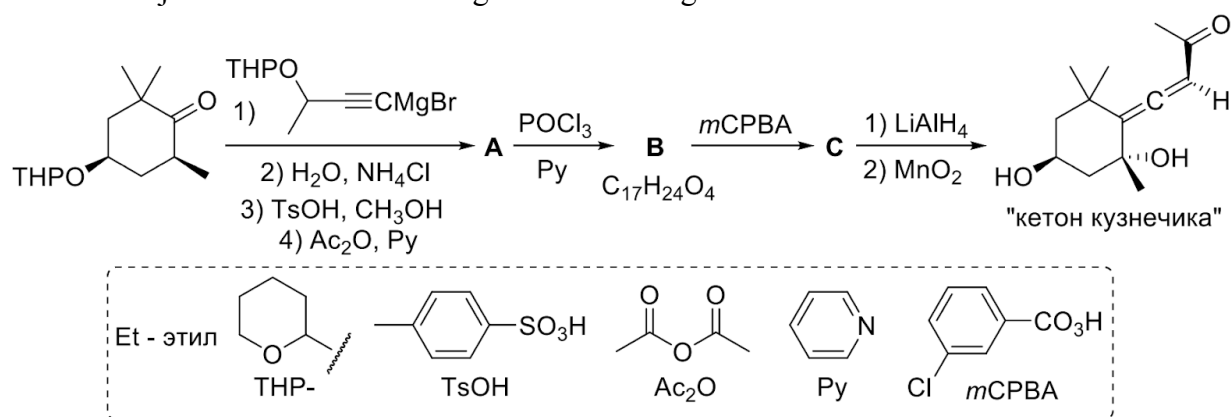
- Substance **G** is a salt of a highly symmetric cation;
- In the ^{13}C NMR spectrum of substance **J**, only two signals are observed at 0.1 and 171.6 ppm, and in the ^{13}C NMR spectrum of **Y**, two signals are observed at 0 and -20.5 ppm. In the ^1H NMR spectrum, both substances give only one signal at 0.1 ppm.

Upon receipt of **K**, a substance is released that is a generally accepted standard in ^1H NMR spectroscopy for measuring chemical shifts.

2019 Russia Tour 2 Organic Task 1

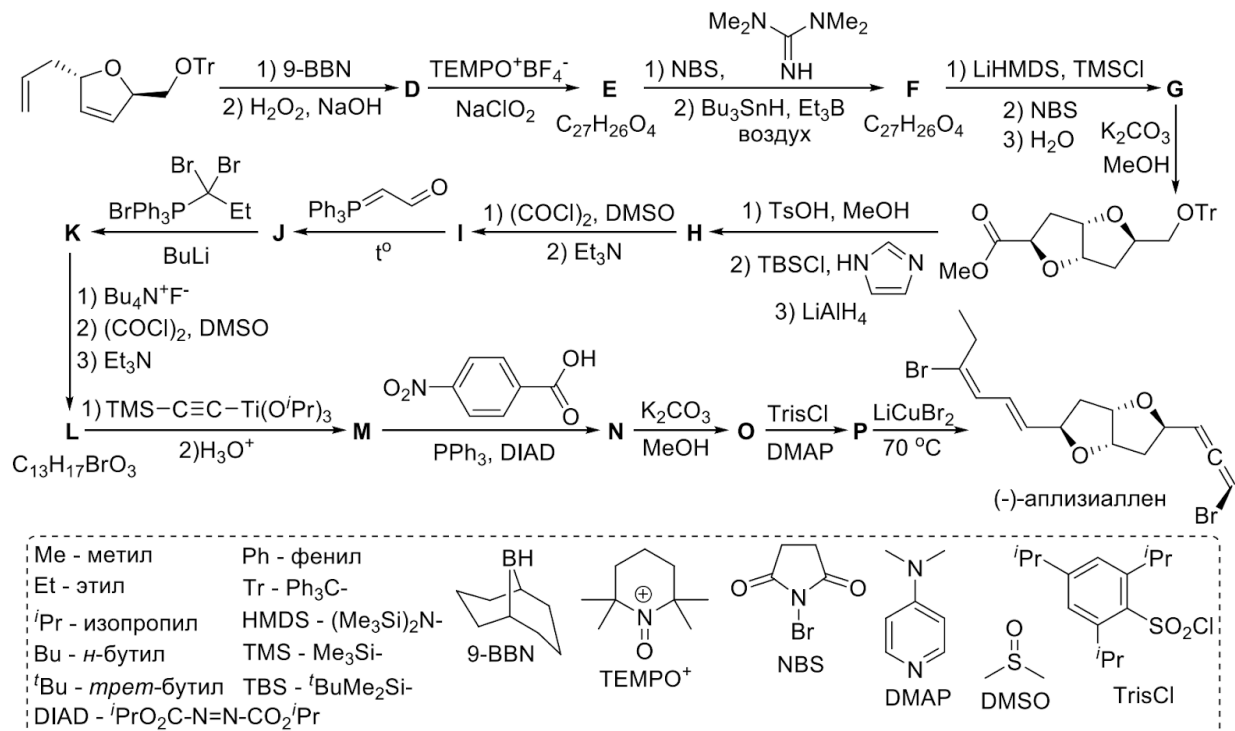
For a long time, it was believed that allene (also called cumulated dienes) should be extremely unstable compounds. For example, the first synthesis of cumulated diene by Burton and von Pehmann in 1887 was originally an attempt to prove the impossibility of the existence of this class of compounds. However, it later emerged that the allens are quite stable, and, moreover, allene fragments are present in about 150 natural compounds. Almost all of these compounds are chiral, and many also exhibit biological activity, due to which they are of interest as objects of complete synthesis.

One of the most famous natural allens is the so-called “grasshopper ketone” (eng. Grasshopper ketone), which was isolated in 1968 from the protective secret of the grasshopper *Romalea microptera* living in the southern United States. The structural fragment of the "grasshopper ketone" is also found in other natural alleles, such as fucoxanthin, peridinine, neoxanthin, etc. The first enantioselective synthesis of the "grasshopper ketone" was carried out by the Japanese scientist Kenji Mori in 1973 according to the scheme given below.



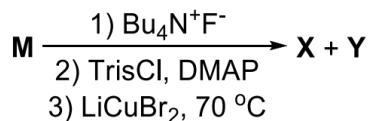
1. Give the structural formulas of compounds A – C. Note that in the IR spectrum of substance A there is a band at 3500 cm^{-1} . Substance B gives only two signals in the $^1\text{H NMR}$ spectrum with chemical shifts greater than 3 ppm, and in the IR spectrum - a band at 2200 cm^{-1} . At the stage of preparation of substance C, two diastereomeric products are formed, of which only one is used to produce the “grasshopper ketone”.

Another example of a natural allen is (-) - apliziallen, isolated in 1985 from the red alga *Laurencia okamurai* Yamada, and later from the mollusk *Aplysia kurodai*. This substance, in addition to cumulated double bonds, also has a structural fragment of cis-2,6-dioxabicyclo [3.3.0] octane, which makes it a very nontrivial object for complete synthesis. For the first time (-) - apliziallen was synthesized by Van and Pagenkopf in 2007, which also clarified its structure. Below is a scheme for the synthesis of (-) - apliziallen from intermediate product H according to Van and Pagenkopf, as well as an alternative scheme for obtaining H proposed in 2016 by a group of scientists from the Osaka Institute of Technology.



2. Give the structural formulas of the compounds D - P. Note that all compounds, except D and E, encrypted in the scheme, contain two non-aromatic cycles in their structure, and in the ¹H NMR spectrum of the substance F there are no signals in the range from 5 to 7 ppm .

The substance M obtained during the synthesis was an inseparable mixture of two epimers with a fourfold predominance of the epimer with the S-configuration of the chiral center formed at this stage. The initial purpose of the synthesis of Van and Pagenkopf was compound X - the enantiomer of the previously proposed structure (-) - aplysiallen. To do this, they carried out the following sequence of transformations with substance M, as a result of which compound X was actually obtained along with the minor diastereomeric product Y:



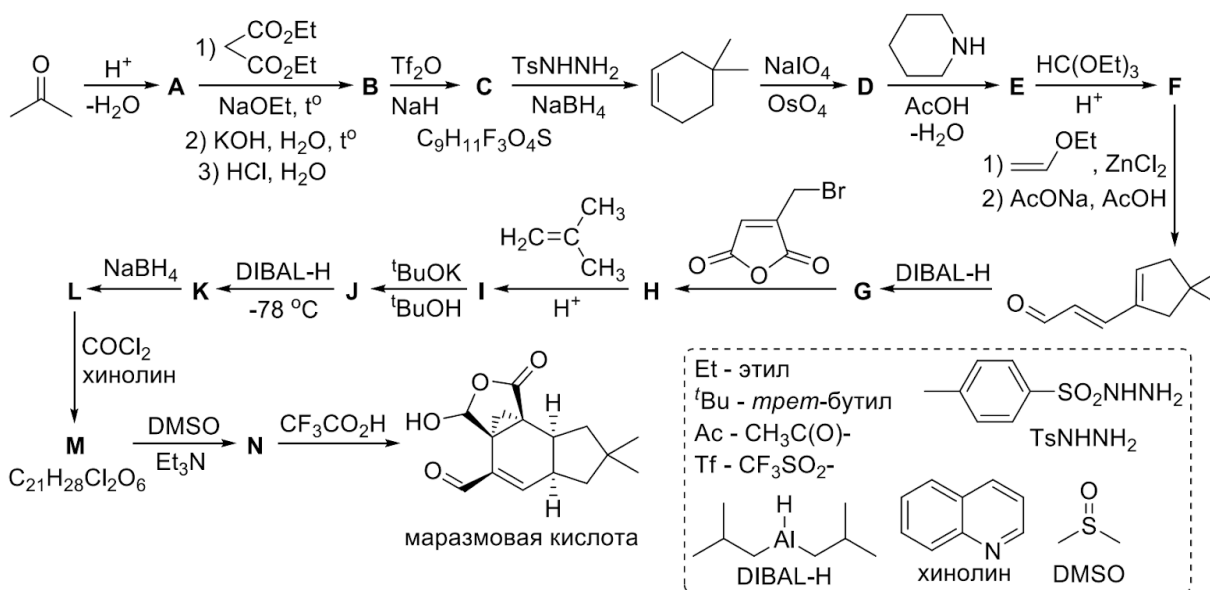
However, after comparing the NMR spectra of compounds X and Y with the spectra of natural (-) - aplysiallen, it became clear that in fact the natural (-) - aplysiallen has the structure Y. Next, Van and Pagenkopf modified the synthesis scheme, which allowed them to obtain compound Y without admixture diastereomers (this scheme is given in paragraph 2). Selectivity was achieved due to the fact that compound N was able to be separated from its epimer N', formed as a by-product, using column chromatography.

3. Give the structural formula that was proposed for (-) - aplysiallen before the synthesis of Van and Pagenkopf.

2019 Russia Tour 2 Organic Task 2

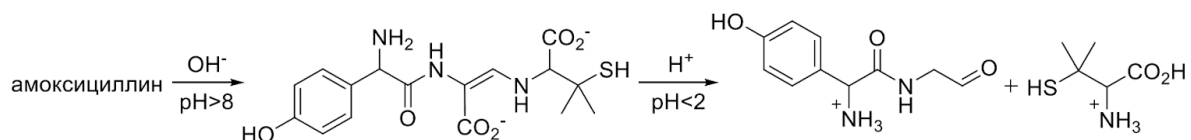
The Nobel Prize is awarded for some discovery or invention. However, at least once the committee awarded the prize for the totality of achievements of the laureate. Robert Burns Woodward for 30 years spent about 20 complex syntheses of natural compounds, which previously seemed impracticable, and also made a tangible contribution to the definition of the structures of numerous substances. With its wording, the committee emphasized the uniqueness of the laureate, and Woodward, in turn, promptly completed the complete synthesis of β -lactam antibiotic cephalosporin C specifically for the Nobel ceremony.

1. One of the successful syntheses by Woodward was the preparation of marasmic acid in 1976. You are invited to decipher the transformation scheme carried out by the laureate and bring the structures of substances A to N. Additionally, it is known that substance B contains one cycle and L - 3 cycles



Woodward, together with another prominent chemist, Robert Robinson, based on penicillin hydrolysis products, first proposed the structure of this antibiotic, which later served as the starting material in one of the methods for the synthesis of cephalosporin C, which has a related chemical structure with it. One of the most popular semi-synthetic broad-spectrum antibiotics of this class is amoxicillin, which is synthesized by attaching 2-amino-2-(4-hydroxyphenyl) acetyl chloride to the core of 6-APA.

2. The diagram below shows the products of hydrolysis of amoxicillin. Like the great chemists, you are invited on the basis of these data to suggest its structure. Additionally, it is known that 6-APC contains two condensed cycles with the number of atoms in each cycle exceeding three. Consider that in both cases of hydrolysis there are no other organic products other than those indicated in the diagram.

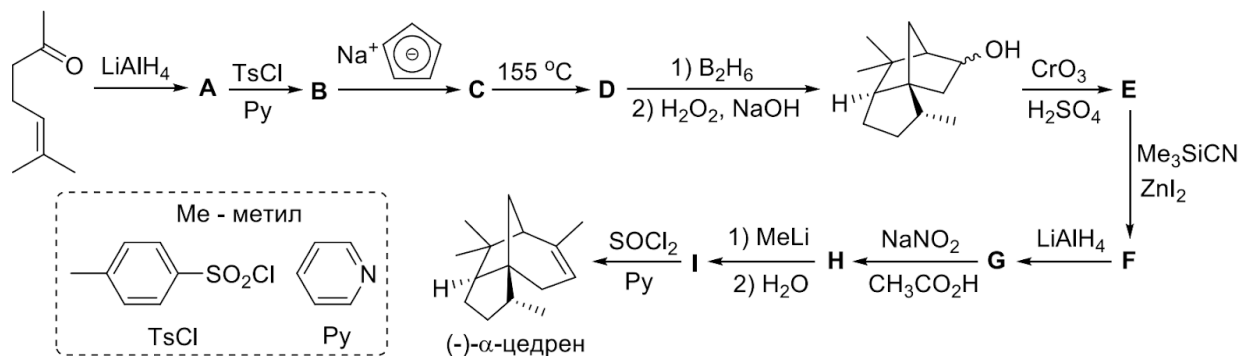


3. How can you spell out the abbreviation 6-APK, based on the structure of the compound? Suggest your option.

Note: At the stage of obtaining the substance H, a mixture of two isomers was formed in a 1: 1 ratio, which was further used without separation. Because of this, substance I was also obtained as a mixture of two isomers, which at the next stage gave the same product J. As the correct answer for compounds H and I, either of two possible isomers is counted

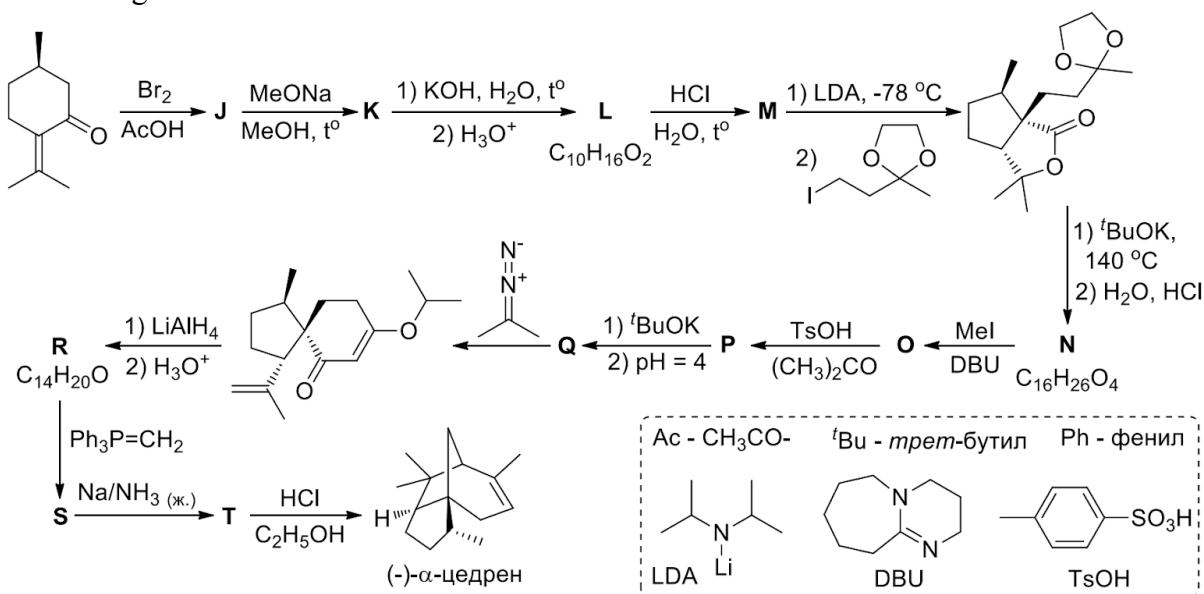
2019 Russia Tour 2 Organic Task 3

(-) - α -Zedren - sesquiterpene, a bright representative of the class of terpenes. It is obtained from wood scraps of virgin cedar growing in the northern states of the United States, and it is also found in some species of juniper. The first complete synthesis of the racemic α -zest was performed by Stork and Clark in 1955. In subsequent years, alternative methods for the synthesis of α -zest were proposed by other synthetic chemists, including the future Nobel laureate Elias James Corey. Below is a diagram of one of these syntheses, carried out in 1978 by Canadian scientists (for simplicity, the diagram shows the structure of the natural enantiomer α -cue, although in fact this way the racemic mixture of enantiomers was obtained)



1. Give the structural formulas of compounds A - I.

In 1983, Solas and Volinski proposed the stereospecific synthesis of (-) - α -peadin from (+) - pulegon through the intermediate formation of another sesquiterpene - (-) - α -acoradiene (T), whose carbocation cyclization in (-) - α -pead at that time was already known. The scheme of this synthesis is given below.

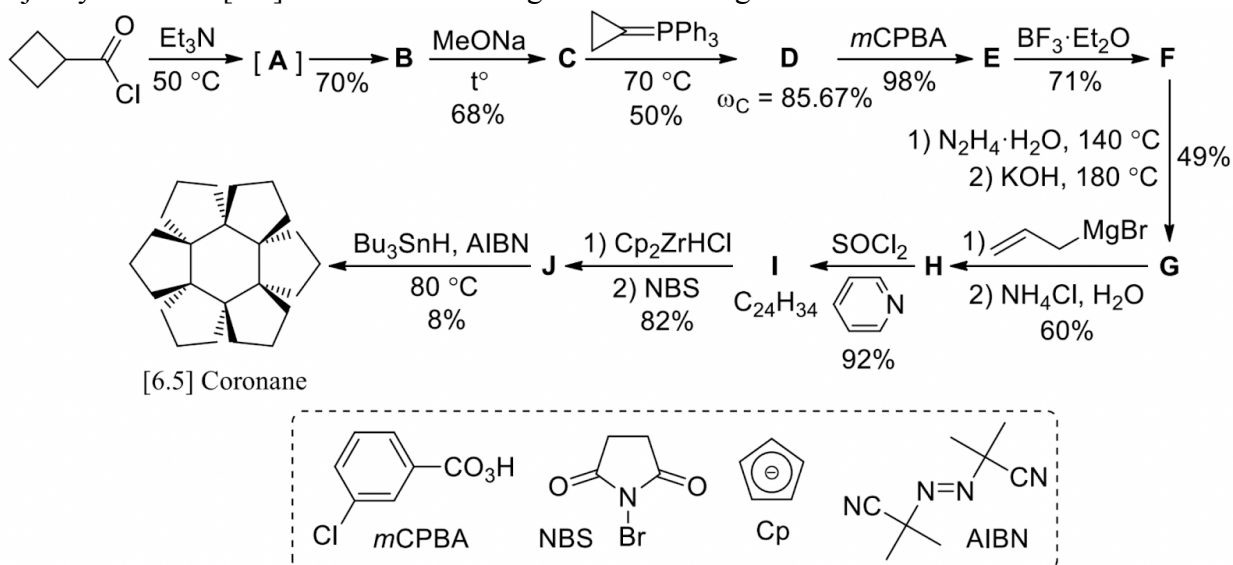


2. Give the structural formulas of compounds J - T. Note that all substances ciphered on the scheme, except for compound J, contain at least one five-membered cycle in their structure. Compounds L, M and N in the ¹H NMR spectrum give the following signals with chemical

shifts of more than 3 ppm: L - one signal at 11.6 ppm, M - no signal, N - four signals at 9.7, 4.8, 4.75 and 3.9 ppm Compounds L and M are isomers.

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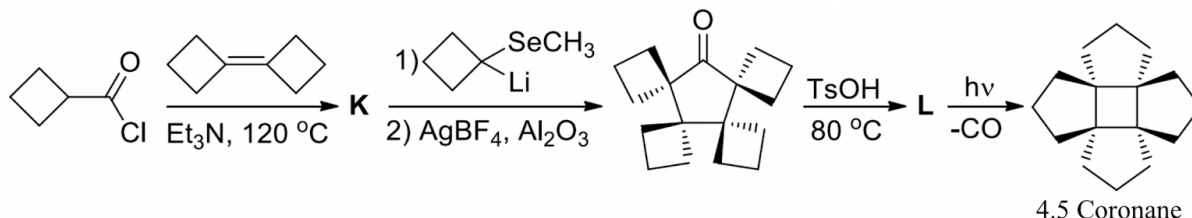
[m.n] Coronanes are polycyclic hydrocarbons with an interesting structure, containing an m-membered central ring, to the sides of which n-membered rings are adjoined. In 1987, Lutz Fitjer synthesized [6.5] coronane according to the scheme given below.



Compounds **B** and **C** have the same empirical formulas and the same number of signals in their NMR spectra (2 signals in the ^1H NMR spectrum and 4 signals in the ^{13}C NMR spectrum), but the molar mass **C** is 1.5 times the molar mass of **B**. In the IR spectrum of compound **F** there are two intense bands in the frequency range of $1650\text{--}1800\text{ cm}^{-1}$, while the **G** spectrum has only one band in this region. None of the compounds **A** – **J** shown in the diagram contains conjugated double bonds or rings with more than 6 carbons. **I** and **J** contain six rings, none of which is four-membered. Regroupings of the adjoined rings occurs in exactly two distinct stages of the [6.5] coronane synthesis.

1. Give the structural formulas of compounds **A**–**J**.
2. Calculate the percent yield of [6.5] coronane given the percent yields in each step shown above.

Shortly after the synthesis of [6.5] coronane, Fitjer synthesized [4.5] coronane from the same precursor (cyclobutanecarboxylic acid chloride) according to the following scheme:



Note that compound **L** does not contain a single four-membered cycle.

3. Give the structural formulas of compounds **K** and **L**.