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Photo : the main building of Moscow State University

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Synthesis of quinine

Outstanding organic chemist **Robert Burns Woodward** over 30 years has carried out about 20 complex syntheses of natural compounds such as quinine, cholesterol, cortisone, strychnine, lysergic acid, reserpine, chlorophyll, cephalosporin, and colchicine that previously seemed unrealizable. For his contribution in organic chemistry he was awarded the Nobel Prize in Chemistry in 1965. The goal of one of the first in a series of extremely complex and elegant syntheses he carried out was **quinine**, an alkaloid of the cinchona tree with a bitter taste. Quinine has antipyretic, analgesic, and antiarethmic properties and is still used in the treatment of malaria. Although the synthesis proved to be successful, it was too long and laborious to be applied on a practical scale. Later, **E**. Jacobsen and his coworkers were able to propose a much simpler enanteoselective synthesis of quinine using catalytic reactions.



Robert Burns Woodward April 10, 1917 – July 8, 1979



Steven E. Jacobsen



State of the second states

Compound	Brut formula	Compound	Brut formula	Compound	Brut formula	Compound	Brut formula
A	C7H9NO	E	C22H32N2O5Si	I	C ₁₇ H ₂₃ NO ₃	L	$C_{28}H_{32}N_2O_5$
В	C ₁₀ H ₉ NO ₂	F	C ₁₅ H ₂₉ NO ₄ Si	J	$C_{17}H_{21}NO_3$	Μ	$C_{31}H_{36}N_2O_6$
С	$C_{10}H_{10}BrNO$	G	$C_{14}H_{31}NO_2Si$	×	$C_{18}H_{22}NO_2$	Ν	$C_{28}H_{30}N_2O_4$
D	$C_{18}H_{27}NO_3Si$	н	C ₂₂ H ₃₅ NO ₄ Si	K	$C_{28}H_{30}N_2O_3$		

1. Write the scheme of transformations presented above, giving the structures of the substances A-N (it is not required to indicate the stereochemistry). Additionally, it is known that the molecular ion (MH^+) of N corresponds to a peak with m / z = 459.2285. The ¹H NMR spectrum of substance B contains the following signals: 11.8 (1H), 7.84 (1H), 7.52 (1H), 7.48 (1H), 7.27 (1H), 6.00 (1H), 3.82 (3H).

Interestingly, in its antiarethmic activity, **quinine** is significantly inferior to its stereoisomer **quinidine** and gives significantly more side effects. Therefore, of all the stereoisomers of **quinine**, it is **quinidine** that is currently used as an antiarethmic agent.

2. How many stereoisomers does quinine have in total? Determine the configuration of chiral centers in its molecule according to the (R, S) - nomenclature.

3. Give the structural formula of **quinidine**, if it is known that the above scheme for the synthesis of **quinine** can be used to obtain **quinidine**, replacing the reagent AD-mix-β with AD-mix-a. These reagents differ in that they use different enantiomers as a chiral ligand.