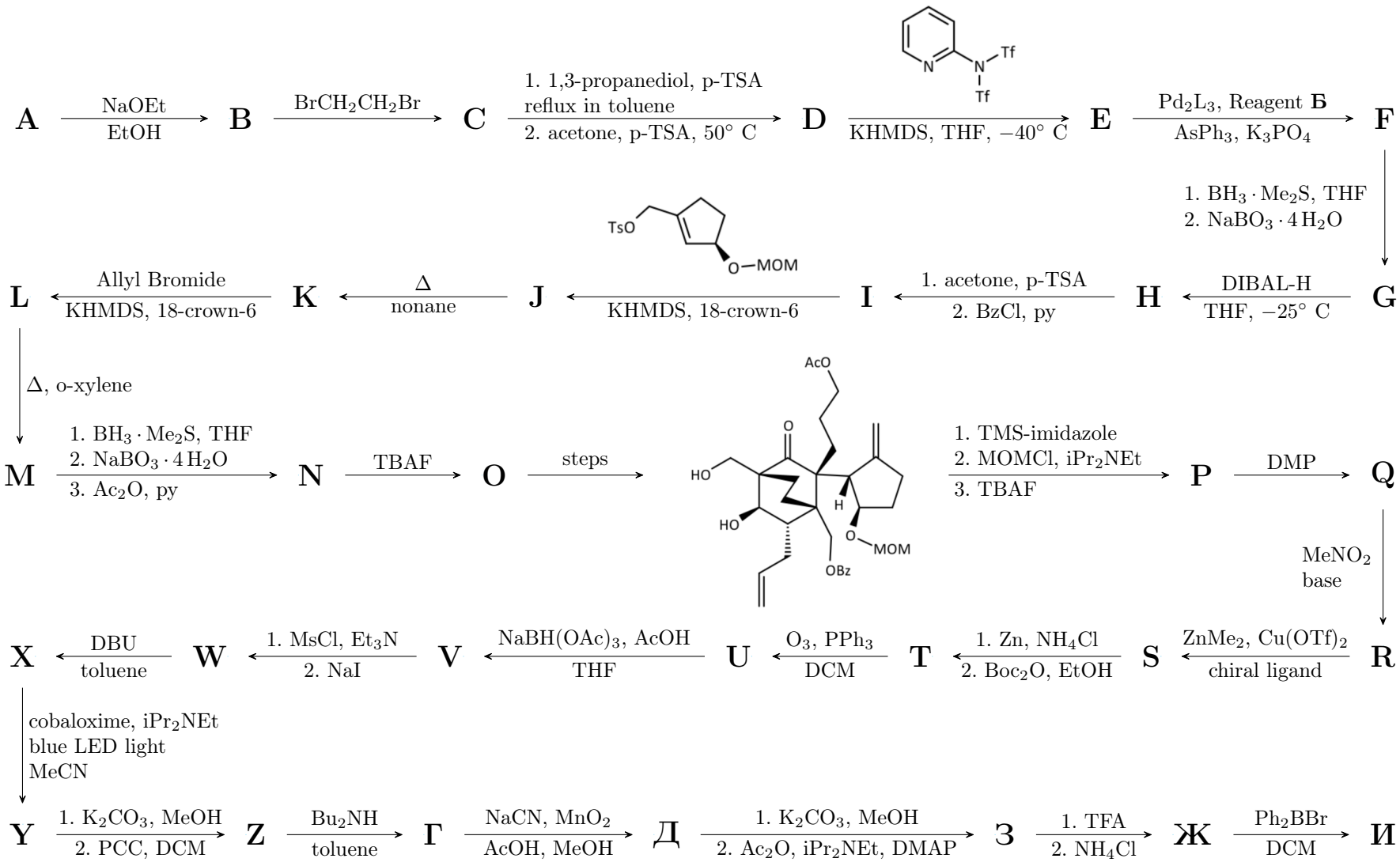
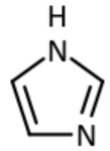
Total Synthesis of a Natural Compound (BCC 2019 Problem 3)

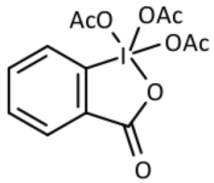


Me = $-CH_3$	Bu = $-CH_2CH_2CH_2CH_3$	Ac = $-COMe$	toluene = PhMe	DIBAL-H = $(iBu_2AlH)_2$
Et = $-CH_2CH_3$	Ph = $-C_6H_5$	Boc = $-CO_2tBu$	THF = $O(CH_2)_4$	o-xylene = o-MeC_6H_4Me
iPr = $-CHMe_2$	Bz = $-COPh$	Ms = $-SO_2Me$	DCM = CH_2Cl_2	18-crown-6 = $(OCH_2CH_2)_6$
allyl = $-CH_2-CH=CH_2$	TMS = $-SiMe_3$	Ts = $-SO_2C_6H_4Me$	py = C_5H_5N	KHMDS = $K^+[N(TMS)_2]^-$
iBu = $-CH(CH_3)(CH_2CH_3)$	TBDPS = $-SiMe_2tBu$	Tf = $-SO_2CF_3$	p-TSA = TsOH	PCC = $[pyH]^+[CrO_3Cl]^-$
tBu = $-CMe_3$	MOM = $-CH_2OCH_3$	acetone = Me_2CO	TFA = CF_3CO_2H	TBAF = $[Bu_4N]^+F^-$

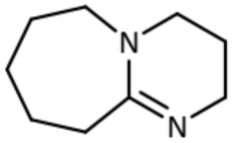
imidazole



DMP

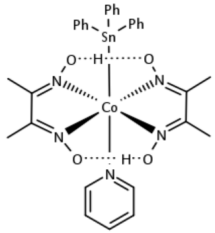


DBU

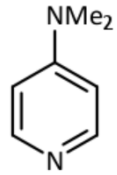


9-BBN

cobaloxime



DMAP



Hints and Information:

- **A** has formula $C_8H_{14}O_4$ and is acyclic.
- The ^{13}C NMR spectrum of **A** has 4 peaks, at 172, 61, 30, and 15 ppm. The ^1H NMR spectrum of **A** has 3 peaks, at 4.12 ppm (quadruplet), 2.74 ppm (triplet), and 1.15 ppm (triplet). The ratio of integrals for these peaks are 1:1:1.5.
- **C** is bicyclic and has chiral centers with configurations S, S.
- **D** has formula $C_{17}H_{24}O_7$
- Reagent **Б** is synthesized from the reaction of TBDPS-protected allyl alcohol with 9-BBN.
- **I** contains three protecting groups.
- The reactions forming **K**, **M**, and **S** are stereoselective.
- In the formation of **S**, the organozinc reagent is used as a nucleophile, resulting in the conversion of a non-chiral secondary carbon into a chiral tertiary carbon with R configuration.
- Ozonolysis in the formation of **U** is complete, and is followed by the conversion of the resulting primary alcohol into a good leaving group, and then to a halide via a Finkelstein reaction.
- The cobalt complex is able to catalyze a coupling reaction which results in the formation of a 7-membered ring.
- The reaction forming **V** is also selective.
- The reaction forming **X** is regioselective.

- **W** contains 8 chiral centers, while **X** and **Y** contain only 6.
- **Y** is pentacyclic, with one cyclic protecting group.
- From **Y** to **И**, two cyclization reactions occur. The first cycle is produced via an aldol condensation and the second is formed after the deprotection of a functional group. Both cyclizations give 5-membered rings.
- After treating **Г** with the indicated reagents, the ester **Д** is formed.
- Compound **И** is the desired natural product with formula $C_{25}H_{31}NO_5$ and is hexacyclic.
- The following changes have been made from the original problem:
  - Some intermediates have had their letterings changed.
  - The problem originally stated that **C** was tricyclic, **Y** was hexacyclic, and **И** was heptacyclic, but this is wrong and is fixed in this version.
  - Some other questions that were multiple choice have been converted to free response form.
  - The reagent/abbreviations box was not provided in the original problem.

Problems:

1. Decipher the scheme. Draw the structures of all unknown intermediates and that of reagent **Б**.
2. Is the reaction forming **B** intermolecular or intramolecular?
3. The reactions forming **D** are carried out in two steps. What is the importance of the second step?
4. In the formation of **C**, only the S,S isomers and R,R isomers are formed. True or False?
5. Why is $AsPh_3$ added to the mixture in the formation of **F**?
6. In the reaction forming **F**, an organopalladium complex is used. The mass percent of Pd in the complex is 23.244% and the ligand can be synthesized from two different organic molecules via a double aldol condensation. Further, a single [2+2] photodimerization reaction of two ligand molecules can give up to 4 different cyclobutane derivatives. The ligand contains three elements, but no sp^3 hybridized atoms, and the mass percent of the element with the greatest coefficient in the ligand is 87.31%. Give the formula and structure of the ligand.
7. How many distinct peaks will be visible in the ^{13}C NMR spectrum of the ligand?
8. Name the reaction forming **K**.
9. How many protecting groups does **N** contain?
10. In the formation of **P**, a three-step sequence was performed, with the first step being selective. Give a brief description of what happens in every step of the synthesis.
11. Name the reaction forming **R**.
12. Out of the following list of reagents, which ones do not remove any protecting groups from **Q**?
    HCl; K_2CO_3; Zn; F^-; NH_3; I_2; H_2, Pd/C; LiOH
13. Which type of selectivity is exhibited in the reaction forming **V** (regio, stereo, or chemoselective)? Is this a reduction or an oxidation?
14. Name the mechanism involved in the formation of **X** from **W**.