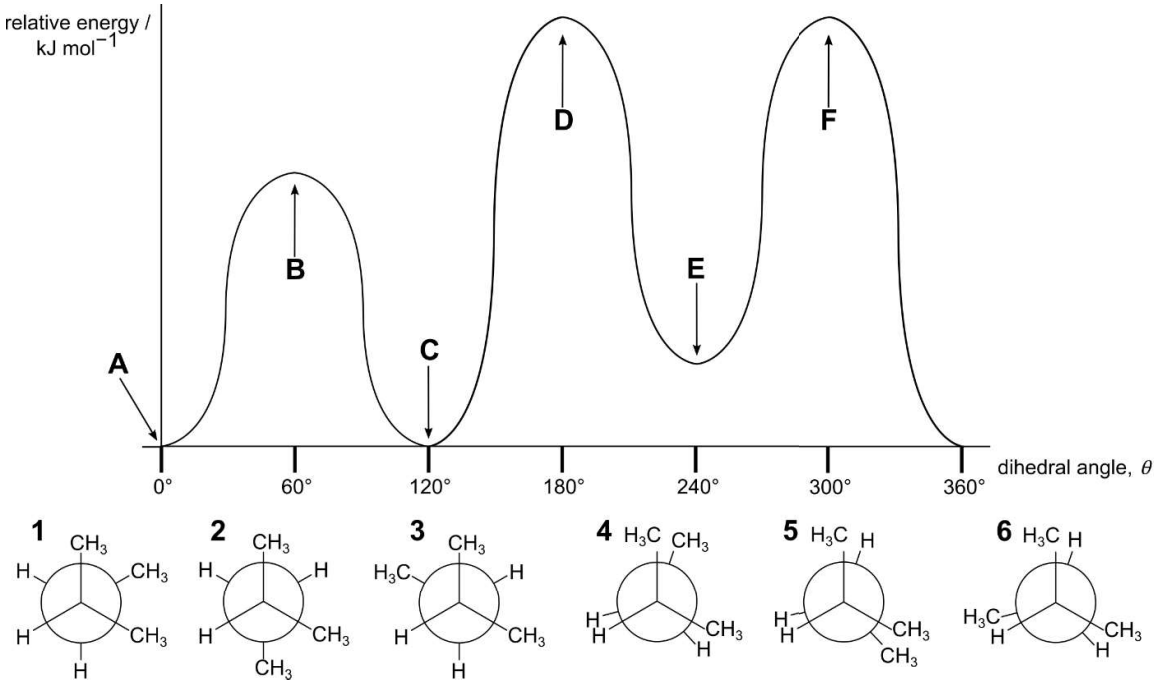
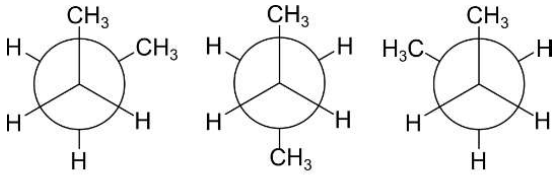
Although θ can take any value between 0° and 360° for rotation around a bond, we often consider just six conformations (three staggered and three eclipsed). The diagram shows the relative energy of the conformations for rotation around the C_2–C_3 bond in methylbutane.



(b) Match the six Newman projections of methylbutane (**1**–**6**) with the points **A**–**F** on the energy diagram. Write only one number in each box.

The energy difference between conformations can be used to approximate the percentage of time a molecule will be found in each conformation by treating the interconversion between conformations as equilibria.

For butane, we will assume that the molecule is always in one of the three staggered conformations: gauche 1 (**G₁**), antiperiplanar (**AP**), or gauche 2 (**G₂**).



gauche 1 **G₁** | anti-periplanar **AP** | gauche 2 **G₂**

The equilbrium **G₁** ⇋ **AP** has a $\Delta G^{\ominus}$ = −3.63 kJ mol^{-1} at 298 K.

$$\Delta G^{\ominus} = -RT\ln K$$

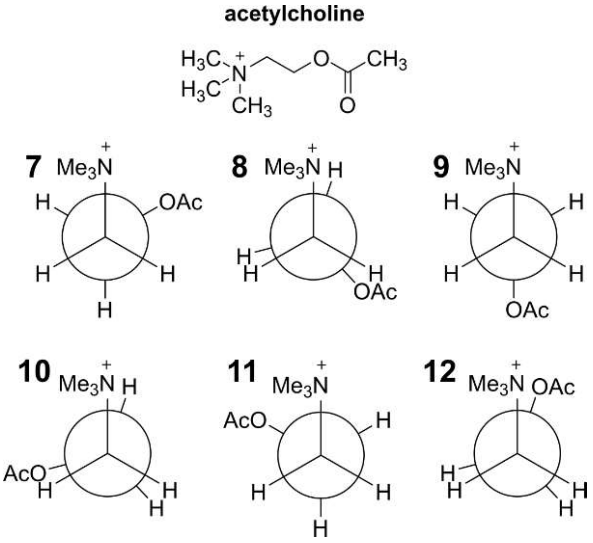
(c) **(i)** Complete the table in the answer booklet by calculating the Gibbs energy change, $\Delta G^{\ominus}$, and the equilibrium constant, K, for each of the three equilibria at 298 K.

G₁ ⇋ **AP** **AP** ⇋ **G₂** **G₂** ⇋ **G₁**

(ii) Hence, calculate the percentage of time that butane is in the anti-periplanar conformer **AP**.

Acetylcholine is a neurotransmitter released by motor neurons to activate muscles.

Six Newman projections of different conformations of acetylcholine are shown. The ethanoate ester group is abbreviated as OAc and the methyl groups are abbreviated as Me.



(d) Group these conformations into sets of equal energy.

For example you could write:

(7 = 8 = 9)

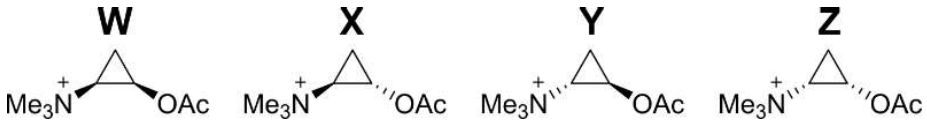
(10 = 11)

12

Include all conformations in your answer.

Although acetylcholine can adopt many conformations in solution, when it binds in muscle receptors it has to adopt a particular conformation. Drugs to treat various diseases seek to block acetylcholine binding.

Many of these drugs are more rigid molecules, where the angle between the $(NMe_3)^+$ and the OAc groups cannot freely change. The drugs which most closely resemble the 3D shape of bound acetylcholine usually bind most strongly in the receptors and so are the most effective blockers.

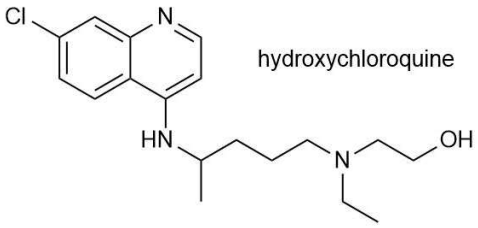


The cyclopropane rings in molecules **W**, **X**, **Y** and **Z** are planar and have very little conformational flexiblity. **W**, **X**, **Y** and **Z** were investigated as acetylcholine blockers.

(e) For each conformation of acetylcholine **7 – 12**, tick whether they are mimicked by any of the cyclopropanes **W**, **X**, **Y** or **Z**. Some conformations may have more than one mimic and some conformations may have no mimics.

5. This question is about Donald Trump and the coronavirus

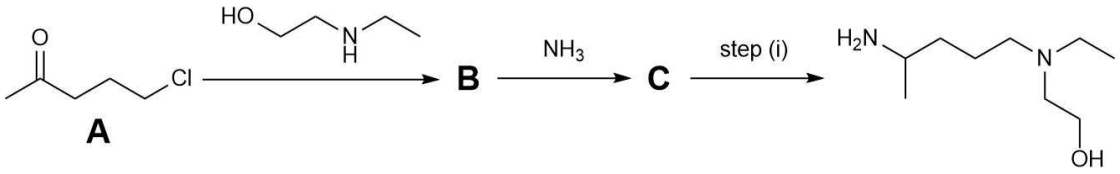
Donald Trump suggested several strategies for preventing or treating a coronavirus infection, which medical experts have disagreed with. These include shining UV light inside the body and injecting disinfectant. In May 2020, Trump said that he was taking hydroxychloroquine. In October 2020, it was reported that he had tested positive for COVID-19.



hydroxychloroquine

Make America Titrate Again

Hydroxychloroquine may be synthesised by the following route. Note in this question not all by-products are shown in the reaction schemes.



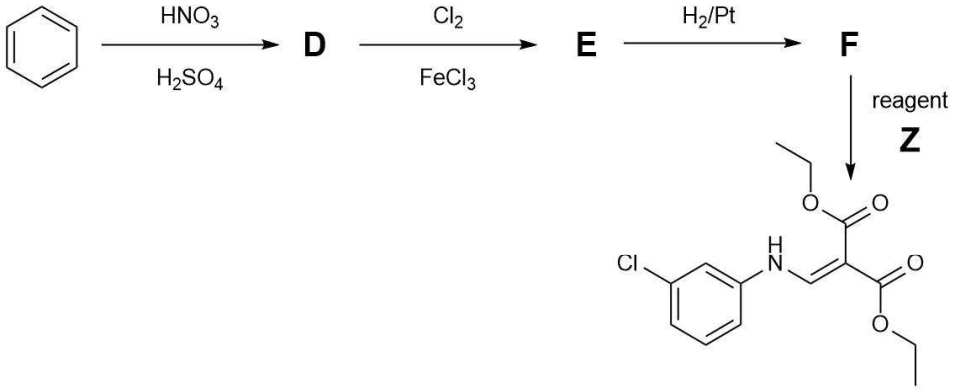
(a) Give the IUPAC name for starting material **A**.

(b) Draw the structures of **B** and **C**.

(c) Tick in the answer booklet the reagents/conditions required to perform step (i).

Br_2 / UV light	$KMnO_4$	H_2 / Ni catalyst	acidified $K_2Cr_2O_7$
OsO_4	ethylamine	O_2 / UV light	H_2SO_4 catalyst

Another starting material in the synthetic route is benzene.



(d) Draw the structures of **D**, **E** and **F**.