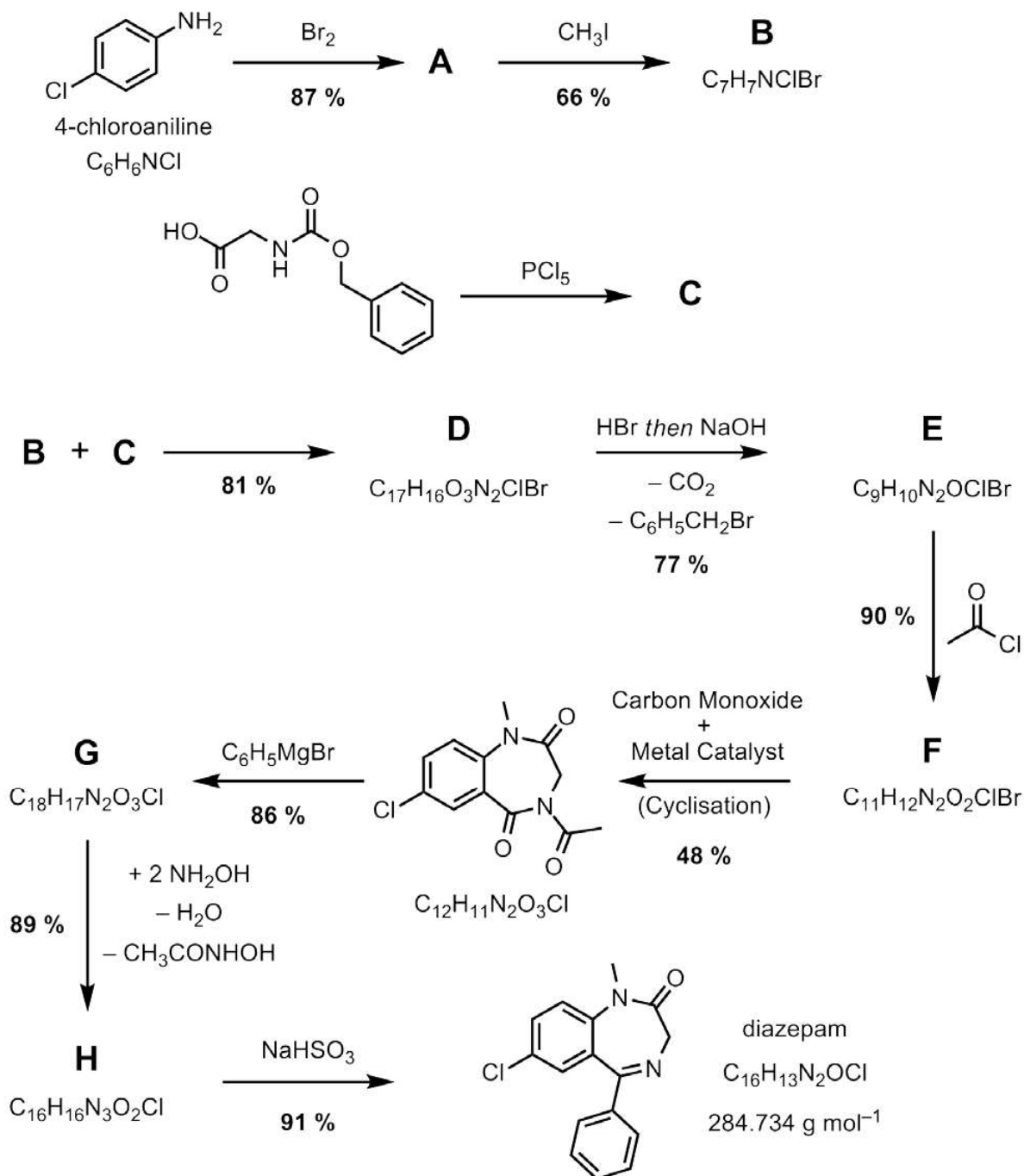


#### 4. This question is about GPs giving out too many drugs

The drugs diazepam (Valium®) and alprazolam (Xanax®) belong to a family of compounds called benzodiazepines which were once hailed as the answer to many ailments. In 1988, The Committee on Safety of Medicines advised GPs to limit their prescriptions of these drugs due to their overuse; however, in England in 2010 more than 6.6 million benzodiazepine prescriptions for anxiety were dispensed. Heath Ledger, Michael Jackson and Whitney Houston are among some of the many people that are believed to have died from drug overdoses that involved benzodiazepines.



The synthesis of diazepam from 4-chloroaniline is shown below. The percentage yield for each step is also shown. By-products are not always shown.



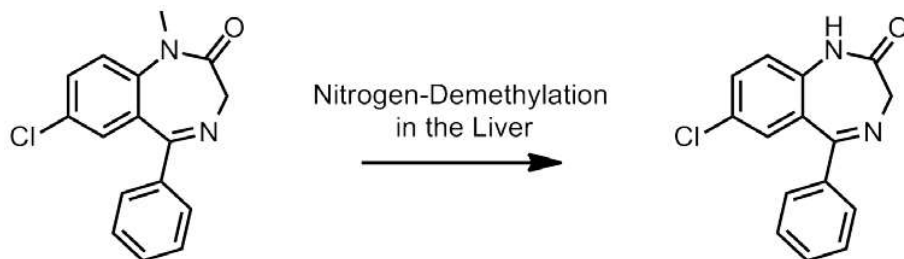
(a) (i) Calculate the overall percentage yield for the conversion of 4-chloroaniline to diazepam.

(ii) A patient was prescribed diazepam for three years at a dose of 5 mg, four times a day.

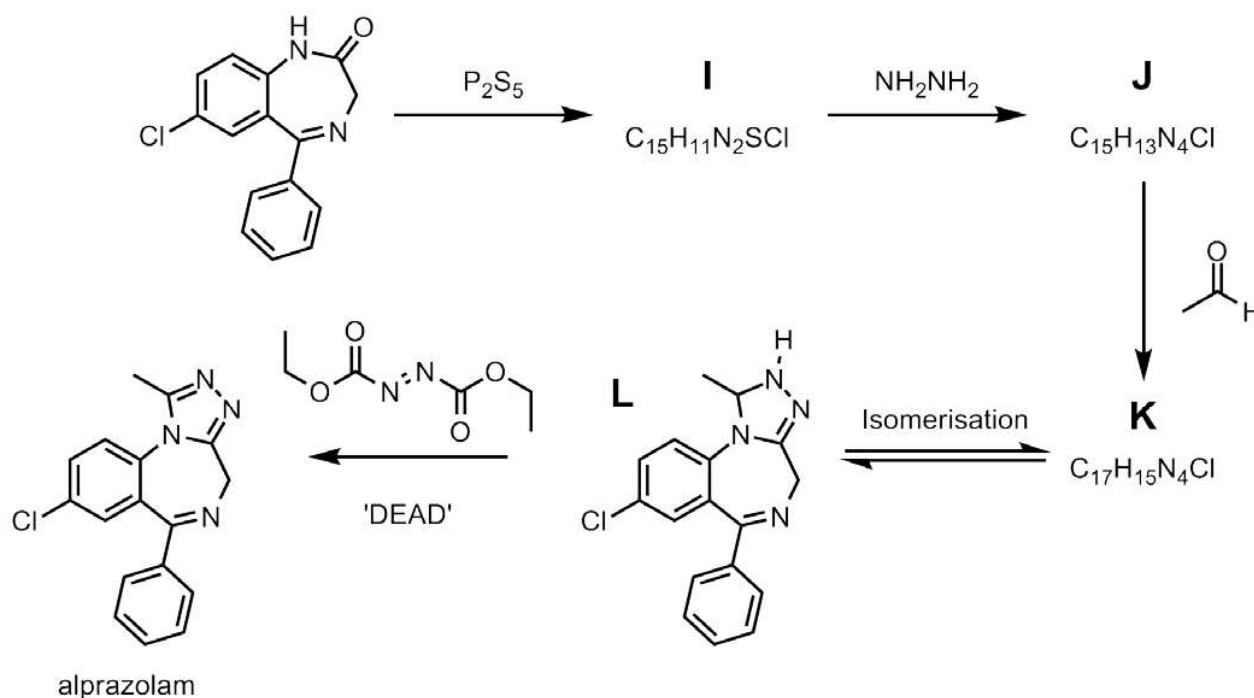
Calculate the mass of diazepam this was, and hence the mass of 4-chloroaniline needed to make the drug for this patient.

(b) Draw the structures of intermediates **A** – **H** in the synthesis of diazepam.

In the liver it was found that diazepam underwent a demethylation reaction. The product of this demethylation reaction was used as inspiration for the synthesis of the drug alprazolam.



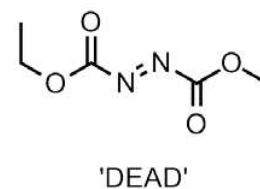
(c) The synthesis of alprazolam is shown below. Draw the structures of intermediates **I**, **J** and **K**



(d) In the final stage of the synthesis, compound **L** is treated with a chemical called 'DEAD' to convert it into alprazolam. DEAD stands for diethyl azodicarboxylate.

How would you classify the reaction of **L** to alprazolam using one of the terms below?

Tick the correct answer in your answer booklet.



Isomerisation

Hydrolysis

Condensation

Oxidation

Reduction