Reactivity of Acid Derivatives:

A,

\[
\text{Cl} \text{-}
\begin{array}{c}
\text{Cl} \\
O \text{-}
\end{array}
\text{vs}
\begin{array}{c}
\text{O} \\
\text{OCH}_3
\end{array}
\]

The acid halide is more reactive than the ester. The acid halide has a great leaving group (that is electronegative and a larger atom, better able to stabilize an anion) and a very large partial positive charge (due to the oxygen and the chlorine attached - both electronegative) making it a strong electrophile. The larger size of the chlorine atom prevents it from doing any resonance donation to the carbonyl group.

The ester is less reactive than the acid halide because the oxygen atom is not as good of a leaving group (electronegative but smaller atom so anion less stable) and the oxygen atom can donate electron density towards the carbonyl carbon, making the partial positive charge smaller.

B.

\[
\begin{array}{c}
\text{Br} \\
\text{Br}
\end{array}
\text{vs}
\begin{array}{c}
\text{O} \\
\text{OCH}_3
\end{array}
\]

The second acid halide is more reactive as the carbonyl carbon on the right is less sterically hindered. The alpha carbon on the right is secondary while the alpha carbon on the left is quaternary.

C.

\[
\begin{array}{c}
\text{O} \\
\text{OCH}_2\text{CH}_3
\end{array}
\text{vs}
\begin{array}{c}
\text{O} \\
\text{NHCH}_2\text{CH}_3
\end{array}
\]

The ester is more reactive than the amide. The ester carbonyl carbon has a larger partial positive charge due to the two electronegative oxygen atoms attached and the minimal resonance donation from the oxygen atom. The oxygen anion leaving group is reasonably stable due to oxygen’s electronegativity.

The amide has a carbonyl with an oxygen atom and a nitrogen atom attached (nitrogen less electronegative so less electron-withdrawing). The nitrogen leaving group (the \(\text{NHCH}_2\text{CH}_3\)) is a very unstable anion due to lower nitrogen electronegativity and poor leaving group) and the nitrogen atom is stronger than oxygen at resonance stabilization so more electron-donation towards the carbonyl carbon, significantly decreasing the size of the partial positive charge on the amide carbonyl even further.
D.

\[ \text{Acid anhydride} \quad \text{vs} \quad \text{Ester} \]

The acid anhydride is more reactive than the ester. Both carbonyl compounds have two oxygen atoms attached and two electron-withdrawing groups on the carbonyl carbon. The acid anhydride has a better, more stable leaving group than the ester (resonance stabilized anion versus anion not resonance stabilized). There is also less resonance donation towards the carbonyl from the leaving group atom (split between two carbonyls in the anhydride).

E.

\[ \text{Acid halide} \quad \text{vs} \quad \text{Acid anhydride} \]

Acid halides are more reactive than acid anhydrides. Both have good leaving groups (\(X^-\) versus \(RCO_2^-\)). The acid halide has two electron-withdrawing groups on its carbonyl, as does the acid anhydride, but the anhydride’s central oxygen atoms' ability to be electron-withdrawing is reduced because the oxygen is centered between two carbonyl groups and cannot be as strongly electron-withdrawing to both carbonyls. The oxygen leaving group of the acid anhydride can also do slight back-donation to the carbonyls, reducing the partial positive charge, making it less reactive.

F.

\[ \text{Acid halide} \quad \text{vs} \quad \text{Amide} \]

The acid halide on the left is more reactive than the amide on the right. The acid halide has two electron-withdrawing groups attached (Br is polarizable), an excellent leaving group and no resonance donation from the halide due to its larger size making its orbitals incompatible to do any resonance with the carbonyl group.

The amide has two electron-withdrawing groups (nitrogen less electronegative), has a poor leaving group (the \(\text{NH}_2\) is an unstable anion) and the nitrogen participates strongly in resonance donation with the carbonyl group, greatly reducing the partial positive charge on the carbonyl carbon.
The ester on the right has a smaller R group and would be more soluble in any aqueous type solutions because it has fewer than six carbons. All else is essentially the same.