
residue of $p=4n+1$ ". This being so, Zagier's proof is rather atypical.

- The theorem was stated by Fermat in 1640; he never published any proof but in all likelihood did possess one, probably based on the principle of infinite descent (which itself is one of Fermat's inventions). The first published proof, by Euler, appeared in the 1740's; it too uses the principle of infinite descent.

Suggested Reading

- ◆ Andre Weil. *Number Theory: An approach through history*, 1984.

Substituent Effect of the Methoxy Group: A Matter of Give and Take

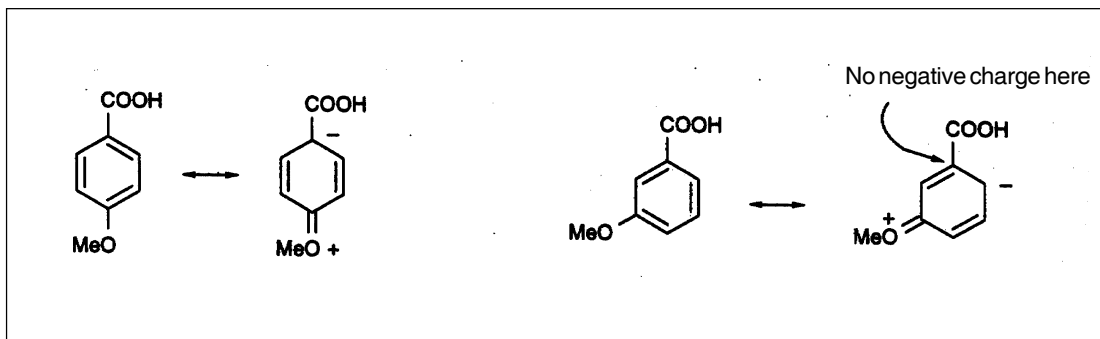
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Oxygen containing functional groups such as hydroxy (HO^-) and alkoxy (RO^-) groups are present in numerous aromatic compounds. The way these groups affect equilibria and kinetic parameters in different reactions depends on a variety of factors. In some cases the groups act as electron donors but in others as acceptors. The differing behaviour can be understood by considering the nature of the electronic interactions in detail. It is important to distinguish between electronic effects in the σ and π frameworks. Two different case histories are given below which illustrate these points.

Case I: Effect on Equilibria

One of the simplest aromatic carboxylic acids, benzoic acid, can be made stronger or weaker by placing an electron withdrawing or a donating group on the aromatic ring, respectively. A methoxy group with its lone pair of electrons which can be used in conjugation is a good donor. Hence, 4-methoxybenzoic



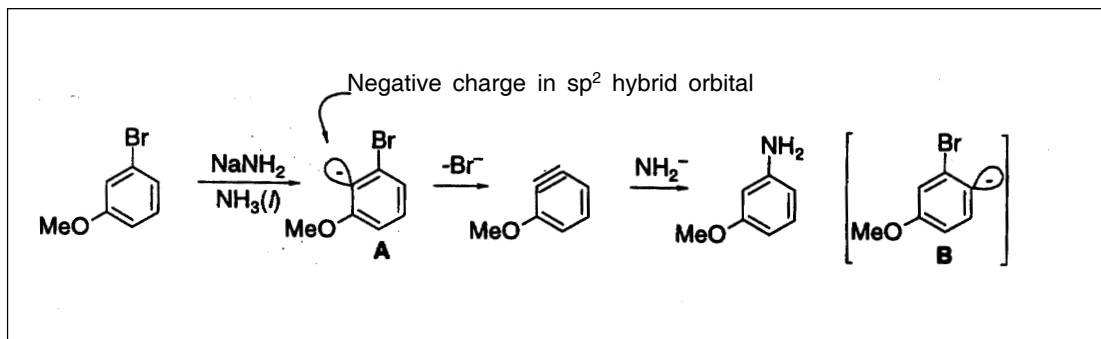


acid is less acidic than benzoic acid. But a methoxy group at the 3-position makes it more acidic. This is not hard to understand. The 4-methoxy group can donate a pair of electrons to the carbon bearing the COOH group through the resonance (or mesomeric) effect. This essentially means that we can draw another resonance structure with a negative charge on C-1 which would destabilize the formation of the carboxylate anion. However, we cannot draw a similar resonance structure with the 3-methoxy group! So the π -donor ability of the group has no effect on the acidity. But another factor has to be taken into account. The oxygen atom, by virtue of its high electronegativity, can inductively *withdraw* electrons through σ -bonds. This happens in addition to the resonance effect. For the 4-isomer, the resonance interaction more than compensates the inductive effect, but in the 3-isomer only the inductive electron withdrawal at C-1 is operative. This effect naturally makes 3-methoxybenzoic acid stronger than benzoic acid.

Case II: Effect on Reaction Rates

When 3-bromoanisole is treated with a strong base such as the NH_2^- , it predominantly forms 3-methoxyaniline. It is known that this reaction goes through a benzyne mechanism with the rate-determining removal of a hydrogen from the carbon next to the one containing the bromine atom. This can happen in two different ways, from C-2 or from C-4. In either case a carbanion





is produced which has the negative charge in an sp^2 hybrid orbital in the plane of the benzene ring which is perpendicular to the π -electron cloud. As a result, no substituent present on the benzene ring can interact with this negative charge involving resonance through the π -cloud. However, the methoxy group can always withdraw electrons through σ -bonds, as stated earlier. Thus, the methoxy group stabilizes carbanion **A** rather than **B**, simply because it is closer to the negative charge in anion **A**.

One question still remains. Once the benzyne is formed, the amide anion can attack either C-2 or C-3. Why does it prefer to attack C-3? We have already answered it! The attack of the amide anion at C-2 will place the negative charge at C-3, whereas the attack at C-3 will place the negative charge at C-2. Once again, the methoxy group inductively stabilizes the latter species because of its proximity to the site of the negative charge.

We can therefore see that the simple methoxy group can behave differently depending upon how it is structurally oriented with respect to the reaction site. One must take into account both the resonance (+*R*) and inductive (-*I*) effects of the group.

[The atoms in the drawings have deliberately not been numbered!]

