

# Rotation about Aromatic Amide Bonds: A Computational Project

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Additivity rules predict the proton at C-3 in the NMR spectrum of 2-nitroacetanilide [**1**] has a larger delta value than that at C-6. This assignment is widely distributed on web sites, e.g. SDBS. When a 4-substituted **1** is studied this is seen to be wrong as pointed out by a group from Temple University and Sadtler Research labs [*J Org Chem* 1968, **33**, 3673-5]. They explained this reversal as due to strong hydrogen bonding between NH and NO<sub>2</sub>, indicated by a shift of the NH signal from 7.5 ppm in acetanilide [**2**] to 10.3 ppm in **1**. While CDCl<sub>3</sub> is the standard solvent for NMR spectra, DMSO dissolves these anilides more readily and for **1** there is a dramatic change in the chemical shift of H-6 to almost coincide with that at H-5. The NH signal at 10.3 ppm remains the same. Hydrogen bonding cannot explain the change in the position of H-6. Rather a change in the angle of the acetamido group to the plane of the benzene ring explains this. Calculations using Gaussian can trace the change of <sup>1</sup>H chemical shifts of the ring protons as the angle of the acetamido group to the plane of the benzene ring is varied. These suggest that in CDCl<sub>3</sub> the energy minimum for this rotation is about 50° while in DMSO it is close to 90° as in **2**. An experiment to demonstrate this consists of adding increments of CDCl<sub>3</sub> to a DMSO solution of **1** and recording the spectrum after each addition. Because the light absorption spectrum of **1** changes markedly on hydrolysis, it has been used as a popular substrate for assaying the aryl acylamidase activity of butylcholinesterase [EC 3.1.5.13] since 1971. More polar solvents decrease the intensity of its absorption indicating a decrease of electron release by the lone pair of electrons on the N atom to the pi system of the ring as the amide group moves closer to 90° to the ring plane.