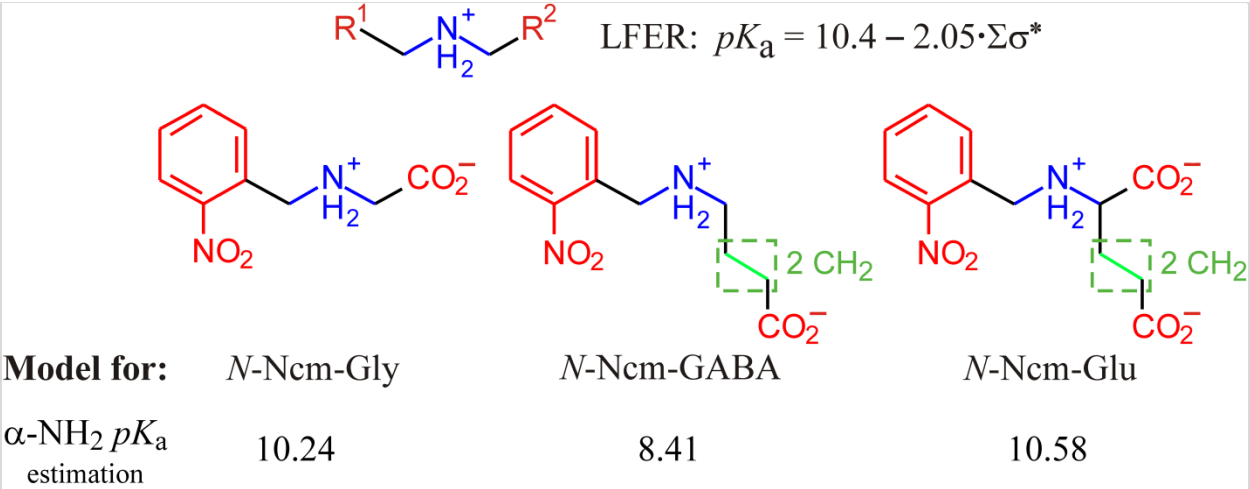
S7 Text. Estimating the pK_a values of the α-amino groups of *N*-Ncm amino acids

The pK_as of the α-amino groups of the *N*-Ncm amino acids can be estimated by using linear free energy relationships (LFER) [2]. The approach is summarized in the figure below.



The Taft equation (LFER) for estimating the pK_a of a secondary amine with the general formula $R^1CH_2NHCH_2R^2$ is $pK_a = 10.4 - 2.05 \cdot \Sigma\sigma^*$ [1], where σ* is a substituent constant, and Σσ* represents the summation of all σ* values applicable to a particular molecule. Generally, each additional CH_2 between a functional group and the acidic or basic center attenuates the σ* of the functional group by a factor of 0.4. Finally, σ* is not available for the 6-nitro-7-coumarinyl group; therefore, we use the σ* for 2-nitrophenyl, which should accurately reflect the effect of a 2-nitroaryl group. Estimation of the amino pK_a for the three *N*-Ncm amino acids is summarized below; the Taft equation and σ* values used are tabulated in Perrin et al. [1].

<u>*N*-Ncm-Gly</u>

2-NO_2Ph σ* = +1.14

CO_2^- σ* = –1.06

$pK_a = 10.4 - 2.05 \cdot [1.14 - 1.06] = 10.236$

<u>*N*-Ncm-GABA</u>

2-NO_2Ph σ* = +1.14

γ-CO_2^- σ* = –1.06, attenuated by $(0.4)^2$ due separation by 2 CH_2 groups

$pK_a = 10.5 - 2.05 \cdot [1.14 - 1.06(0.4)^2] = 8.411$

<u>*N*-Ncm-Glu</u>

2-NO_2Ph σ* = +1.14

α-CO_2^- σ* = –1.06

γ-CO_2^- σ* = –1.06, attenuated by $(0.4)^2$ due separation by 2 CH_2 groups

$pK_a = 10.5 - 2.05 \cdot [1.14 - 1.06 - 1.06(0.4)^2] = 10.584$

1. Perrin DD, Dempsey B, Serjeant EP. *pKa Prediction for Organic Acids and Bases*: Springer Netherlands; 1981.