Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.


## Electronic Supplementary Information

# New Ethionamide boosters and EthR2: structural and energetic analysis

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TABLE S1. Selected second-order perturbation theory analysis of Fock matrix in NBO basis of BDM72719 - Trp100 complex. The red text depicts the LP!BD* interaction.

| Donor (i) | Acceptor (j) | $E^{(2)}$ kcal/mol |
|---|---|---|
| **from unit 1 to unit 2** | | |
| BD(2) C1-C2 | BD*(2) C40-C48 | 0.07 |
| BD(1) C3-H17 | RY*(3) C38 | 0.07 |
| BD(1) C4-O14 | RY*(1) H49 | 0.06 |
| BD(2) C10-C13 | BD*(2) C40-C48 | 0.06 |
| LP*(1) C4 | RY*(1) H51 | 0.05 |
| LP*(1) C4 | BD*(2) C46-C50 | 0.05 |
| LP(1) O14 | BD*(1) C48-H49 | 0.06 |
| LP(3) O14 | BD*(1) C40-C48 | 0.05 |
| LP(3) O14 | BD*(2) C40-C48 | 0.08 |
| LP(3) O14 | BD*(1) C46-C50 | 0.07 |
| LP(3) O14 | BD*(2) C46-C50 | 0.09 |
| BD*(2) C1-C2 | BD*(2) C40-C48 | 0.85 |
| **from unit 2 to unit 1** | | |
| BD(2) C40-C48 | BD*(2) C1-C2 | 0.05 |
| BD(2) C46-C50 | LP*(1) C4 | 0.06 |

TABLE S2. Selected second-order perturbation theory analysis of Fock matrix in NBO basis of BDM72719 - Phe126. The red text depicts the LP→BD* interaction.

| Donor (i) | Acceptor (j) | $E^{(2)}$ kcal/mol |
|---|---|---|
| **from unit 1 to unit 2** | | |
| BD(1) C5-C6 | RY*(3) C44 | 0.11 |
| BD(1) C5-H20 | RY*(1) H45 | 0.06 |
| BD(1) C5-H20 | RY*(1) H47 | 0.06 |
| BD(1) C5-H20 | BD*(1) C40-C44 | 0.06 |
| BD(1) C5-H20 | BD*(2) C40-C44 | 0.07 |
| BD(1) C5-H20 | BD*(2) C42-C46 | 0.09 |
| BD(1) C6-C7 | RY*(1) C44 | 0.06 |
| BD(1) C6-C7 | RY*(3) C44 | 0.25 |
| BD(1) C6-H22 | RY*(2) O49 | 0.07 |
| BD(1) C6-H22 | BD*(2) C40-C44 | 0.08 |
| BD(1) C7-H23 | RY*(1) H33 | 0.06 |
| BD(1) C7-H25 | BD*(1) C44-H45 | 0.17 |
| BD(1) C7-H25 | BD*(1) C44-C46 | 0.06 |
| **from unit 2 to unit 1** | | |
| BD(1) C32-C48 | RY*(1) H22 | 0.06 |
| BD(1) C40-C44 | RY*(2) C7 | 0.06 |
| BD(2) C40-C44 | BD*(1) C6-H21 | 0.09 |
| BD(2) C40-C44 | BD*(1) C6-H22 | 0.06 |
| BD(2) C40-C44 | BD*(1) C7-H24 | 0.19 |
| BD(2) C42-C46 | BD*(1) C6-H22 | 0.05 |
| BD(1) C44-H45 | BD*(1) C7-H25 | 0.18 |
| BD(1) C44-C46 | RY*(1) H20 | 0.07 |
| BD(1) C46-H47 | BD*(1) C5-H20 | 0.12 |
| LP(1) O49 | BD*(1) C6-H22 | 0.08 |
| BD*(2) C40-C44 | BD*(1) C6-H21 | 0.05 |

TABLE S3. Selected second-order perturbation theory analysis of Fock matrix in NBO basis of BDM72719 - Ile164. The red text depicts the LP→BD* interaction.

| Donor (i) | Acceptor (j) | $E^{(2)}$ kcal/mol |
|---|---|---|
| **from unit 1 to unit 2** | | |
| BD(1) C3-H16 | RY*(1) H33 | 0.08 |
| BD(1) C3-H16 | BD*(1) C32-H33 | 0.14 |
| BD(1) C3-H16 | BD*(1) C36-H38 | 0.09 |
| BD(1) C3-H16 | BD*(1) C40-H41 | 0.14 |
| BD(1) C3-H8 | BD*(1) C40-H41 | 0.12 |
| LP(1) N9 | BD*(1) C36-H38 | 0.73 |
| **from unit 2 to unit 1** | | |
| BD(1) C32-H33 | RY*(1) H16 | 0.07 |
| BD(1) C32-H33 | BD*(1) C3-H16 | 0.14 |
| BD(1) C36-H38 | RY*(3) N9 | 0.07 |
| BD(1) C36-H38 | BD*(1) C3-H16 | 0.11 |
| BD(1) C40-H41 | BD*(1) C3-H17 | 0.05 |

TABLE S4. Selected second-order perturbation theory analysis of Fock matrix in NBO basis of BDM72719 - Ile113. The red text depicts the LP→BD* interaction.

| Donor (i) | Acceptor (j) | $E^{(2)}$ kcal/mol |
|---|---|---|
| **from unit 1 to unit 2** | | |
| BD(1) C5-H19 | BD*(1) C34-C36 | 0.22 |
| BD(1) C5-H19 | BD*(1) C36-H38 | 0.07 |
| BD(1) C6-C7 | RY*(1) H38 | 0.06 |
| BD(1) C7-H23 | BD*(1) C36-H38 | 0.10 |
| BD(1) C7-H24 | RY*(1) H38 | 0.19 |
| BD(1) C7-H24 | RY*(4) H38 | 0.06 |
| BD(1) C7-H24 | BD*(1) C36-H38 | 0.68 |
| BD(1) C7-H24 | BD*(1) C43-H46 | 0.41 |
| BD(1) C7-H25 | RY*(1) H38 | 0.22 |
| BD(1) C7-H25 | RY*(4) H38 | 0.06 |
| BD(1) C7-H25 | RY*(2) O48 | 0.06 |
| BD(1) C7-H25 | BD*(1) C36-H38 | 0.37 |
| **from unit 2 to unit 1** | | |
| BD(1) C34-C36 | RY*(1) H19 | 0.08 |
| BD(1) C36-H37 | RY*(2) H19 | 0.11 |
| BD(1) C36-H37 | BD*(1) C5-H19 | 0.24 |
| BD(1) C36-H38 | RY*(1) H19 | 0.07 |
| BD(1) C36-H38 | RY*(2) H19 | 0.18 |
| BD(1) C36-H38 | BD*(1) C5-N11 | 0.07 |
| BD(1) C36-H38 | BD*(1) C5-H19 | 0.21 |
| BD(1) C36-H38 | BD*(1) C7-H23 | 0.27 |
| BD(1) C43-H46 | BD*(1) C7-H24 | 0.36 |
| BD(2) C47-O48 | BD*(1) C7-H25 | 0.05 |
| LP(1) O48 | BD*(1) C7-H25 | 0.15 |
| LP(2) O48 | BD*(1) C7-H25 | 0.24 |

TABLE S5. Selected second-order perturbation theory analysis of Fock matrix in NBO basis of BDM72719 - Ala130. The red text depicts the LP→BD* interaction.

| Donor (i) | Acceptor (j) | $E^{(2)}$ kcal/mol |
|---|---|---|
| **from unit 1 to unit 2** | | |
| BD(1) C6-H21 | RY*(1) H33 | 0.06 |
| BD(1) C6-H21 | BD*(1) C32 -H33 | 0.09 |
| BD(1) C6-H22 | BD*(1) C34 -H37 | 0.29 |
| BD(1) N8-H26 | BD*(1) C34 -H35 | 0.16 |
| BD(1) N11-H28 | RY*(3) C34 | 0.07 |
| BD(1) N11-H28 | BD*(1) C34-H36 | 0.31 |
| LP(1) N8 | RY*(1) O39 | 0.06 |
| LP(1) N11 | BD*(1) C32-H33 | 0.13 |
| LP(1) N11 | BD*(1) C34-H36 | 0.14 |
| BD*(1) C4-O14 | BD*(1) C32-H33 | 0.14 |
| **from unit 2 to unit 1** | | |
| BD(1) C32-H33 | BD*(1) C6-H21 | 0.06 |
| BD(1) C34-H35 | RY*(3) H28 | 0.10 |
| BD(1) C34-H35 | BD*(1) N8-H26 | 0.37 |
| BD(1) C34-H35 | BD*(1) N11-H28 | 0.88 |
| BD(1) C34-H36 | BD*(1) N11-H28 | 0.17 |
| BD(1) C34-H37 | RY*(3) N11 | 0.06 |
| BD(1) C34-H37 | RY*(3) H28 | 0.10 |
| BD(1) C34-H37 | BD*(1) C6-H22 | 0.18 |
| BD(1) C34-H37 | BD*(1) N11-H28 | 0.52 |
| LP(1) N30BD*(1) C6-H210.06 | | |

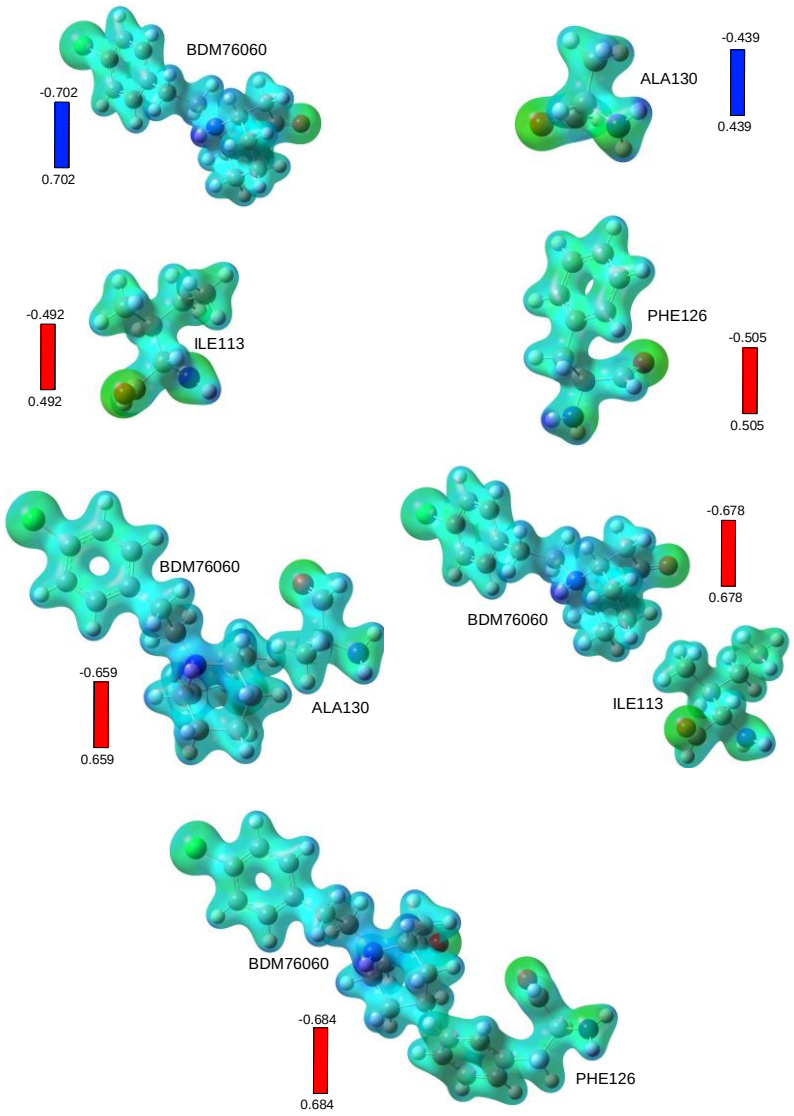


FIG. S1. The electrostatic potential maps show the ligand BDM76060 and the most relevant amino acids, as well as the protein-bound ligands.