MOLECULAR MODELING: PREDICTION OF THE STRUCTURE OF HOST-GUEST COMPLEXES

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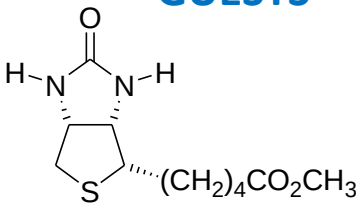
The molecular recognition features of urea derivatives, (+)-biotin methyl ester (**1**), 2-imidazolidone (**2**), *N*,*N*'-trimethylenurea (**3**) and barbital (**4**), with synthetic receptors containing 2,6-bisamidopyridine (**5**-**6**) or 2,5-bisamidopyrrole (**7**-**8**) bearing pyridyl or 1,8-naphthyridyl groups, have been studied by Monte Carlo conformational search with the AMBER force field. The most probable conformation and the associated energy of the complexes have been obtained. The main driving forces for complexation between the host and the guest will be analyzed.

GUESTS



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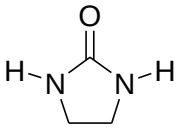

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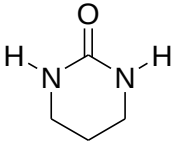

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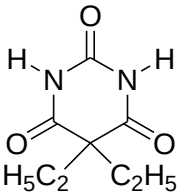

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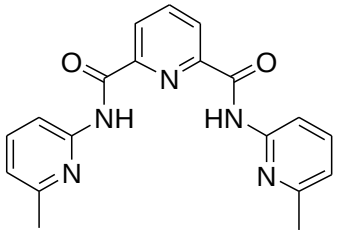
HOSTS



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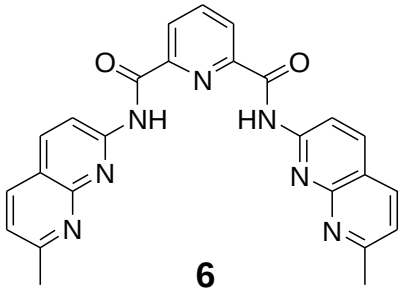

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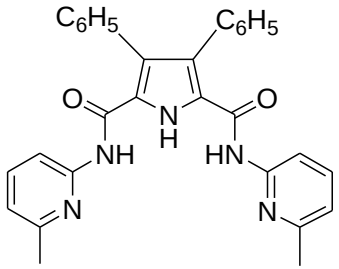

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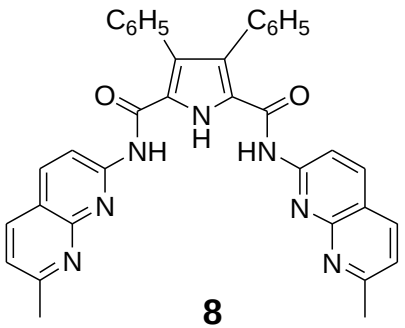

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Minimum energy structure for some complexes is shown. We can observe that the interaction mode for the complexes with (+)-biotin methyl ester (**1**), 2-imidazolidone (**2**) and *N*,*N*'-trimethylenurea (**3**) is much alike and in accordance with the usual binding mode for this kind of compounds - through the urea moiety. However, that of barbital (**4**) uses only the carbonyl group.

Hosts **6** and **8,** bearing naphthyridine units, give rise to more stable complexes than those formed by hosts **5** and **7**, containing pyridine units, due to the extra hydrogen bonds between the NH urea groups and the N8' naphthyridine nitrogens. On the other hand, in the complexes formed by hosts **7** and **8** the additional hydrogen bond arising from the pyrrolic NH compensates energetically the necessary conformational change in receptor to bind guests.

Interaction energy values $-E_{min}$ (kJ mol^{-1}) for the complexes of hosts **5**-**8** with guests **1**-**4**.

	5	**6**	**7**	**8**
Methyl biotin (**1**)	68.0	70.5	64.8	72.0
2-imidazolidone (**2**)	51.7	57.5	43.7	52.1
N,*N*'-trimethyleneurea (**3**)	57.7	59.5	46.2	54.8
barbital (**4**)	74.8	108.5	59.1	90.9