Ligand efficiency

`Motivation:` Investigate the upper-bound potency (IC50) respect to LE values

> ΔG_dissociation = -RT *ln(Kd)*
> *ΔG_inhibition = -RT* ln(Ki)
>
> Ki = IC50 / {1+([S]/Km)}
> RT ~ 0.6 (T=300K)
>
> ln(x) = 2.303 * log(x)
>
> LE = (ΔG) / N
> LE = -RT *ln(IC50) / N*
> *LE ~ 1.3818* {-log(IC50)} / N = 1.3818 *pIC50 / N ~ 1.4* pIC50 / N

references

(1) Hopkins, A., Keseru, G., Leeson, P. et al. The fole of efficiency metrics in drug discovery. Nat. Rev. Drug. Discov. 2014, 13, 105-121
(2) Nissink, J. W. Simple Size-Independent Measure of Ligand Efficiency. J. Chem. Inf. Model. 2009, 49, 1617-1622

In [1]:
```
import os, sys, math
import numpy as np
import matplotlib.pyplot as plt
```

In [2]:
```
def IC50_to_pIC50(x):
    """
    x: IC50 [nM]
    """
    x = x * 10**(-9)
    return -np.log10(x)
```

In [3]:
```
def pIC50_to_IC50(x):
    """
    x: pIC50
    return IC50 in nM
    """
    return 10**(-x) * 10**9
```

In [4]:
```
RT=0.6
```

In [5]:
```
np.log(10)
```

Out[5]:
```
2.302585092994046
```

In [6]:
```
CONST = np.log(10) * RT
```

In [7]:
```
CONST
```

Out[7]:
```
1.3815510557964275
```

convert LE and HAC into IC50

In [8]:
```
LE=0.27
HAC=33
pIC50=6.24
```

In [9]:
```
pIC50_to_IC50(pIC50)
```

Out[9]:
```
575.4399373371566
```

In [10]:
```
IC50_to_pIC50(100)
```

Out[10]:
```
7.0
```

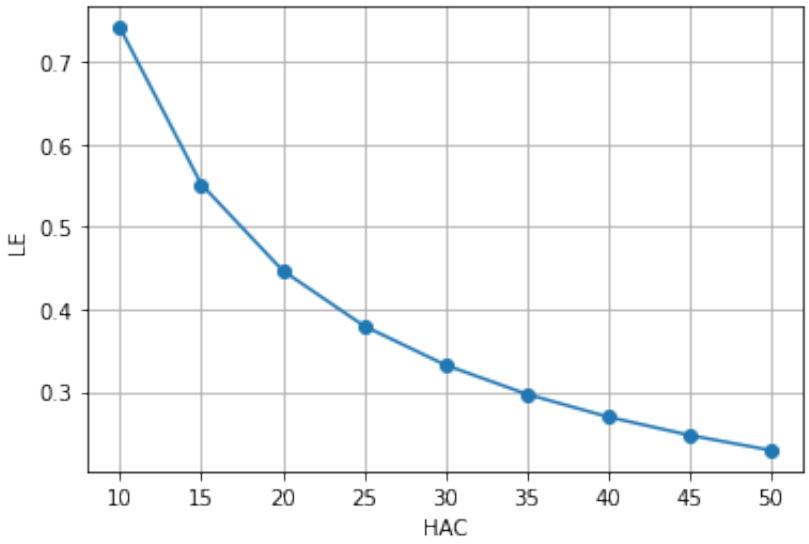
maximum LE

ref.(2)

> LEmax = exp(1.4)/N^0.73

In [11]:
```
N = np.arange(10,51, 5)
LE = [np.exp(CONST)/n**0.73 for n in N]
```

In [12]:
```
plt.plot(N, LE, marker='o')
plt.xlabel("HAC")
plt.ylabel("LE")
plt.grid()
plt.show()
```



maximum pIC50 (IC50) evaluated from LEmax

`assumption:` HAC=40 is roughly equal to MW of 450~500 (see figure from ref.2)

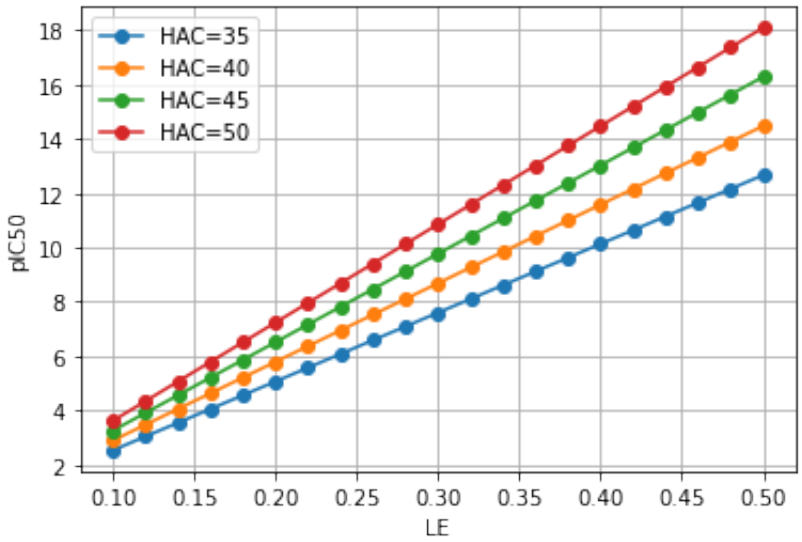
> pIC50 = HAC * LE / 1.3818

In [13]:
```
HAC_1=35
HAC_2=40
HAC_3=45
HAC_4=50

labels = ["HAC=35", "HAC=40", "HAC=45", "HAC=50"]
```

In [14]:
```
LE = np.arange(0.1,0.51,0.02)
```

In [15]:
```
pIC50_1 = [ HAC_1*x/CONST for x in LE ]
pIC50_2 = [ HAC_2*x/CONST for x in LE ]
pIC50_3 = [ HAC_3*x/CONST for x in LE ]
pIC50_4 = [ HAC_4*x/CONST for x in LE ]
```

In [16]:
```
plt.plot(LE, pIC50_1, marker='o')
plt.plot(LE, pIC50_2, marker='o')
plt.plot(LE, pIC50_3, marker='o')
plt.plot(LE, pIC50_4, marker='o')
plt.legend(labels)

plt.xlabel("LE")
plt.ylabel("pIC50")
plt.grid()
plt.show()
```



In [17]:
```
pIC50_to_IC50(6)
```

Out[17]:
```
1000.0
```

In [ ]:
```

```