

```
In [1]: import pickle
from rdkit import Chem
from rdkit.Chem import Draw
from rdkit.Chem.Draw import IPythonConsole
from rdkit.Chem import rdFMCS
from rdkit.Chem.Draw import rdDepictor

from IPython.display import display
import matplotlib.pyplot as plt
from IPython.display import HTML
import pandas as pd

IPythonConsole.ipython_useSVG=True
rdDepictor.SetPreferCoordGen(True)
#IPythonConsole.drawOptions.minFontSize=20
```

```
In [2]: with open('predictions/w_logs.pkl', 'rb') as file: w_te_data = pickle.load(fi
with open('predictions/wo_logs.pkl', 'rb') as file: wo_te_data = pickle.load(
original = pd.read_csv('predictions/chem_departm_output_wo_tie_embedding/outp
```

```
In [3]: def view_difference(mol1, mol2):
    mcs = rdFMCS.FindMCS([mol1, mol2])
    mcs_mol = Chem.MolFromSmarts(mcs.smartsString)
    match1 = mol1.GetSubstructMatch(mcs_mol)
    target_atm1 = []
    for atom in mol1.GetAtoms():
        if atom.GetIdx() not in match1:
            target_atm1.append(atom.GetIdx())
    match2 = mol2.GetSubstructMatch(mcs_mol)
    target_atm2 = []
    for atom in mol2.GetAtoms():
        if atom.GetIdx() not in match2:
            target_atm2.append(atom.GetIdx())
    return Draw.MolsToGridImage([mol1, mol2], highlightAtomLists=[target_atm1,
```

# Generation

## Notes:

- Predict the next fragment when probability  $p > 0.5$
- The logic takes top-5 attachments from combinations of top-5 motifs and its possible configs. E.g., motif C1=CC=CC=C1 has 2 possible configs, C1=[CH:1]C=C[CH:2]=C1 or C1=[CH:1]C=CC=C1. The first config could be connected to other motifs that the connections are marked by :X, X is a number. The second config is the end motif that couldn't be connected to other motifs. Atoms marked by different mark numbers are connected together. No two atoms with same mark numbers are used for connection.
- For every attachment, it's checked for validity:
  - If the to-connect motif and to-be-connected (aka predicted motif) share common atoms for connections.
  - No self-loop.
  - If all atoms in the to-be-connected motif exist in the to-connect motif, no need to attach them.
- To view prediction logs of other molecules, subtract 2 from the molecule's index in Excel file.

In [4]:

```

def view(data, i, _original):
    print('Original: {}'.format(_original[i]))
    display(Draw.MolsToGridImage([Chem.MolFromSmiles(_original[i])]))

    sample = data[i]
    # step 0
    step_f0 = sample[0]
    print('*****Sample {}th*****'.format(i))
    print('-----Step-0-----')
    print('Root motif: {}'.format(step_f0['root']))
    print('Top 5 root motif configs:', '\n'.join([str(x) for x in step_f0['top-5-root-attachments']]))

    # display
    mol = Chem.MolFromSmiles(step_f0['top-5-root-attachments'][0][0])
    print('Displaying partial graph (aka molecule): {}'.format(step_f0['partial-graph']))
    display(Draw.MolsToGridImage([mol]))
    print('-----')

    # the remaining steps
    for i, step_f in enumerate(sample[1:]):
        print('-----Step-{}-----'.format(i + 1))
        if 'Generate fragment' in step_f:
            print('Generate next fragment p = {}'.format(step_f['Generate fragment']))
        else:
            print('Skip, current fragment has no next fragment to be attached')
            continue

        if 'top-5-inter-cands' in step_f:
            print('Top 5 next motifs to attach:')
            for fragment in step_f['top-5-inter-cands']:
                print('Molecule {} and its specific config {} w/ p={}'.format(fragment[0], fragment[1], step_f['p']))
                display(Draw.MolsToGridImage([Chem.MolFromSmiles(fragment[0])]))
                print('-----')
                if 'Attaching Fragment' in step_f:
                    frag = step_f['Attaching Fragment']

                    sub_mol = Chem.MolFromSmiles(step_f['partial-graph'])
                    print('Attaching fragment {} of config {}'.format(frag[0], frag[1]))
                    print('Latest partial graph: {}'.format(step_f['partial-graph']))
                    print('Latest graph (left) vs graph in last step (right)')
                    display(view_difference(sub_mol, mol))
                    mol = sub_mol
                    print('-----')
                else:
                    print("Skip, the best next fragment to be attached to the current fragment is {}".format(frag[1]))

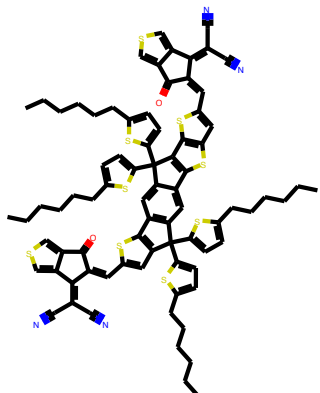
```

In [11]:

```
view(wo_te_data, 12, original)
```

Original: CCCCCCC1=CC=C(S1)C2(C(S3)=CC=C3CCCCC)C(C(SC(/C=C(C4=O)/C(C5=CSC=C45

```
)=C(C#N)\C#N)=C6)=C6S7)=C7C8=CC9=C(C(SC(/C=C(C%10=O)/C(C%11=CSC=C%10%11)=C(C#N)\C#N)=C%12)=C%12C9(C(S%13)=CC=C%13CCCCC)C(S%14)=CC=C%14CCCCC)C=C28
```



\*\*\*\*\*Sample 12th\*\*\*\*\*

-----Step-0-----

Root motif: CN

Top 5 root motif configs: ('[NH2:1][CH3:2]', tensor(3.4918))

('[CH3:1][NH2:2]', tensor(-2.9572))

('C[NH2:1]', tensor(-13.9794))

('N[CH3:1]', tensor(-18.6545))

('C([OH:1])[CH3:2]', tensor(-977.5619))

Displaying partial graph (aka molecule): CN

-----Step-1-----

Generate next fragment p = 1.0

Top 5 next motifs to attach:

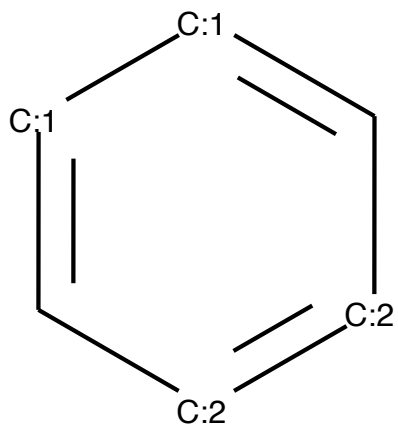
Molecule CC and its specific config [CH3:1][CH3:2] w/ p=-0.018690187484025955

-----  
Molecule C=O and its specific config [O:1]=[CH2:2] w/ p=-4.199256420135498

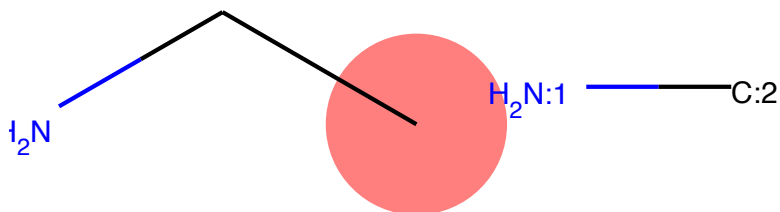
-----  
Molecule C=C and its specific config [CH2:1]=[CH2:2] w/ p=-6.180079460144043

-----  
Molecule C=O and its specific config O=[CH2:1] w/ p=-6.762899398803711

-----  
Molecule C1=CC=CC=C1 and its specific config C1=[CH:1][CH:1]=C[CH:2]=[CH:2]1 w  
/ p=-9.228087425231934

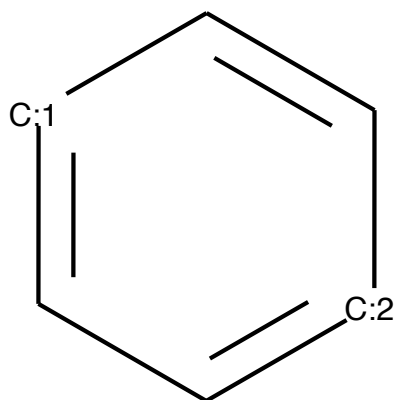


-----  
 Attaching fragment [CH3:1][CH3:2] of config ['C[CH3:1]']  
 Latest partial graph: CCN  
 Lastest graph (left) vs graph in last step (right)

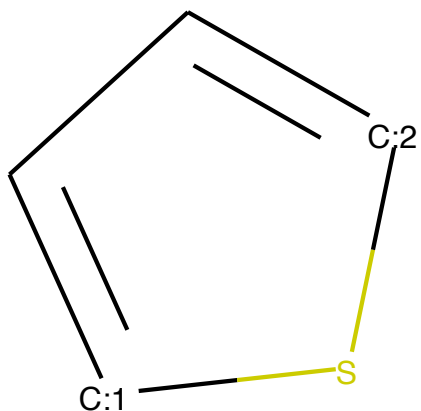


-----  
 -----Step-2-----  
 Generate next fragment p = 1.0  
 Top 5 next motifs to attach:  
 Molecule C#N and its specific config N#[CH:1] w/ p=-0.3776191174983978

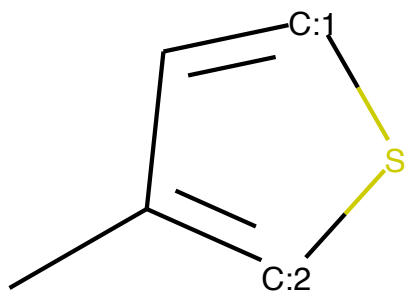
-----  
 Molecule C1=CC=CC=C1 and its specific config C1=[CH:1]C=C[CH:2]=C1 w/ p=-1.649  
 0508317947388



-----  
 Molecule C1=CSC=C1 and its specific config C1=[CH:1]S[CH:2]=C1 w/  $p=-2.462209939956665$



-----  
 Molecule CC1=CSC=C1 and its specific config CC1=[CH:2]S[CH:1]=C1 w/  $p=-3.976339101791382$

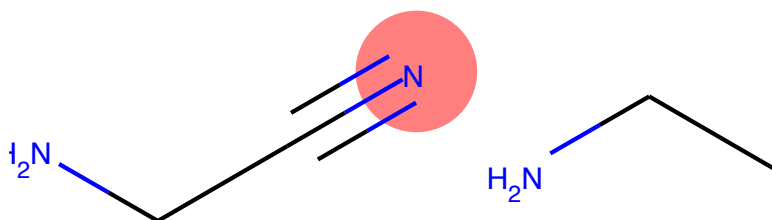


-----  
 Molecule C=O and its specific config O=[CH2:1] w/  $p=-4.291350841522217$

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Attaching fragment N#[CH:1] of config ['N#[CH:1]']
Latest partial graph: N#CCN
Lastest graph (left) vs graph in last step (right)

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-----Step-3-----
Generate next fragment p = 3.489314508442476e-07
-----Step-4-----
Generate next fragment p = 4.766485074193274e-19
-----Step-5-----
Generate next fragment p = 1.0
Top 5 next motifs to attach:
Molecule C=C and its specific config [CH2:1]=[CH2:2] w/ p=-0.32256531715393066

```

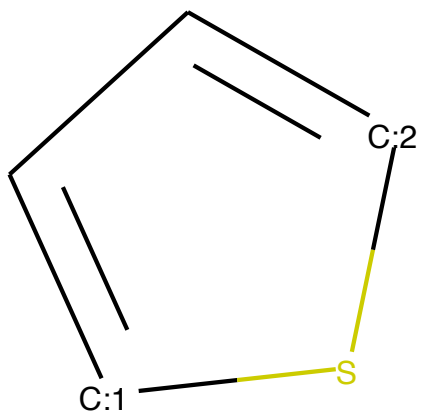
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Molecule CC and its specific config [CH3:1][CH3:2] w/ p=-1.2986748218536377

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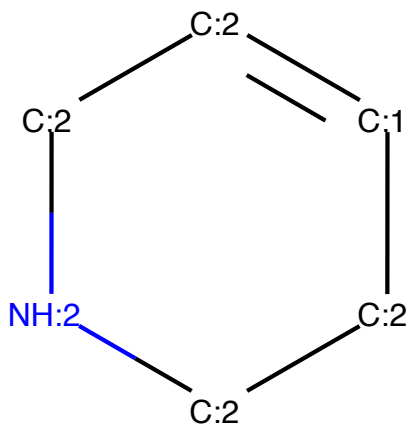


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Molecule C1=CSC=C1 and its specific config C1=[CH:1]S[CH:2]=C1 w/  $p=-6.360332489013672$



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Molecule C=O and its specific config O=[CH2:1] w/  $p=-7.436509132385254$

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Molecule C1=CCNCC1 and its specific config [CH:1]1=[CH:2][CH2:2][NH:2][CH2:2][CH2:2]1 w/  $p=-9.168729782104492$



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Skip, the best next fragment to be attached to the current fragment does not yield a valid sub-molecule . Go back to the previous fragment.

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In [ ]: