FARMEBS
10. SIMPOZIJ STUDENATA FARMACIJE I MEDICINSKE BIOKEMIJE 2022

Osnove kvantno-kemijskih izračuna

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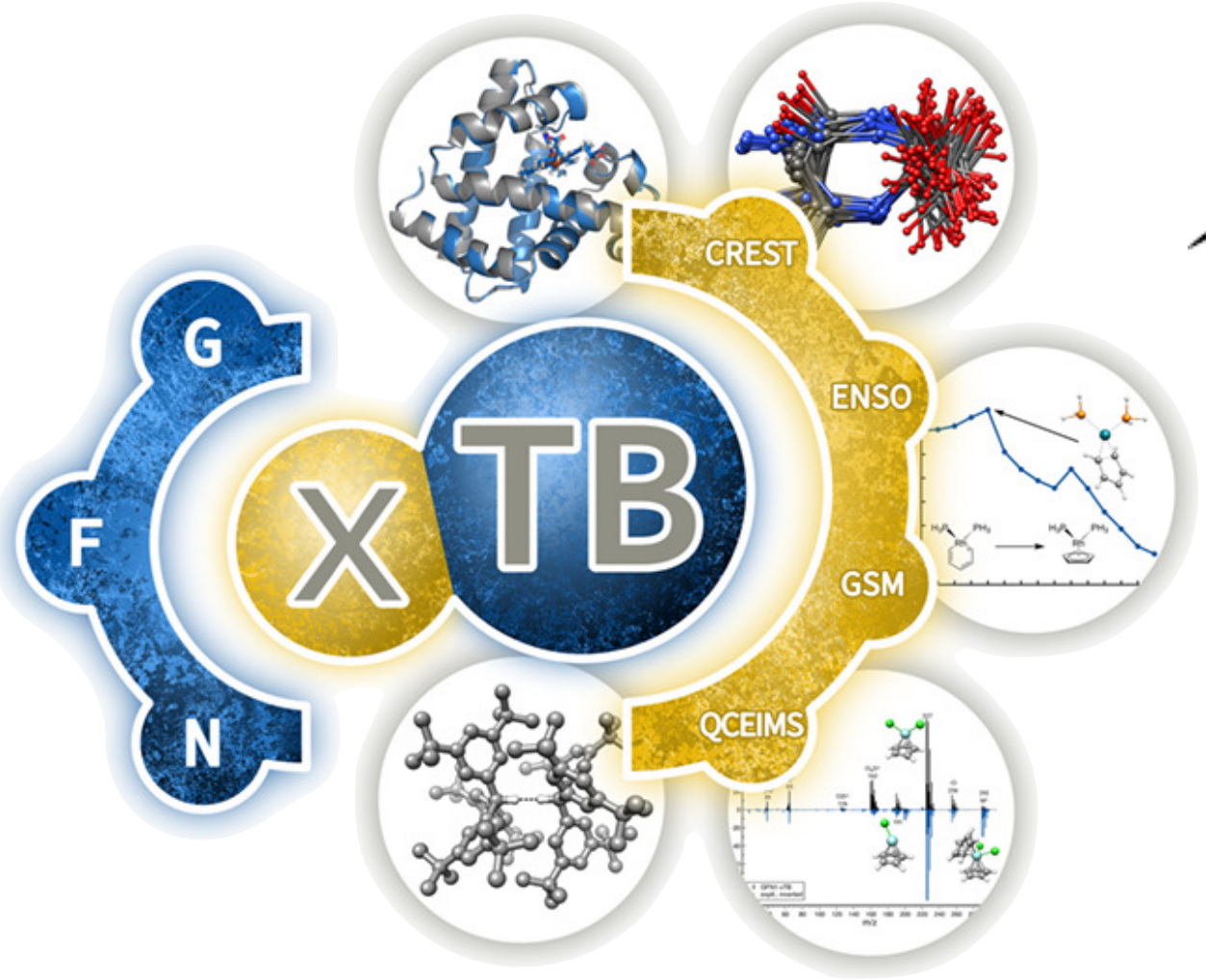
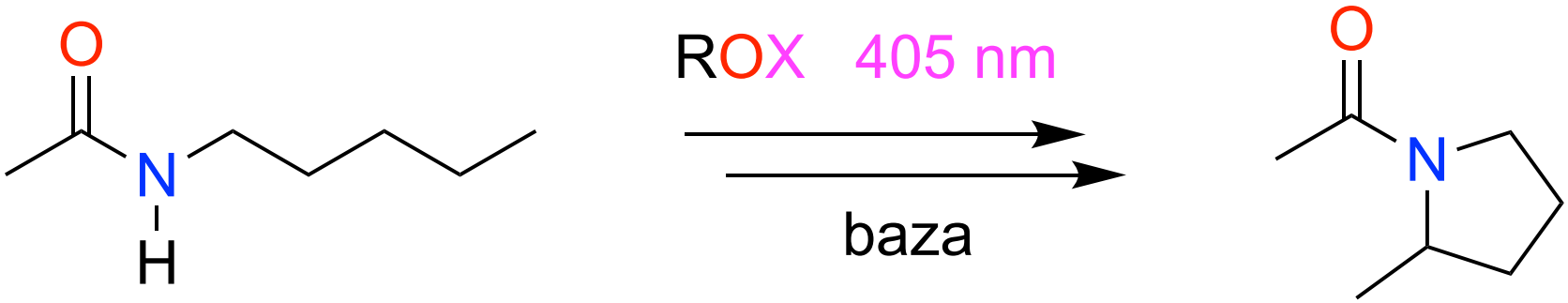


ORCA

G

Hofmann–Löffler–Freytag reakcija



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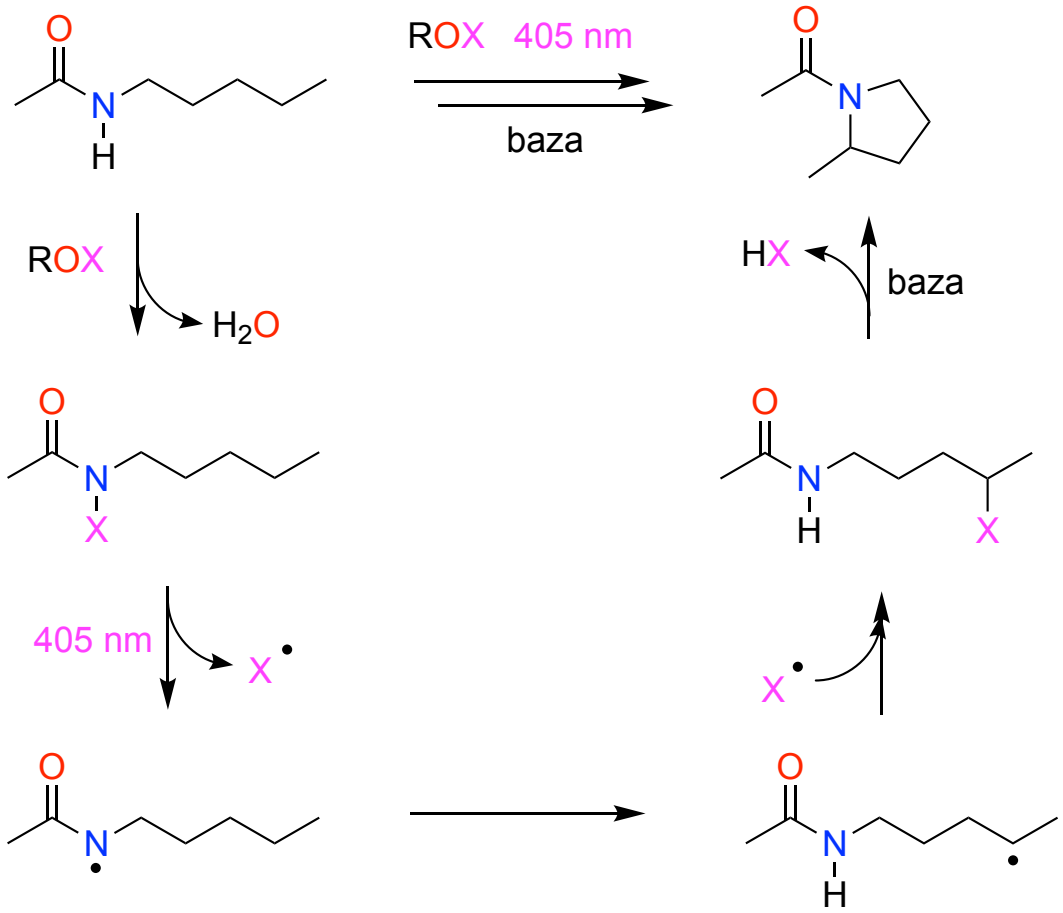
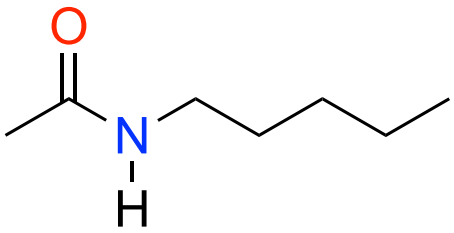
Hofmann–Löffler–Freytag reakcija



Reaktant



CRTANJE!

- konformacijska analiza reaktanata
- Boltzmannova raspodjela
- tautomerne forme i ravnoteža
- utjecaj otapala - implicitno, eksplicitno, kombinirano
  - prva solvatacijska ljuska
  - ostale ljuske
- odabir odgovarajuće teorijske razine

CRTANJE

Avogadro

- besplatan
- interface s drugim programima
- uključeni FF optimizator
- vizualizacija orbitala/frekvencija
- konformacijska analiza

IQmol

besplatan

uključen FF optimizator

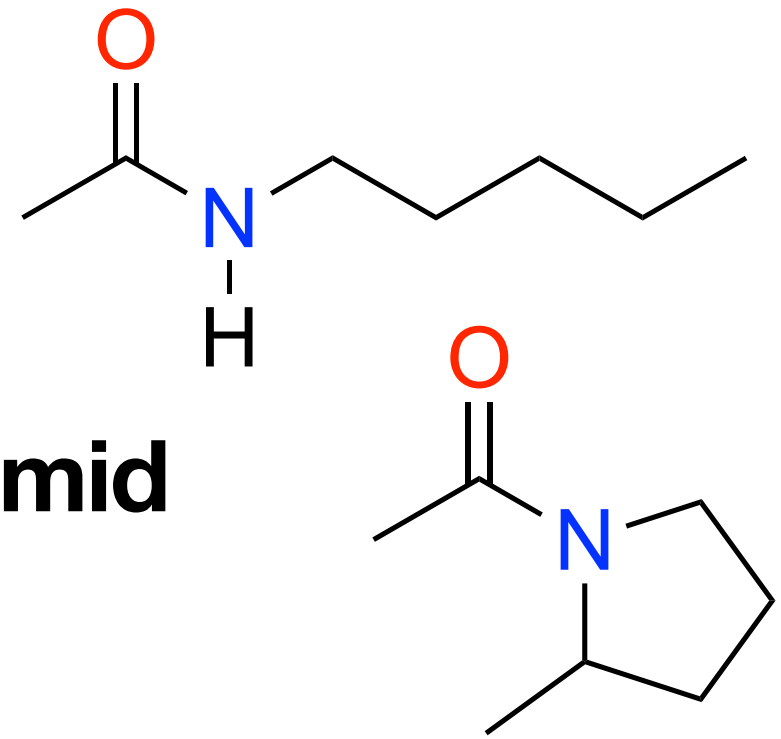
direktno pokretanje računa QChem

.xyz format

Crtanje molekula

N-pentilacetamid

2-metilpiridinilacetamid



Optimizacija

G16 i ORCA input

ime.com

```
%nproc=4
%mem=8gb
%chk=ime.chk
# opt freq b3lyp/SVP

naslov

0 1
A x.x y.y z.z
```

ime.script

```
#!/bin/sh
#$ -N ime
#$ -l memory=4
#$ -cwd
#$ -pe mpi 2
#$ -o ime.out
#$ -e ime.err
export PATH=…
dog16 ime
```

ime.inp

```
! B3LYP SV(P) OPT FREQ
%pal nprocs 4 end
%maxcore 8000
* XYZ 0 1
A x.x y.y z.z
*
```

ime.script

```
#!/bin/sh
#$ -N ime
#$ -o ime.err
#$ -j Y
#$ -l memory=8
#$ -pe mpi 4
#$ -cwd
module load orca/5.0.3
run-orca-isabella.sh ime.inp > ime.out
```

qsub ime.script

Traženje prijelaznog stanja - iz nacrtane strukture

G16 i ORCA input

ime.com

```
%nproc=4
%mem=8gb
%chk=ime.chk
# opt=(calcfc,ts,noeigentest)
freq b3lyp/SVP

naslov

0 1
A x.x y.y z.z
```

ime.inp

```
! B3LYP SV(P) OPTTS FREQ
%pal nprocs 4 end
%maxcore 8000
* XYZ 0 1
A x.x y.y z.z
*
```

ime.script

```
qsub ime.script
```

Traženje prijelaznog stanja - iz reaktanata/produkata

G16 i ORCA input

ime.com

```
%nproc=4
%mem=8gb
%chk=ime.chk
# opt=(qst2) freq b3lyp/SVP

reaktant

0 1
A x.x y.y z.z

produkt

0 1
A x.x y.y z.z
```

ime.script

```
%nproc=4
%mem=8gb
%chk=ime.chk
# opt=(qst3) freq b3lyp/SVP

reaktant

0 1
A x.x y.y z.z

produkt

0 1
A x.x y.y z.z

TS

0 1
A x.x y.y z.z
```

ime.inp

```
! B3LYP SV(P) NEB-TS FREQ
%pal nprocs 4 end
%maxcore 8000
%NEB NEB_END_XYZFILE "produkt.xyz"
END
* XYZfile 0 1 reaktant.xyz
```

ime.script

```
! B3LYP SV(P) NEB-TS FREQ
%pal nprocs 4 end
%maxcore 8000
%NEB NEB_END_XYZFILE “produkt.xyz"
NEB_TS_XYZFILE "mislimTS.xyz" END
* XYZfile 0 1 reaktant.xyz
```

U skripti obavezno navesti koji podaci i gdje se prebacuju

Traženje prijelaznog stanja - pretraživanje PES-a

G16 i ORCA input

ime.com

```
%nproc=4
%mem=8gb
%chk=ime.chk
# opt=(modredundant) b3lyp/SVP

naslov

0 1
A x.x y.y z.z

B 1 2 S 15 -0.01
```

ime.script

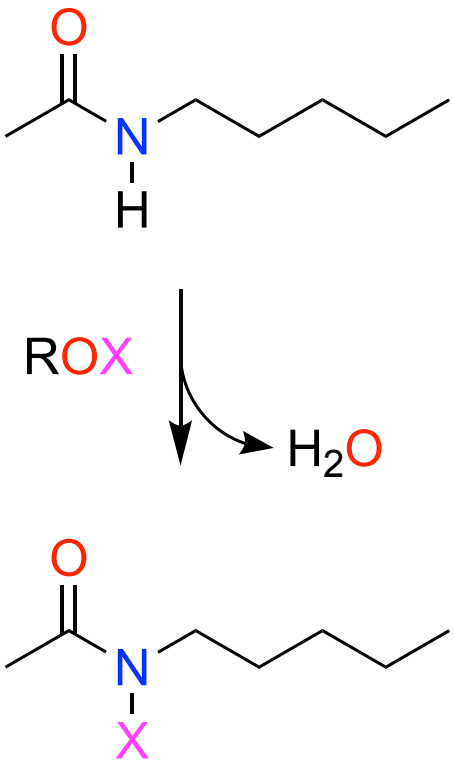
Brojanje atoma u ORCA-i ide od 0!

ime.inp

```
! B3LYP SV(P)
! ScanTS
%geom
scan B 1 0 = 2.0, 1.0, 10 end
end
%pal nprocs 4 end
%maxcore 8000
* XYZ 0 1
A x.x y.y z.z
*
```

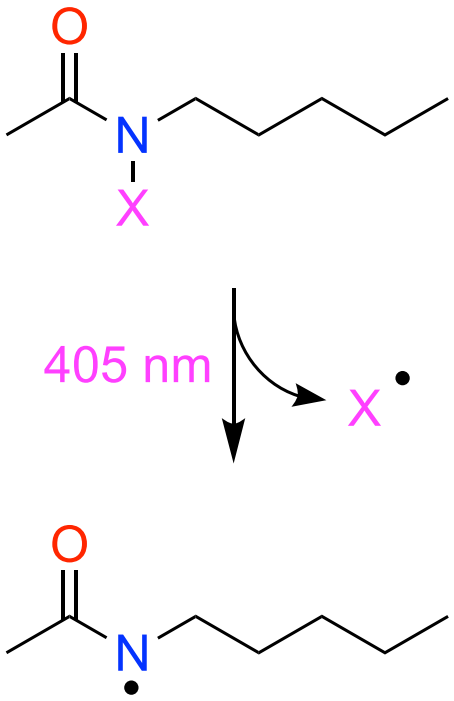
Više o skriptiranju
https://tldp.org/LDP/abs/html/

Halogeniranje



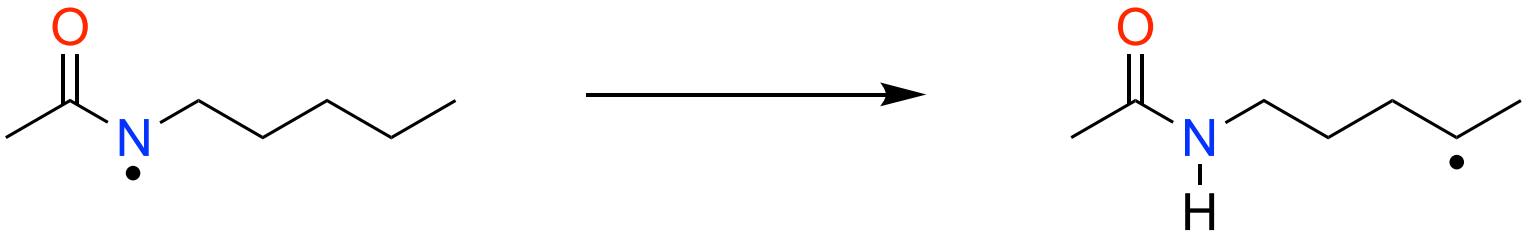
- određivanje reakcijskih parametara za HOCl
- prijelazno stanje kloriranja za amido i imido formu
- IRC računi
- globalni, lokalni minimumi
- termodinamika i kinetika reakcije
- promjena halogena
- promjena R-supstituenta (npr. AcOX)

Homolitičko cijepanje N-halogen veze



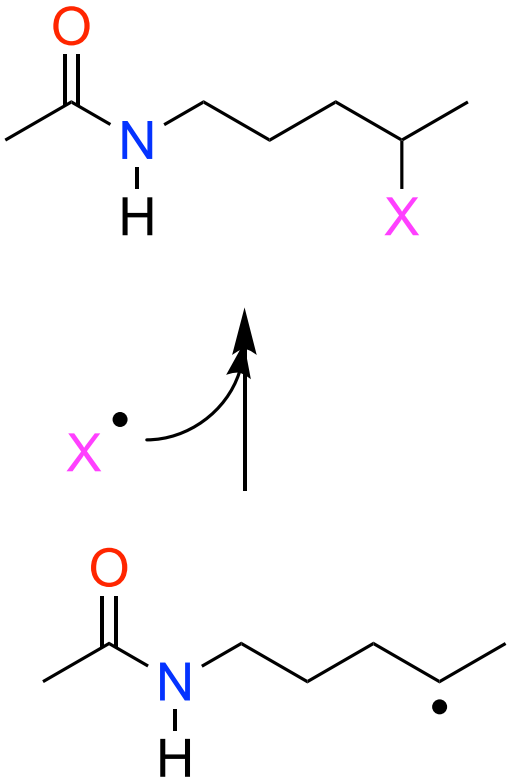
- skeniranje reakcijske koordinate
- plohe potencijalne energije
- singlet vs triplet
- elektronski prijelazi
- promjena redosljeda popunjavanja orbitala

Prijenos atoma vodika (HAT)



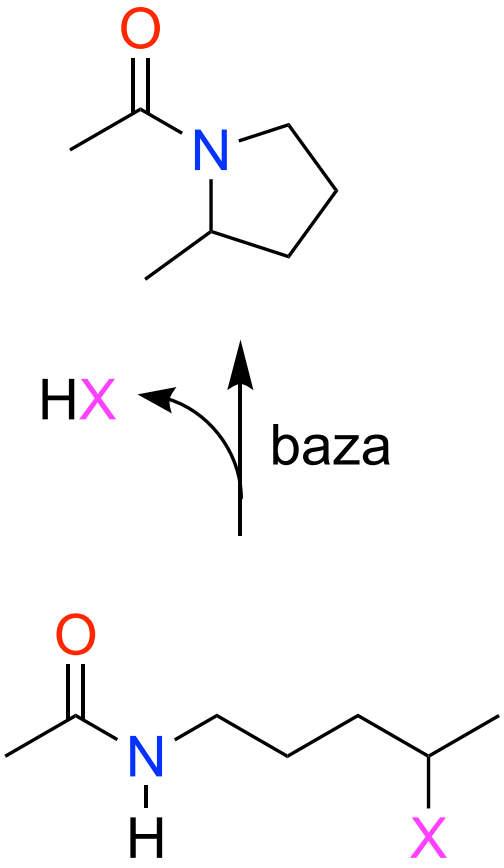
- stabilnost N- i C- radikala (termodinamika)
- određivanje kompeticijskih reakcija
  - 1,2-HAT, 1,3-HAT, 1,4-HAT i 1,5-HAT
- intra- vs inter-HAT (dodatni modelni sustavi)

Stvaranje C-halogen veze



- skeniranje reakcijske koordinate
- plohe potencijalne energije
- singlet vs triplet
- elektronski prijelazi
- računanje spektara
  - IR, NMR/EPR, UV/Vis
  - obavezno standard

Zatvaranje peteročlanog prstena

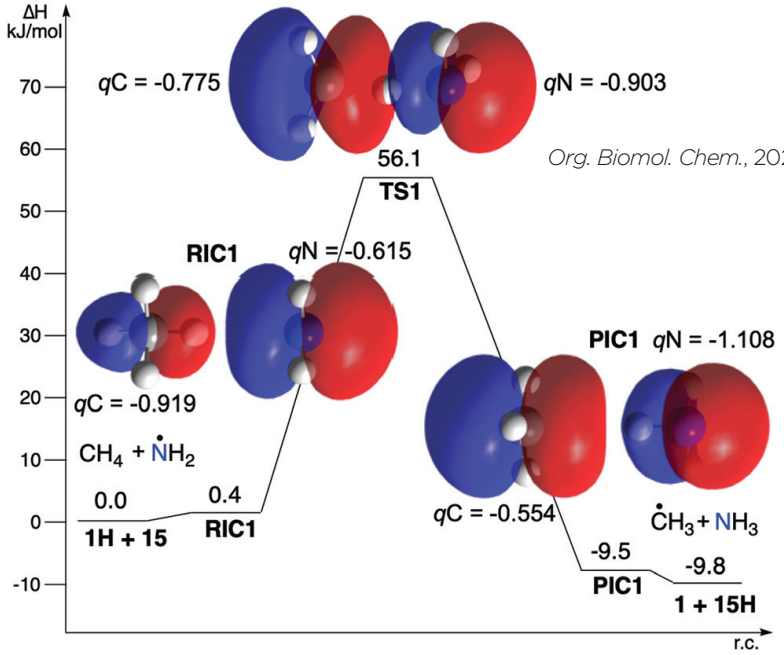


- S_N2 reakcija
- uloga baze
- uloga otapala
- stabilnost produkata
- teorijska razina
- provjera u odnosu na eksperimentalne podatke

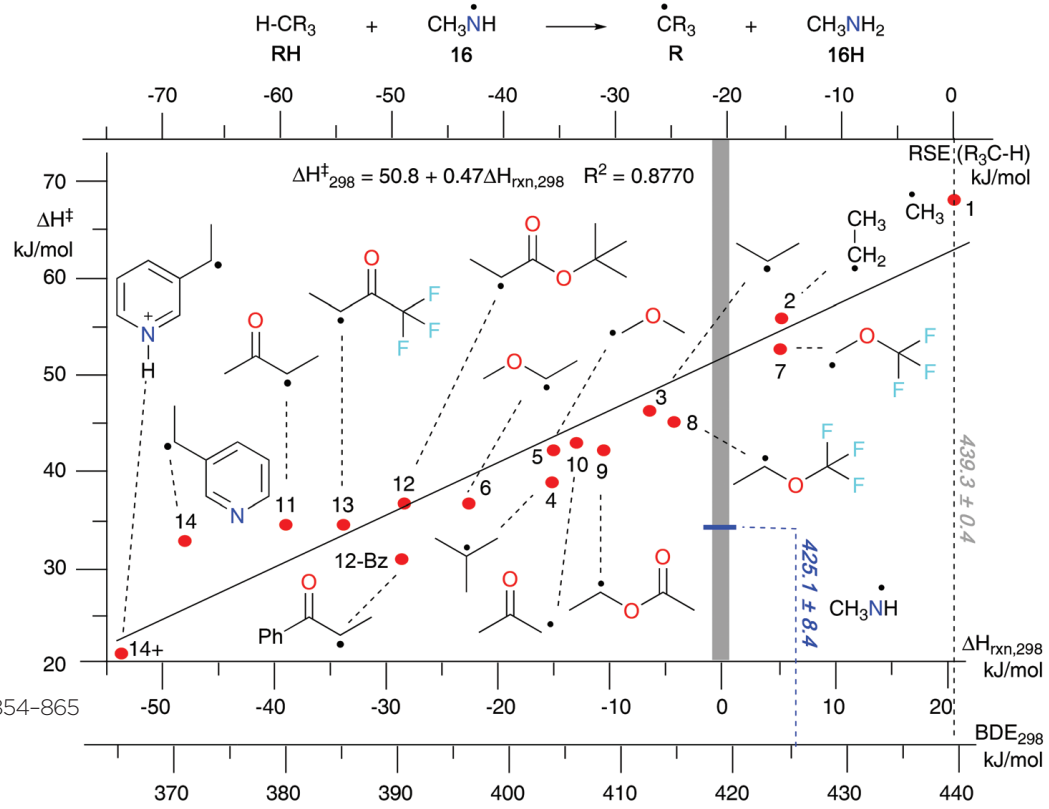
Prikaz rezultata

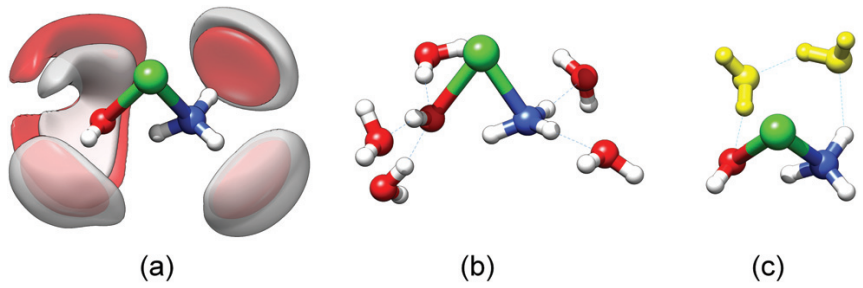
Table 3 RSE, $\Delta H_{rxn,298}$, and $\Delta H^{\ddagger}_{298}$ values for all systems shown in Chart 3

Species	RSE (*N*-rad)	RSE (*C*-rad)	BDE $(N-H)_{calc.}$	BDE $(C-H)_{calc.}$	$\Delta H_{rxn,298}$	$\Delta H^{\ddagger}_{298}$
L1	−33.8	−71.0	416.3	368.3	−47.9	45.7
L1+	−40.5	−89.4	409.6	349.9	−59.6	46.0
L2	−58.4	−71.1	391.7	368.3	−23.4	54.2
L2+	−71.7	−89.0	378.4	350.3	−28.0	54.0
L3	−26.1	−66.7	424.0	372.7	−43.0	30.1
L4	−2.0	−63.5	448.1	375.8	−82.9	18.5
L5	2.0	−75.2	452.0	364.1	−87.2	16.2
L6	15.4	−73.7	465.5	365.6	−99.3	4.8



Org. Biomol. Chem., 2021, **19**, 854–865





Org. Biomol. Chem., 2015, **13**, 11740–11752

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