IUPAC InChI Project:

Redesign of Handling of Tautomerism for InChI V2

Marc Nicklaus and Devendra Dhaked

Not Just an Academic Question

FICuS[1], FICTS ⟶ Tautomeric pairs (conflicts)

[1] Sitzmann *et al.* SAR QSAR Environ. Res. **2008**, *19*, 1–9

Aldrich Market Select (AMS) database :

5,755,574 molecules (2012-09 version)

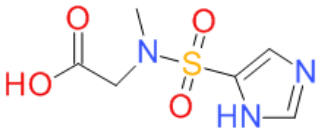
31,156 conflicts ⟶ **62,872 molecules**

n-tuples	Conflicts
2	30,619
3	514
4	21
5	1

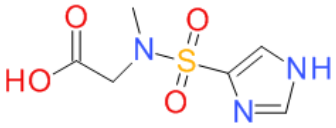
Examples (prices per 1 g):

$313

$350



$188



$300

Same original supplier!

Guasch, L. *et al.*
JCIM *56*, **2016**, 2149–2161.

Status

- Proposed transforms (“rules”) based on:
  - Existing 20 tautomerism transforms in CACTVS
  - Ca. 25 new rules not (yet) covered by CACTVS, based on experimental studies
- Checked for occurrence rates in ~250M cpds:
- Most rules found applicable to >100 cpds.
- See also InChI V2 Discussion Thu 1:00 – 1:45 pm and Breakout Group Fri 8:30 – 10:00 am

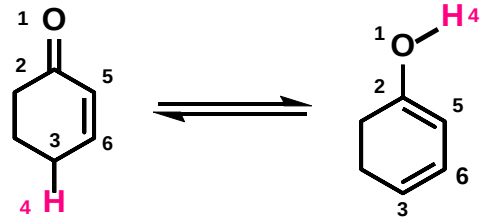
- Acknowledgements: Wolf-Dietrich Ihlenfeldt

Current CACTVS Tauto Rules

rule 2: 1.5 (thio)keto/(thio)enol

[O,S,Se,Te;X1:1]=[Cz1H0:2][C:5]=[C:6][CX4z0,NX3:3][#1:4]>>
[#1:4][O,S,Se,Te;X2:1][Cz1:2]=[C:5][C:6]=[Cz0,N:3]

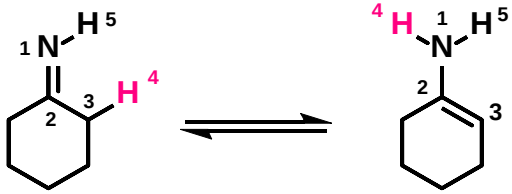
Occurrence rate: ~1%



rule 3: simple (aliphatic) imine

[#1,a,O:5][NX2:1]=[Cz{1-2}:2][CX4R{0-2}:3][#1:4]>>
[#1,a,O:5][NX3:1]([#1:4])[Cz:2]=[C:3]

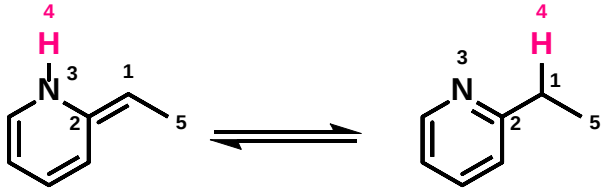
Occurrence rate: ~13%



rule 4: special imine

[Cz0R0X3:1]([C:5])=[C:2][Nz0:3][#1:4]>>
[#1:4][Cz0R0X4:1]([C:5])[c:2]=[nz0:3]

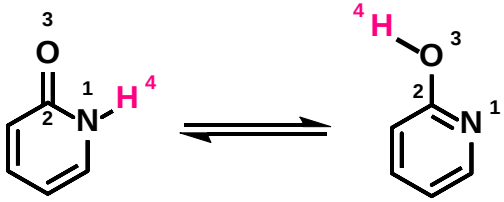
Occurrence rate: ~2%



rule 5: 1.3 aromatic heteroatom H shift

[#1:4][N:1][C;e6:2]=[O,NX2:3]>>
[NX2,nX2:1]=[C,c;e6:2][O,N:3][#1:4]

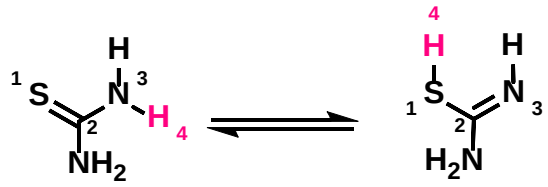
Occurrence rate: ~9%



rule 6: 1.3 heteroatom H shift

[CX{2-3}z{0-1},N,n,S,s,O,o,Se,Te:1]=[NX2,nX2,CX3,c,P,p:2] [N,n,S,O,Se,Te:3][#1:4]>>
[#1:4][CX4z{0-1},N,n,S,O,Se,Te:1][NX2,nX2,CX3z{0-1},c,P,p:2]=[N,n,S,s,O,o,Se,Te:3]

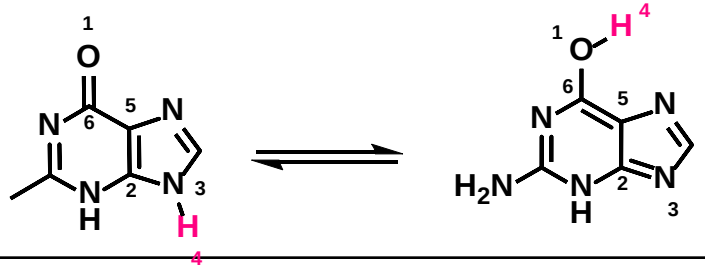
Occurrence rate: >66%



rule 7: 1.5 (aromatic) heteroatom H shift (1)

[nX2,NX2,S,O,Se,Te:1]=[C,c,nX2,NX2:6][C,c:5]=[C,c,nX2:2][N,n,S,s,O,o,Se,Te:3][#1:4]>>
[#1:4][N,n,S,O,Se,Te:1][C,c,nX2,NX2:6]=[C,c:5][C,c,nX2:2]=[NX2,S,O,Se,Te:3]

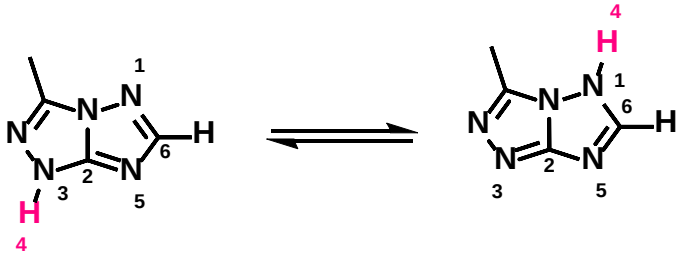
Occurrence rate: ~9%



rule 8: 1.5 aromatic heteroatom H shift (2)

[n,s,o:1]=[c,n:6][c:5]=[c,n:2][n,s,o:3][#1:4]>>
[#1:4][n,s,o:1][c,n:6]=[c:5][c,n:2]=[n,s,o:3]

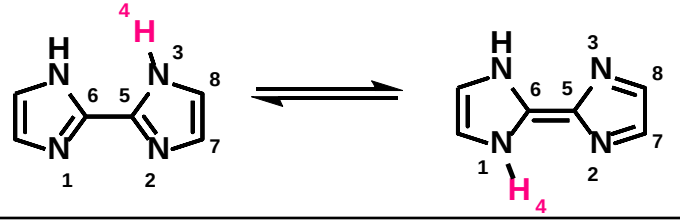
Occurrence rate: ~2%



rule 9: 1.7 (aromatic) heteroatom H shift

[nX2,NX2,S,O,Se,Te,Cz0X3R0:1]=[c,C,NX2,nX2:6][C,c,NX2,nX2:5]=[C,c,NX2,nX2:2][C,c,NX2,nX2:7]=[C,c,NX2,nX2:8][N,n,S,s,O,o,Se,Te,CX4z0:3][#1:4]>>
[#1:4][N,n,S,O,Se,Te,Cz0X4:1][C,c,NX2,nX2:6]=[C,c:5][C,c,NX2,nX2:2]=[C,c,NX2,nX2:7][C,c,NX2,nX2:8]=[NX2,S,O,Se,Te,CX3z0R0:3]

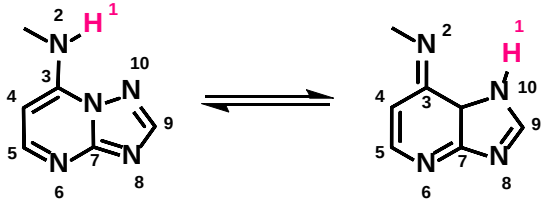
Occurrence rate: ~48%



rule 10: 1.9 (aromatic) heteroatom H shift

[#1:1][n,N,O:2][c,nX2,C:3]=[c,nX2,C:4][c,nX2:5]=[c,nX2:6][c,nX2:7]=[c,nX2:8][c,nX2,C:9]=[n,N,O:10]>>
[N,n,O:2]=[C,c,nX2:3][c,nX2:4]=[c,nX2:5][c,nX2:6]=[c,nX2:7][c,nX2:8]=[c,nX2:9][n,O:10][#1:1]

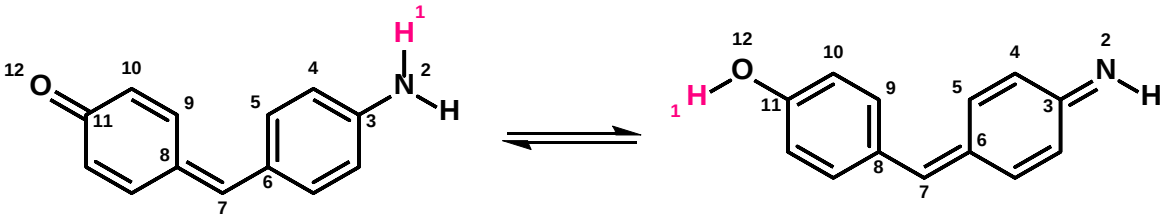
Occurrence rate: ~3%



rule 11: 1.11 (aromatic) heteroatom H shift

[#1:1][n,N,O:2][c,nX2,C:3]=[c,nX2,C:4][c,nX2:5]=[c,C,nX2:6][c,C,nX2:7]=[c,C,nX2:8][c,nX2,C:9]=[c,C,nX2:10][c,C,nX2:11]=[nX2,NX2,O:12]>>
[NX2,nX2,O:2]=[C,c,nX2:3][c,C,nX2:4]=[c,C,nX2:5][c,C,nX2:6]=[c,C,nX2:7][c,C,nX2:8]=[c,C,nX2:9][c,C,nX2:10]=[c,C,nX2:11][nX2,O:12][#1:1]

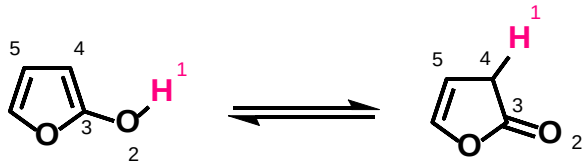
Occurrence rate: ~1%



rule 12: 1.5 furanones

[#1:1][O,S,N:2][c,C;z2;r5:3]=[C,c;r5:4][c,C;r5:5]>>
[O,S,N:2]=[Cz2r5:3][C&r5R{0-2}:4]([#1:1])[C,c;r5:5]

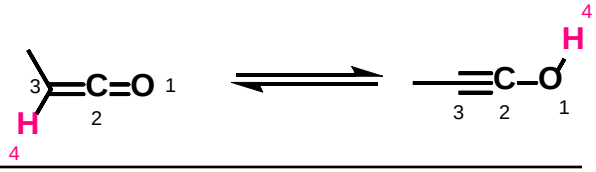
Occurrence rate: ~6%



rule 13: keten-ynol exchange

[O,S,Se,Te;X1:1]=[C:2]=[C:3][#1:4]>>
[#1:4][O,S,Se,Te;X2:1][C:2]#[C:3]

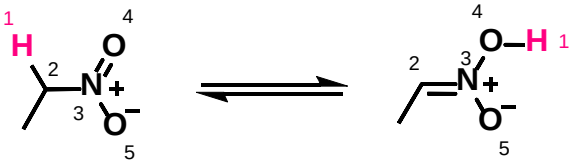
Incidences: >4,500



rule 14: ionic nitro/aci-nitro

[#1:1][C:2][N+:3]([O-:5])=[O:4]>>
[C:2]=[N+:3]([O-:5])[O:4][#1:1]

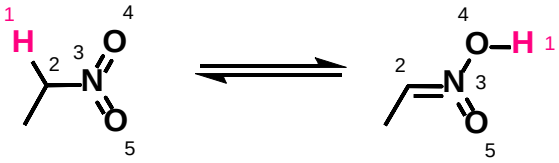
Occurrence rate: ~0.2%



rule 15: 1.3 pentavalent nitro/aci-nitro

[#1:1][C:2][N:3](=[O:5])=[O:4]>>
[C:2]=[N:3](=[O:5])[O:4][#1:1]

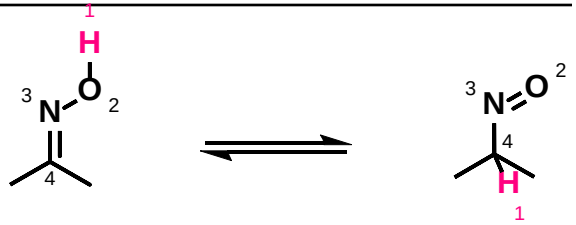
Occurrence rate: ~0.1%



rule 16: oxime/nitroso

[#1:1][O:2][N+0z1:3]=[C:4]>>
[O:2]=[N+0z1:3][C:4][#1:1]

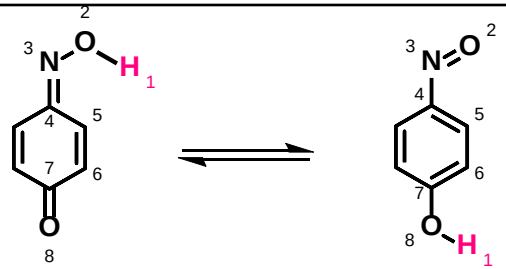
Occurrence rate: ~0.4%



rule 17: nitroso/oxime via phenyl

[#1:1][O:2][Nz1:3]=[C:4][C:5]=[C:6][C:7]=[O:8]>>
[O:2]=[Nz1:3][c:4]=[c:5][c:6]=[c:7][O:8][#1:1]

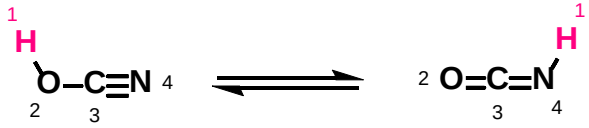
Incidences: >600



rule 18: cyanuric acid

[#1:1][O:2][C:3]#[N:4]>>
[O:2]=[C:3]=[N:4][#1:1]

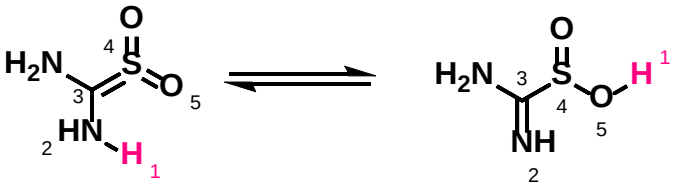
Incidences: >400



rule 19: formamidinesulfonic acid

[#1:1][O,N:2][C:3]=[S,Se,Te:4]=[O:5]>>
[O,N:2]=[C:3][S,Se,Te;v{2-4}:4][O:5][#1:1]

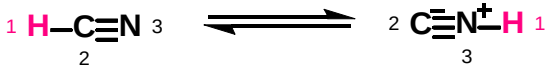
Incidences: >500



rule 20: isocyanide

[#1:1][C0:2]#[N0:3]>>
[C-:2]#[N+:3][#1:1]]

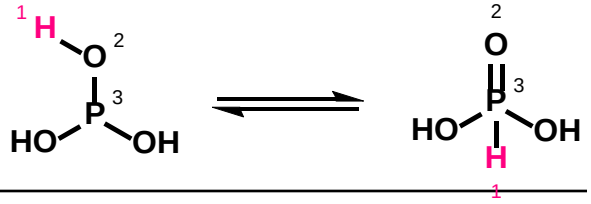
Incidences: >300



rule 21: phosphonic acid

[#1:1][NX3,O:2][P;v3:3]>>[NX2,O:2]=[P;v5:3][#1:1]

Incidences: >23,000



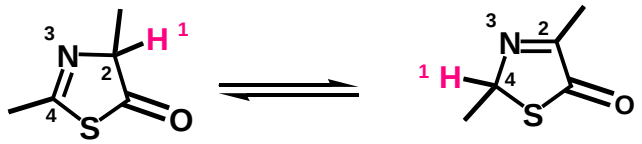
Note: Rule expanded by “N” vs. current standard CACTVS rule.

New Proposed Tauto Rules

rule 22: imine via imine

[#1:1][CX4:2][NX2:3]=[CX3:4]>>
[CX3:2]=[NX2:3][CX4:4][#1:1]

Occurrence rate: ~2%

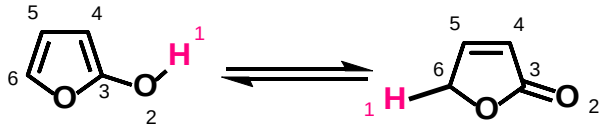


Lin et al. Eur. J. org. Chem. 2002, 557-563; Kolehmainen et al. Pol. J. Chem., *77*, 31-45

rule 23: 1,5 furanones

[#1:1][O,S,NX3:2][cX3;z2;r5:3]=[c;r5:4][c;r5:5]=[c;z{1-2};r5;R{1-2}:6]>>
[O,S,NX2:2]=[CX3;z2;r5:3]1[C;r5:4]=[C;r5:5][Cz{1-2};r5;R{1-2}:6][#1:1]

Occurrence rate: ~2%

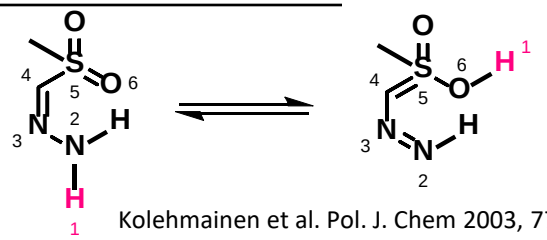


Rossa et al. Tetra. Lett. 2009, 50, 12-14; Brandsma et al. Tetra. Lett. 1998, 39, 2433-2436

rule 24: sulfonylhydrazine/diazenylsulfinic acid

[#1:1][OX2,SX2,NX3:2][NX2:3]=[C:4][SX4:5]=[O:6]>>
[OX1,SX1,NX2:2]=[NX2:3][C:4]=[SX4:5][O:6][#1:1]

Incidences: >800

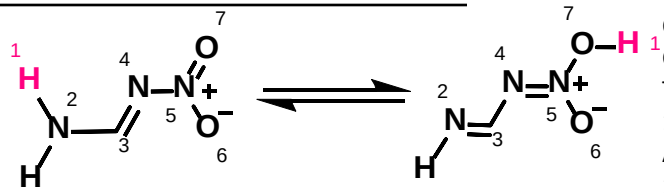


Kolehmainen et al. Pol. J. Chem 2003, 77, 31-45

rule 25: N-nitro/N-nitronic acid

[#1:1][OX2,SX2,PX3,NX3:2][C:3]=[NX2:4][N+:5]([O-:6])=[O:7]>>
[OX1,SX1,PX2,NX2:2]=[C:3][NX2:4]=[N+:5]([O-:6])[O:7][#1:1]

Incidences: >1,100

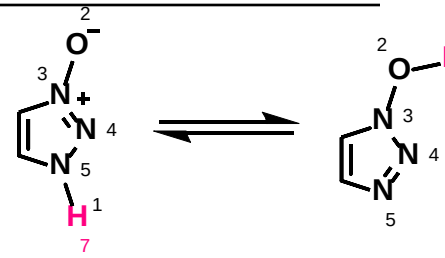


Cholerton et al. J. Chem. Soc., Perkin Trans. 2 1984, 1761-1766, Richter et al. Analyst, 1994, 119, 1371-1374

rule 26: 1.4 N-oxide/N-hydroxide

[#1:1][OX2:2][N;z{1-2};X3!$(N=O);H0:3][CX3,c,n,NX2:4]=[n,NX2:5]>>
[O&-:2][N+;z{1-2};X3;H0:3]=[c,CX3,n,NX2:4][n,NX3:5][#1:1]

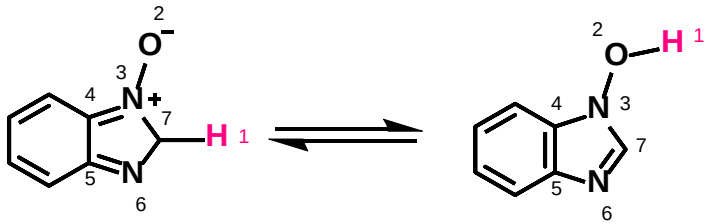
Incidences: >7,000



Boiani et al. J. Phys. Chem. A 2004, 108, 11241-11248; Pfister-Guillouzo et al. Spectrochim. Acta, Part A 224, 1995, 51, 1801-1807

rule 27: 1.6 N-oxide/N-hydroxide(1)

[#1:1][OX2:2][NX3r5:3][c,C;r5:4]=[c,C;r5:5][NX2r5:6]=[CX3:7]>>
[O&-&H0:2][NX3z1&+;r5:3]=[c,C;r5:4][c,C;r5:5]=[NX2r5:6][CX4:7][#1:1]

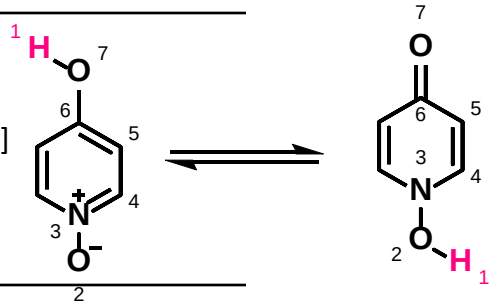


Incidences: >900

(same as for rule 26)

rule 28: 1.6 N-oxide/N-hydroxide(2)

[#1:1][O:2][NX3r6:3][C;r6:4]=[C;r6:5][C;z1;r6:6]=[O,NX2,S:7]>>
[O&-&H0:2][n&+,N&+;X3;z1;r6:3]=[c,C;r6:4][c,C;r6:5]=[c,C;z1;r6:6][O,NX3,S:7][#1:1]

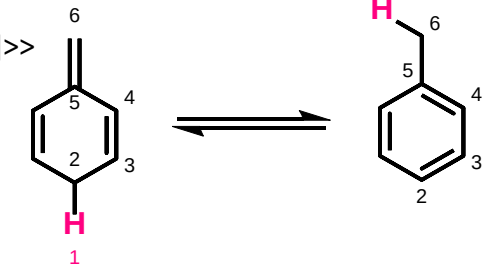


Incidences: >1,600

Katritzky et al. Heterocyc., 1991, 32, 329-369

rule 29: acene

[#1:1][CX4;R{1-2};r6:2][C;r6;R{1-3}:3]=[C;r6;R{1-3}:4][CX3;r6;R{1-2}:5]=[C;!a;R{0-1};X3:6]>>
[c;r6;R{1-2}:2]=[c;r6;R{1-3}:3][c;r6;R{1-3}:4]=[cX3;r6;R{1-2}:5][CX4;!a;R{0-1}:6][#1:1]



Occurrence rate: ~40%

Korth et al. J. Org. Chem. 2015, 80(16), 8206-8216; Takahashi et al. J Am. Chem. Soc. 2007, 129(51), 15752-15753.

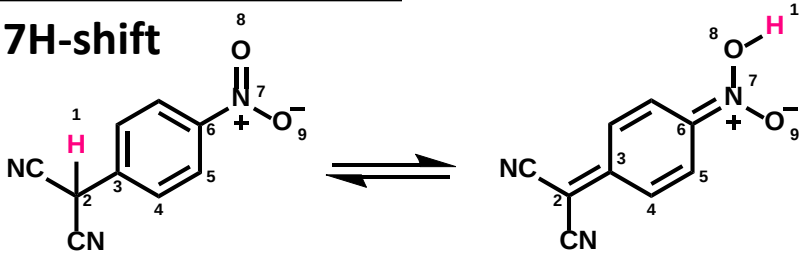
rule 31: This is a variant of rule 9

[nX2,NX2,S,O,Se,Te,Cz0X3R0:1]=[c,C,NX2,nX2:6][C,c,NX2,nX2:5]=[C,c,NX2,nX2:2][C,c,NX2,nX2:7]=[C,c,NX2,nX2:8][N,n,S,s,O,o,Se,Te,CX4z0:3][#1:4]>>
[#1:4][N,n,S,O,Se,Te,Cz0X4:1][C,c,NX2,nX2:6]=[C,c:5][C,c,NX2,nX2:2]=[C,c,NX2,nX2:7][C,c,NX2,nX2:8]=[NX2,S,O,Se,Te,CX3z0R0:3]

Occurrence rate: ~12%

rule 32: nitro/aci-nitro via aromatic ring (1): 1, 7H-shift

[#1:1][CX4:2][c:3]=[c:4][c:5]=[c:6][N+:7]([O-:9])=[O:8]>>
[CX3:2]=[C:3][C:4]=[C:5][C:6]=[N+:7]([O-:9])[O:8][#1:1]

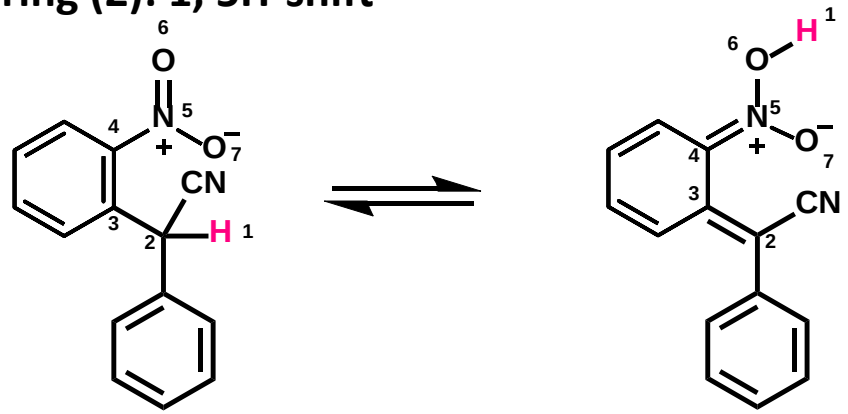


Occurrence rate: ~0.3%

Suzuki, H.; Koide, H.; Ogawa, T. Bull. Chem. Soc. Jpn. 1988, 61 (2), 501–504.

rule 33: nitro/aci-nitro via aromatic ring (2): 1, 5H-shift

[#1:1][CX4:2][c:3]=[c:4][N+:5]([O-:7])=[O:6]>>
[CX3:2]=[C:3][C:4]=[N+:7]([O-:7])[O:6][#1:1]

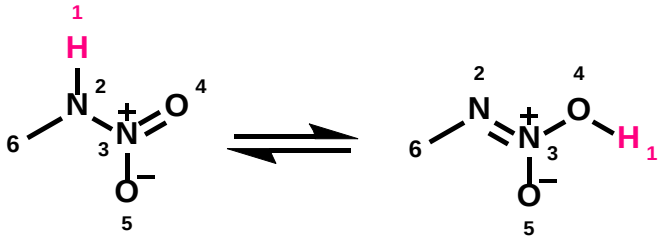


Occurrence rate: >0.1%

Schwörer, M.; Wirz, J. Helv. Chim. Acta 2001, 84 (6), 1441–1458; Filimonov, S. I.; Chirkova, Z. V.; Sharunov, V. S.; Abramov, I. G.; Stashina, G. A.; Firgang, S. I.; Suponitsky, K. Y. Chem. Heterocycl. Compd. 2012, 48 (3), 427–435.

rule 34: nitramide/N-nitronic acid

[#1:1][N:2][N+:3]([O-:5])=[O:4]>>
[N:2]=[N+:3]([O-:5])[O:4][#1:1]

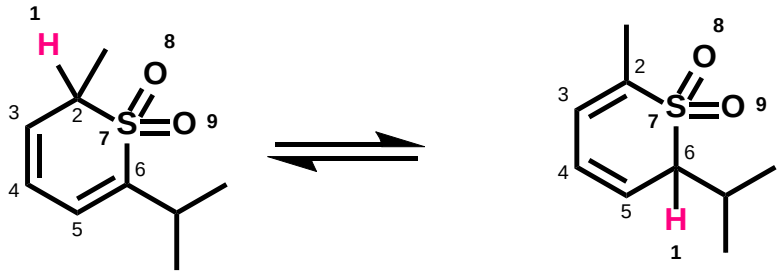


Incidences: >4,500

Arrowsmith, C. H.; Kresge, a. J.; Tang, Y. C. J. Am. Chem. Soc. 1991, 113 (1), 179–182; Cox, R. A. Can. J. Chem. 1996, 74 (10), 1779–1783.

rule 35: sulfone-based aliphatic compounds

[#1:1][CX4z1:2][CX3:3]=[CX3:4][CX3:5]=[CX3:6][SX4:7](=[O])(=[O])>>
[CX3z1:2]=[CX3:3][CX3:4]=[CX3:5][CX4:6]([#1:1])[SX4:7](=[O])(=[O])

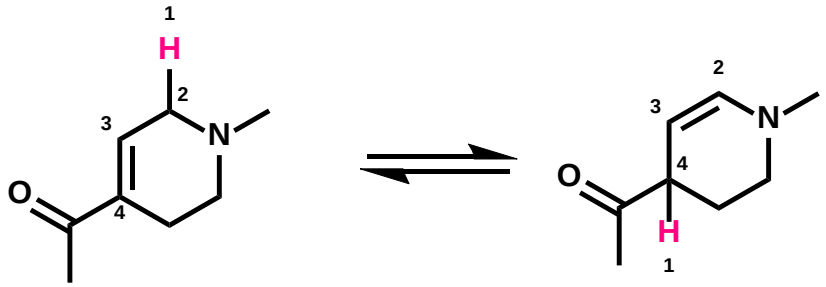


Occurrence rate: ~0.2%

Stanovnik, B.; Tisler, M.; Katritzky, A. R.; Denisko, O. V. Adv. Heterocycl. Chem. 2001, 81, 254.
Finlay, J. D.; Hall, C. R.; Smith, D. J. H. Tetrahedron Lett. 1977, 18 (13), 1149–1150.

rule 36: allylamines vs. enamine

[#1:1][CX4z1:2]([NX{2-3}:5])[CX3:3]=[CX3:4]>>
[CX3z1:2]([NX{2-3}:5])=[CX3:3][CX3:4][#1:1]

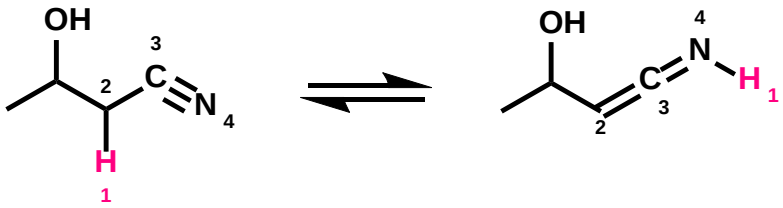


Occurrence rate: ~57%

Stanovnik, B.; Tisler, M.; Katritzky, A. R.; Denisko, O. V. Adv. Heterocycl. Chem. 2001, 81, 254;
Martinez, S. J.; Joule, J. A. Tetrahedron 1978, 34 (19), 3027–3036.

rule 39: nitrile/keteneimine: 1,3H-shift

[#1:1][CX4:2]([CX{3-4}]=,-[OX{1-2}])[CX2:3]#[NX1:4]>>
[CX3:2]([CX{3-4}]=,-[OX{1-2}])=[C:3]=[NX2:4][#1:1]

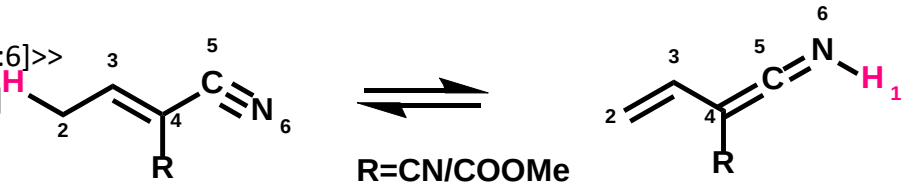


Incidences: >36,500

Giussi, J. M.; Ponzinibbio, A.; Cortizo, M. S.; Allegretti, P. E. *Spectrochim. Acta - Part A Mol. Biomol. Spectrosc.* **2010**, *77* (2), 367–373; Giussi, J. M.; Gastaca, B.; Albesa, A.; Cortizo, M. S.; Allegretti, P. E. *Spectrochim. Acta Part A Mol. Biomol. Spectrosc.* **2011**, *78* (2), 868–873; Giussi, J. M.; Gastaca, B.; Lavecchia, M. J.; Schiavoni, M.; Cortizo, M. S.; Allegretti, P. E. *J. Mol. Struct.* **2015**, *1081*, 375–380.

rule 40: nitrile/keteneimine :1,5H-shift

[#1:1][CX4:2][CX3:3]=[CX3;$([CX{2-3}]=,#[N,O]):4][CX2:5]#[NX1:6]>>
[CX3:2]=[CX3:3][CX3;$([CX{2-3}]=,#[N,O]):4]=[C:5]=[NX2:6][#1:1]

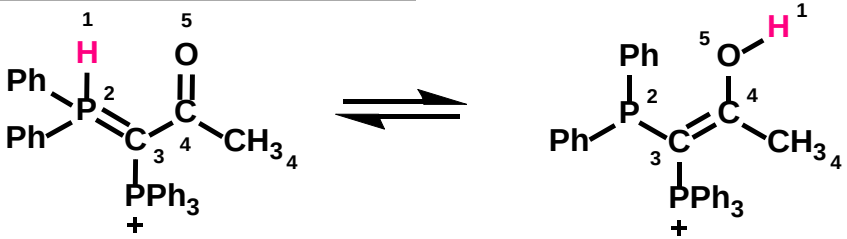


Incidences: 0

Saraví Cisneros, H.; Laurella, S.; Ruiz, D. L.; Ponzinibbio, A.; Allegretti, P. E.; Furlong, J. J. P. Int. J. Spectrosc. 2009, 2009, 1–18; Cisneros, H. S.; Erben, M. F.; Della Védova, C. O.; Laurella, S.; Allegretti, P. E.; Furlong, J. J. P. Eur. J. Mass Spectrom. 2011, 17 (2), 125–143.

rule 41: tetrad phosphorus-carbon

[#1:1][PX4:2]=[CX3;$([PX4+]):3][CX3z1:4]=[O:5]>>
[PX3:2][CX3;$([PX4+]):3]=[CX3z1:4][OX2:5][#1:1]

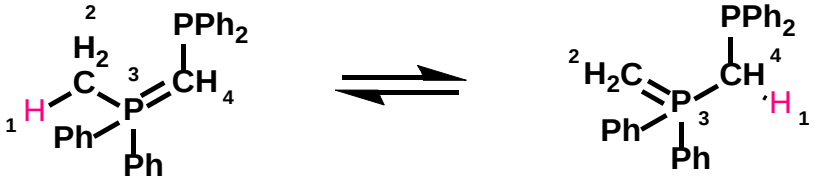


Incidences: 0

Mastryukova, T. A.; Kabachnik, M. I. Russ. Chem. Rev. 1983, 52 (11), 1012–1029.

rule 42: triad phosphorus-carbon

[#1:1][CX4:2][PX4:3]=[CX3z2;$([PX3]):4]>>
[CX3:2]=[PX4:3][CX4z2;$([PX3]):4][#1:1]

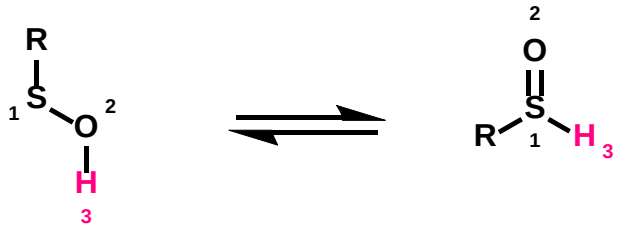


Incidences: 0

Mastryukova, T. A.; Kabachnik, M. I. Russ. Chem. Rev. 1983, 52 (11), 1012–1029.

rule 45: sulfenyl/sulfinyl: 1,2H-shift

[Sv2X2:1][OX2][#1:3]>>
[Sv4X3]([#1:3])=[OX1:2]

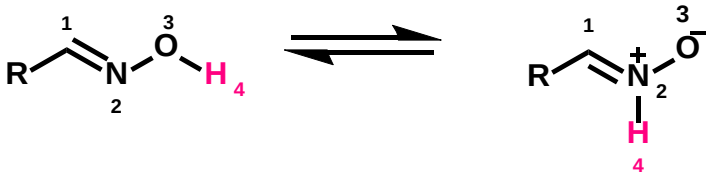


Incidences: >820

Kumar, M. R.; Farmer, P. J. ACS Chem. Biol. 2017, 12 (2), 474–478; Davis, F. A.; Billmers, R. L. J. Org. Chem. 1985, 50 (14), 2593–2595

rule 46: oxim/nitrone: 1,2H-shift

[CX3:1]=[NX2:2][OX2:3][#1:4]>>
[CX3:1]=[NX3+:2]([OX1-:3])[#1:4]

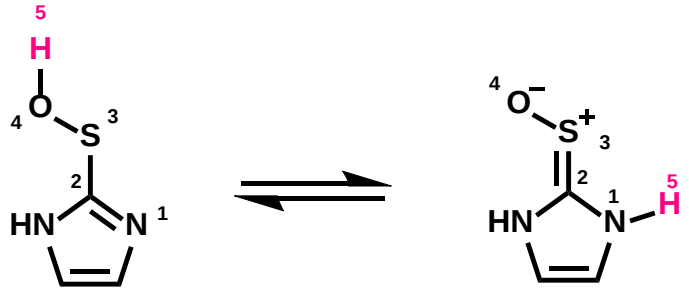


Occurrence rate: ~0.3%

Liu, W.; Zhang, C.; Zhang, H.; Zhao, N.; Yu, Z.; Xu, J. J. Am. Chem. Soc. 2017, 139 (25), 8678–8684; Osborn, H. M. I.; Gemmell, N.; Harwood, L. M J. Chem. Soc. Perkin Trans. 1 2002, 0 (22), 2419–2438; Grigg, R.; Heaney, F.; Markandu, J.; Surendrakumar, S.; Mark, T.-P.; William, W. J. Tetrahedron 1991, 47 (24), 4007–4030.

rule 47: sulfenyl /S-oxide: 1,4H-shift

[NX2]=[CX3z{2-3}:2][SX2:3][OX2:4][#1:5]>>
[#1:5][NX3:1][CX3z{2-3}:2]=[SX2+:3][OX-:4]

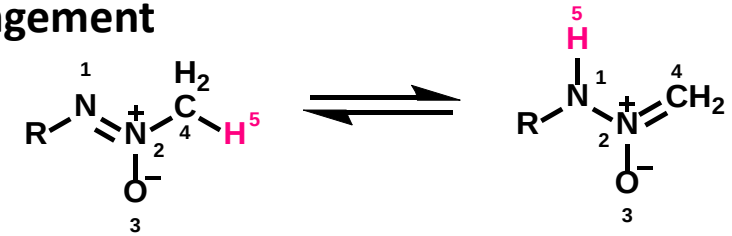


Incidences: >30

Kumar, M. R.; Farmer, P. J. ACS Chem. Biol. 2017, 12 (2), 474–478; Chipiso, K.; Simoyi, R. H. J. Phys. Chem. A 2016, 120 (21), 3767–3779.

rule 48: nitrone/azoxy or Behrend rearrangement

[CX3,NX2:1]=[NX3+:2]([O-:3])[CX4:4][#1:5]>>
[#1:5][CX4,NX3:1][NX3+:2]([O-:3])=[CX3:4]



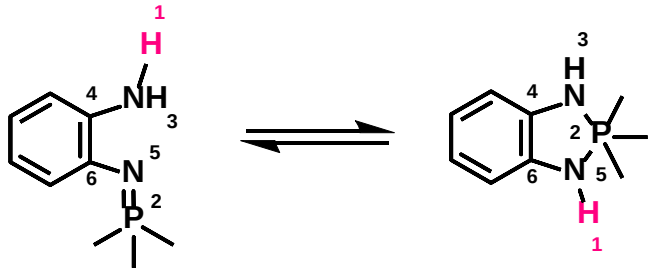
Incidences: >4,200

Freeman, J. P. J. Org. Chem. 1962, 27 (8), 2881–2884; Smith, P. A. S.; Gloyer, S. E. J. Org. Chem. 1975, 40 (17), 2504–2508; Raczyńska, E. D.; Kosińska, W.; Ośmiałowski, B.; Gawinecki, R. Chem. Rev. 2005, 105 (10), 3561–3612.

Special Cases
- consider for InChI V2?

rule 30: 5_endo_tet

[#1:1][NX3;R:3]1[*R:4]~[*R:6][O,N,S,Se,Te;R:5][PX5R;z2:2]1>>
[PX4;!R;z1:2]=[NX2;!R;+0:3][*:4]~[*:6][O,N,S,Se,Te;!R:5][#1:1]

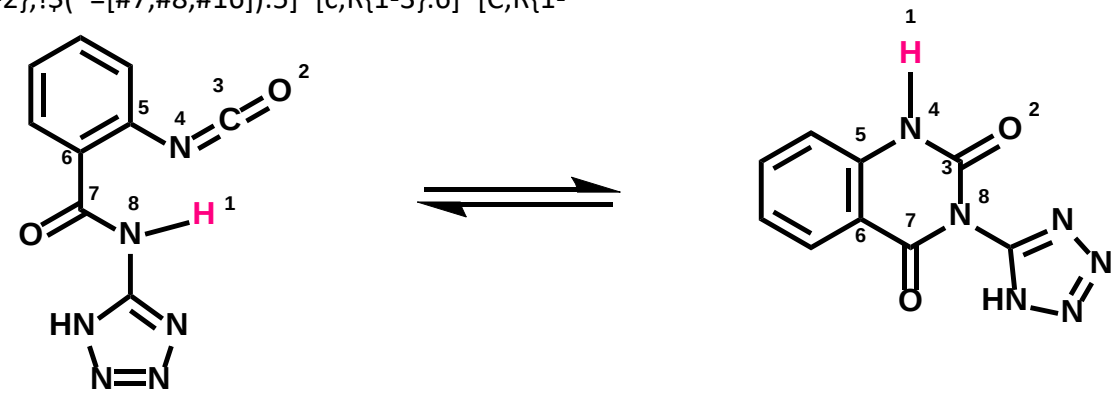


Incidences: >70

Stegmann, H.; Haller, R. *Eur. J.* **1977**, *110* (12), 3817–3828.

rule 37: 6-endo-dig

[OX:2]=[CX2;z2:3]=[NX2;!R:4][c;R{0-1};!$(*=[#7,#8,#16]):5]~[c;R{0-1}:6]~[C;R{0-1}:7][NX3;!R:8][#1:1]>>
[O:2]=[CX3;z3;R:3]1[NX3;R:4]([#1:1])[c;R{1-2};!$(*=[#7,#8,#16]):5]~[c;R{1-3}:6]~[C;R{1-2}:7][NX3;R:8]1

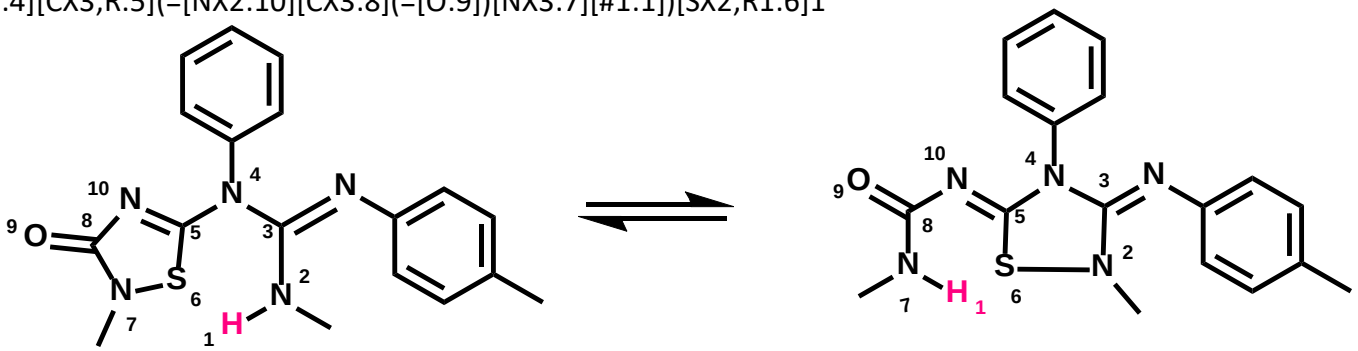


Incidences: >34,500

Peet, N. P. J. Heterocycl. Chem. 1987, 24 (1), 223–225;
Kurasawa, Y.; Takada, A.; Ho, S. K. Heterocycles 1995, 41 (8), 1805–1832.

rule 38: Thiadiazoline

[#1:1][NX3:2][CX{2-3}:3][NX3:4][CX3;R1:5]1[SX2;R1:6][NX3;R1:7][CX3;R1:8](=[O:9])[NX2:10]=1>>
[NX3;R:2]1[CX{2-3};R:3][NX3;R:4][CX3;R:5](=[NX2:10][CX3:8](=[O:9])[NX3:7][#1:1])[SX2;R1:6]1

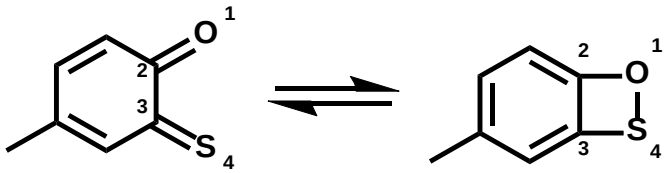


Incidences: >30

L'Abbé, G.; Albrecht, E. Chem. 1992, 29 (2), 451–454.

rule 43: Benzoxathiete (Valence tautomerism)

[OX1:1]=[CX3:2][CX3:3]=[SX{1-2}z{0-1}:4]>>
[OX2:1]1[c:2]=[c:3][SX{2-3}z{1-2}:4]1

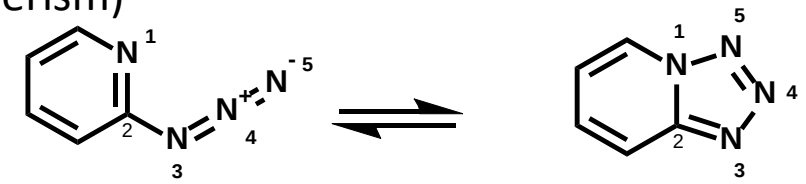


Incidences: >2,100

Naghipur, A.; Reszka, K.; Lown, J. W.; Sapse, A.-M. Can. J. Chem. 1990, 68 (11), 1950–1960; Naghipur, A.; Reszka, K.; Sapse, A. M.; Lown, J. W. J. Am. Chem. Soc. 1989, 111 (1), 258–268.

rule 44: Tetrazole–azide (Valence tautomerism)

[nX2:1]=[cz{2-3}:2][NX2z1:3]=[N+X2z2:4]=[N-X1:5]>>
[NX3:1]1[Cz{2-3}:2]=[NX2z1:3][NX2z2:4]=[NX2z2:5]1

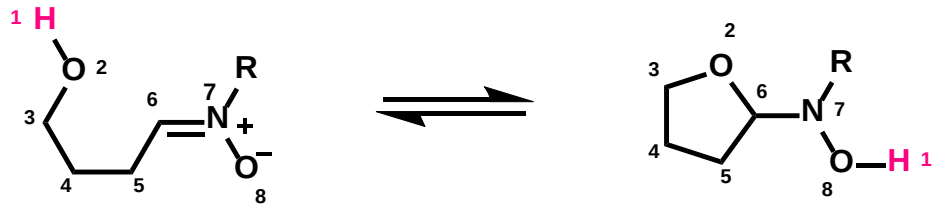


Occurrence rate: ~0.9%

Cmoch, P.; Wiench, J. W.; Stefaniak, L.; Webb, G. A. J. Mol. Struct. 1999, 510 (1–3), 165–178; Smirnova, N. B.; Postovskii, I. Y.; Vereshchagina, N. N.; Lundina, I. B.; Mudretsova, Heterocycl. Compd. 1970, 4 (1), 130–131; Dabbagh, H. A.; Lwowski, W. J. Org. Chem. 2000, 65 (22), 7284–7290; Alkorta, I.; Blanco, F.; Elguero, J. Tetrahedron 2010, 66 (27–28), 5071–5081.

rule 49: 5_exo_trig: 1,4H-shift

[#1:1][NX3,OX2:2][CX4:3][CX4:4][CX4:5][CX3:6]=[NX3+:7][OX1-:8]>>
[NX3,OX2:2]1[CX4:3][CX4:4][CX4:5][CX4:6]1[NX3:7][OX2:8][#1:1]

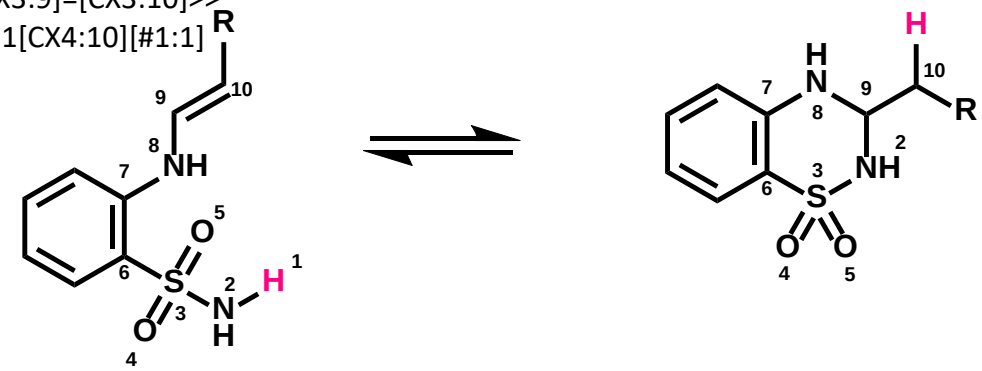


Incidences: >270

Coşkun, N.; Asutay, O. Tetrahedron Lett. 2007, 48 (29), 5151–5155; Coşkun, N.; Aksoy, Ç. Tetrahedron Lett. 2009, 50 (25), 3008–3012; Cicchi, S.; Corsi, M.; Marradi, M.; Goti, A. Tetrahedron Lett. 2002, 43 (15), 2741–2743.

rule 50: 6_exo_trig

[#1:1][NX3:2][SX4:3](=[O:4])(=[O:5])[c:6][c:7][NX3:8][CX3:9]=[CX3:10]>>
[NX3:2]1[SX4:3](=[O:4])(=[O:5])[c:6][c:7][NX3:8][CX4:9]1[CX4:10][#1:1]



Incidences: >20,800

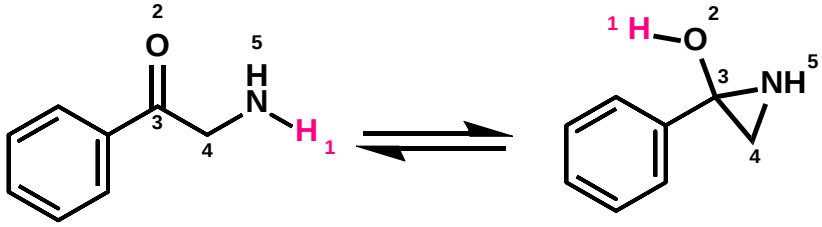
Maloshitskaya, O. A.; Sinkkonen, J.; Alekseyev, V. V.; Zelenin, K. N.; Pihlaja, K. Tetrahedron 2005, 61 (30), 7294–7303.

Ring-Chain Rules
(not proposed for InChI V2)

Guasch L, Sitzmann M, Nicklaus MC.
Enumeration of ring-chain tautomers based on SMIRKS rules.
J Chem Inf Model. **2014**;54(9):2423-32. doi: 10.1021/ci500363p.

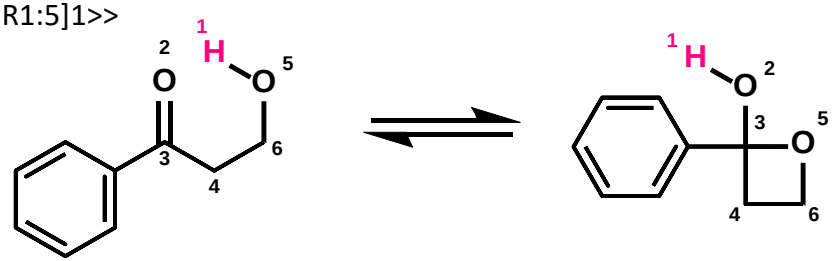
RC1: 3_exo_trig

[#1:1][O,N,S,Se,Te:2][#6R1;!c;z2:3]1[#6;!c;R1:4][O,N,S,Se,Te;R1:5]1>>
[O,N,S,Se,Te:2]=[C;!R;z1:3][#6;!R:4][O,N,S,Se,Te;!R:5][#1:1]



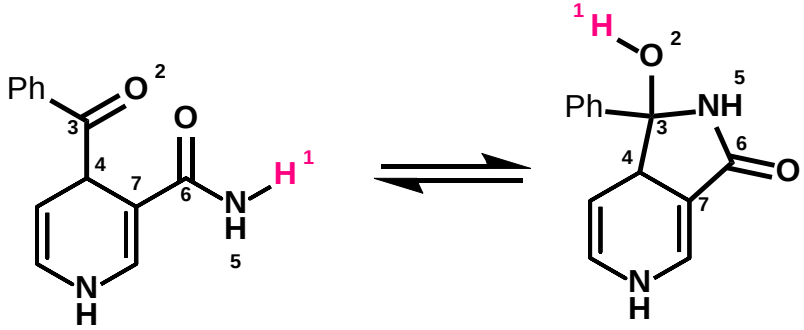
RC2: 4_exo_trig

[#1:1][O,N,S,Se,Te:2][#6R1;!c:3]1[#6;R1:4]~[C;R1:6][O,N,S,Se,Te;R1:5]1>>
[O,N,S,Se,Te:2]=[C;!R:3][C;!R:4][C;!R:6][O,N,S,Se,Te;!R:5][#1:1]



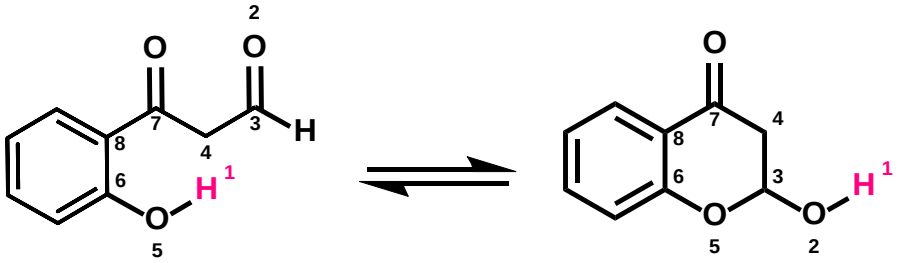
RC4: 5_exo_trig

[#1:1][O,N,S,Se,Te:2][#6R1;!c:3]1[*:4]~[*:7]~[R1:6][O,N,S,Se,Te;R:5]1>>
[O,N,S,Se,Te:2]=[C;!R:3][R{0-1}:4]~[R{0-1}:7][!R:6][O,N,S,Se,Te:5][#1:1]



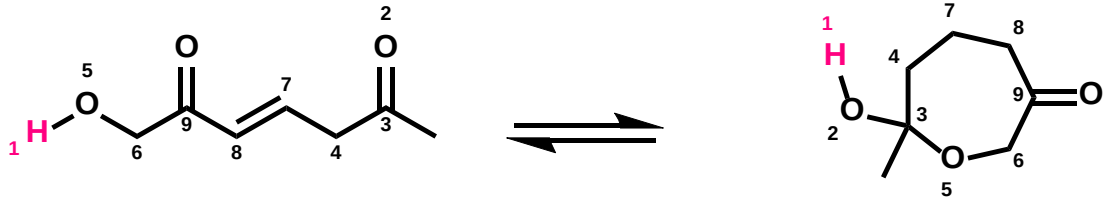
RC4: 6_exo_trig

[#1:1][O,N,S,Se,Te:2][#6R1;!c:3]1[*:4]~[*:7]~[*;R1:8]~[C;R1:6][O,N,S,Se,Te;R:5]1>>
[O,N,S,Se,Te:2]=[C;!R:3][R{0-1}:4]~[R{0-1}:7]~[!R:8]~[!C:6][O,N,S,Se,Te:5][#1:1]



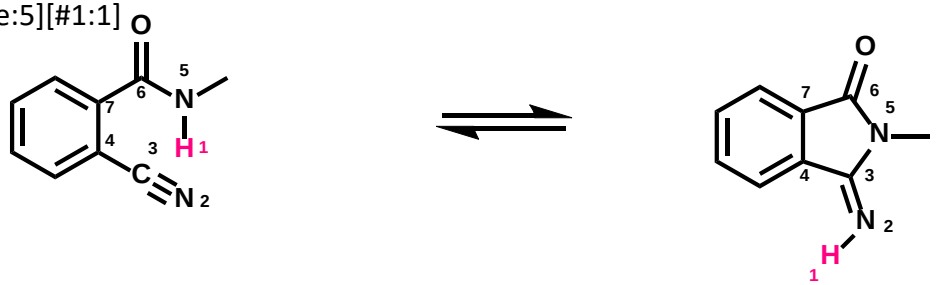
RC5: 7_exo_trig

[#1:1][O,N,S,Se,Te:2][#6R1;!c:3]1[*:4]~[*:7]~[*;R1:8]~[*;R1:9]~[R1:6][O,N,S,Se,Te;R:5]1>>
[O,N,S,Se,Te:2]=[C;!R:3][R{0-1}:4]~[R{0-1}:7]~[!R:8]~[!R:9]~[!R:6][O,N,S,Se,Te:5][#1:1]



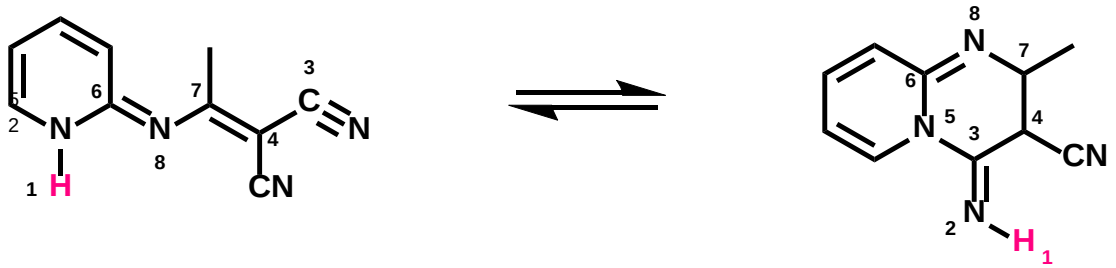
RC6: 5_exo_dig

[#1:1][N:2]=[#6R1;!c:3]1[*:4]~[*:7]~[#6R1:6][O,N,S,Se,Te;R:5]1>>
[N;X1:2]#[C;!R:3][R{0-1}:4]~[R{0-1}:7]~[#6;!R:6][O,N,S,Se,Te:5][#1:1]



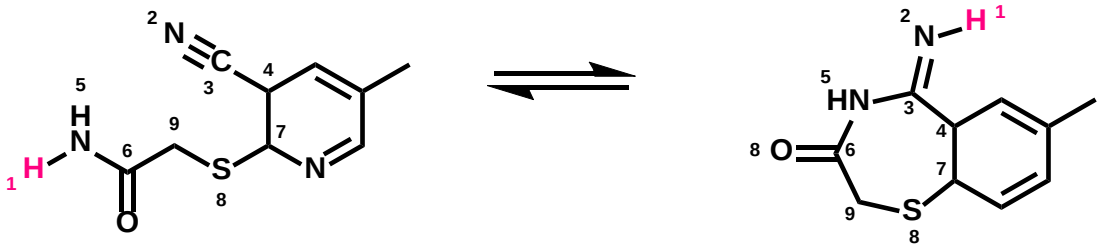
RC7: 6_exo_dig

[#1:1][N:2]=[#6R1;!c:3]1[*:4]~[*:7]~[*;R1:8]~[#6R1:6][O,N,S,Se,Te;R:5]1>>
[N;X1:2]#[C;!R:3][R{0-1}:4]~[R{0-1}:7]~[*;!R:8]~[#6;!R:6][O,N,S,Se,Te:5][#1:1]



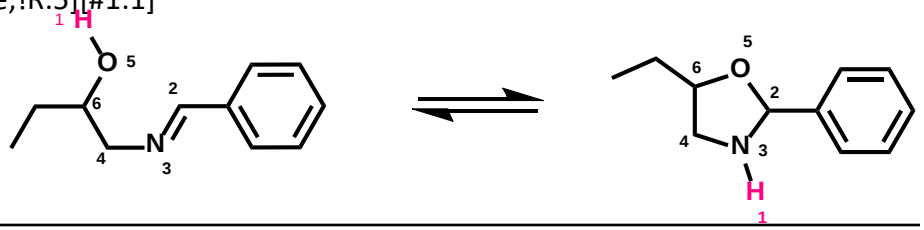
RC8: 7_exo_dig

[#1:1][N:2]=[#6R1;!c:3]1[*:4]~[*:7]~[*;R1:8]~[*;R1:9]~[#6R1:6][O,N,S,Se,Te;R:5]1>>
[N;X1:2]#[C;!R:3][R{0-1}:4][R{0-1}:7][*;!R:8][*;!R:9][#6;!R:6][O,N,S,Se,Te:5][#1:1]



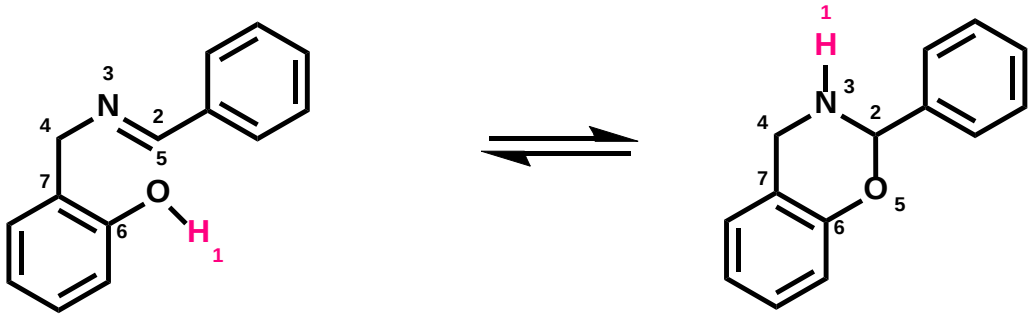
RC9: 5_endo_trig

[#1:1][N;R1;X3:3]1[!a:4]~[R:6][O,N,S,Se,Te;R:5][#6R;z2;X4:2]1>>
[C;!R;z1;X3:2]=[N;!R,X2;+0:3][*:4]~[*:6][O,N,S,Se,Te;!R:5][#1:1]



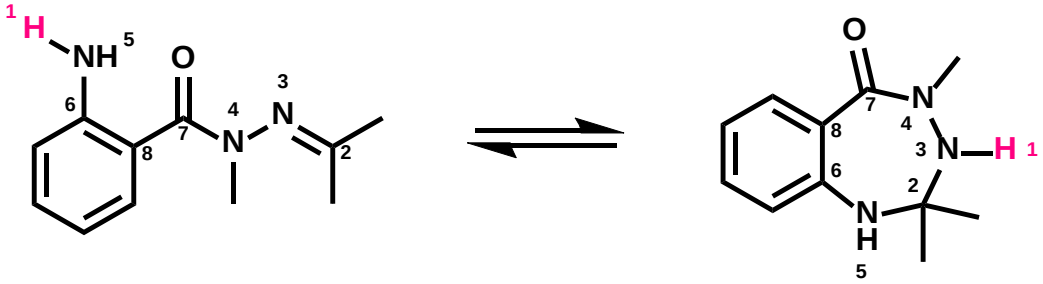
RC10: 6_endo_trig

[#1:1][N;R1;X3:3]1[!a:4]~[*:7]~[*;R1:6][O,N,S,Se,Te;R:5][#6R;z2;X4:2]1>>
[C;!R;z1;X3:2]=[N;!R;+0:3][R{0-1}:4]~[*;R{0-1}:7]~[!R:6][O,N,S,Se,Te:5][#1:1]



RC11: 7_endo_trig

[#1:1][N;R1;X3:3]1[!a:4]~[*:7]~[*;R1:8]~[R1:6][O,N,S,Se,Te;R:5][#6R;z2;X4:2]1>>
[C;!R;z1;X3:2]=[N;!R;+0:3][R{0-1}:4]~[*;R{0-1}:7]~[*;!R:8]~[!R:6][O,N,S,Se,Te:5][#1:1]



What about zwitterionic tautomers?