Zeneth 8: A faster, more intuitive, degradation predictive system

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Contents

• Zeneth 8 overview
  Knowledge manager
  Predictor

• Transformations and patterns
• Degradant scoring
• Excipient functionality

• New scientific developments
  Stereochemistry
  $pK_a$ calculator

• Demonstration
Expert knowledge-based system for the prediction of forced degradation

- **Query compound**
- **Knowledge base**
  - Transformations [507]
  - Excipients [189]
  - References [546]
- **Environmental conditions**
  - $\text{H}_2\text{O}$ (hydrolysis)
  - $\text{O}_2$, $\text{H}_2\text{O}_2$, AIBN (oxidation)
  - Light (photochemistry)
  - pH
  - Temperature
- **“Predictor”**
- **Other constraints**
- **Potential degradants**

List of transformations available for processing:

- Condensations and additions
- Eliminations and fragmentations
- Hydrolyses
- Isomerisations and rearrangements
- Oxidations
- Photochemical reactions
<table>
<thead>
<tr>
<th>ID</th>
<th>Transformation Name</th>
<th>Category</th>
<th>Created</th>
<th>Modified</th>
</tr>
</thead>
<tbody>
<tr>
<td>z151</td>
<td>Decarbonylation of alpha-oxo ester</td>
<td>Eliminations and fragmentations</td>
<td>16/10/2018 11:36</td>
<td>19/03/2019 07:25</td>
</tr>
<tr>
<td>z152</td>
<td>Vinylogous retro-aldol reaction</td>
<td>Eliminations and fragmentations</td>
<td>16/10/2018 11:36</td>
<td>19/03/2019 07:26</td>
</tr>
<tr>
<td>z153</td>
<td>Cyclisation to hemiaminal, hemiacetal or hemimercaptal</td>
<td>Condensations and additions</td>
<td>16/10/2018 11:36</td>
<td>19/03/2019 07:28</td>
</tr>
<tr>
<td>z154</td>
<td>Isomerisation of N-(acylmethyl) imine</td>
<td>Isomerisations and rearrangements</td>
<td>16/10/2018 11:36</td>
<td>21/08/2019 18:31</td>
</tr>
<tr>
<td>z155</td>
<td>Baeyer-Villiger rearrangement of ketone</td>
<td>Oxidations</td>
<td>16/10/2018 11:36</td>
<td>19/03/2019 07:33</td>
</tr>
<tr>
<td>z156</td>
<td>Oxidation of alpha-diketone to acid anhydride</td>
<td>Oxidations</td>
<td>16/10/2018 11:36</td>
<td>19/03/2019 07:40</td>
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<tr>
<td>z157</td>
<td>Lossen rearrangement of hydroxamic acid or derivative</td>
<td>Eliminations and fragmentations</td>
<td>16/10/2018 11:36</td>
<td>01/04/2019 14:17</td>
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<tr>
<td>z158</td>
<td>Photochemical hydrolysis of trifluoromethyl group</td>
<td>Photochemical reactions</td>
<td>16/10/2018 11:36</td>
<td>19/03/2019 07:43</td>
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<tr>
<td>z159</td>
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<td>16/10/2018 11:36</td>
<td>07/10/2019 16:03</td>
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<tr>
<td>z160</td>
<td>Oxidation of pyrazole or thiazole with singlet oxygen</td>
<td>Oxidations</td>
<td>16/10/2018 11:36</td>
<td>19/03/2019 07:47</td>
</tr>
</tbody>
</table>

Total transformations: 507
Knowledge manager

Transformation name:* Photodecarboxylation of aryloxyacetic acid

ID:* z457

Transformation category: Photochemical reactions

Description image:

![Chemical structure diagram]

R1 = aromatic carbon
R2, R3 = aliphatic carbon (not multiply bonded and not attached to a heteroatom) or aromatic carbon or hydrogen

Comments:

Aryloxyacetic acids can undergo photolytic decarboxylation. The mechanism has been postulated to involve an initial photoexcitation of the carboxylate anion followed by decarboxylation to the excited state of the aryloxy carbocation. This carbocation is then protonated (from any donor present) and then returns to the ground state [Miranda et al., Vaya et al]. The reaction has been observed for fenofibrin acid [Miranda et al].

References:


Mechanistic studies on the photoallergy mediated by fenofibrin acid: photoreactivity with serum albumins. Vaya I, Andreu I, Morje VT, Jimenez MC and Miranda MA, 2016, Chemical Research in Toxicology, 29, 40-46


Created date and time: 16/10/2018 11:36

Last modified date and time: 26/02/2019 16:57
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<th>Title</th>
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<th>Volume</th>
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<td>Abdel-Malik MM and de Mayo P</td>
<td>Canadian Journal of Chemistry</td>
<td>1984</td>
<td>62</td>
<td>1275-1278</td>
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Total references: 554
# Knowledge manager

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<th>Type</th>
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<tbody>
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<td>(1)</td>
<td>Regular</td>
<td>✔️ (1)</td>
<td>01/03/2019 12:00</td>
<td>01/03/2019 12:00</td>
<td>☑️</td>
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<td>01/03/2019 12:00</td>
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<tr>
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<td>01/03/2019 12:00</td>
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<td>01/03/2019 12:00</td>
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<td>01/03/2019 12:00</td>
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<td>01/03/2019 12:00</td>
<td>☑️</td>
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<td>Regular</td>
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<td>01/03/2019 12:00</td>
<td>01/03/2019 12:00</td>
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</tr>
<tr>
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<td>01/03/2019 12:00</td>
<td>01/03/2019 12:00</td>
<td>☑️</td>
</tr>
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<td></td>
<td>01/03/2019 12:00</td>
<td>01/03/2019 12:00</td>
<td>☑️</td>
</tr>
</tbody>
</table>

Total structures: 7
Transformation patterns

**z457: Photodecarboxylation of aryloxyacetic acid**

[Chemical structure image]

**Explora pattern language**

**Pattern**

1. **Prediction**
   - breakBond(10, 15);
   - hideStructure(15);
   - breakBond(8, 9);
   - setBondType(9, 10, DOUBLE);
   - hideStructure(9);
   - setCharge(8, -1);
   - captureIntermediate("");
   - setIntermediateTypeMechanistic();
   - setIntermediateAsPresumed();
   - unsetCharge(8);
   - setScore(0.7);

**Script**

Atom 13: requiredBondType(AROMATIC)

Atoms 16, 17: (heteroCount == 0 and allowedBondType(SINGLE)) or requiredBondType(AROMATIC)

Explora pattern language
Zeneth prediction

Query Compound

Environmental Conditions
• Water
• pH 3

“Predictor”

Knowledge Base

Structure perception:
valences, rings, aromaticity

Match pattern
and conditions

“Hydrolysis of acetal”

pH profile
• requires water
• catalysed by acid

No Prediction

Generate potential degradants

Prediction score = 700
Degradant likelihood/scoring

Many transformations have a pH profile:

- Rule 34: If [transformation 030] is [certain] then [transformation 030 products] is [hydrolysis with pH profile 5]
- Rule 121: If [conditions: water] is [certain] then [hydrolysis with pH profile 5] is [likelihood with pH profile 5]
- Rule 80: If [pH >= 8] is [certain] then [likelihood with pH profile 5] is [very unlikely]
- Rule 81: If [6 <= pH < 8] is [certain] then [likelihood with pH profile 5] is [unlikely]
- Rule 82: If [4 <= pH < 6] is [certain] then [likelihood with pH profile 5] is [equivocal]
- Rule 83: If [2 <= pH < 4] is [certain] then [likelihood with pH profile 5] is [likely]
- Rule 84: If [pH < 2] is [certain] then [likelihood with pH profile 5] is [very likely]

Formula of yellow line = MAX (1 − pH / 10, 0.1); x 1000 → score

pH 3.9 → likely
pH 3 → likely
pH 2 → likely
pH 1.9 → very likely
Child degradant can never have a higher score than the parent

**Individual step likelihoods**

- Q → D1
  - 500 (Eq)

**“Lowest step” pathway likelihoods**

1st Gen.

- D1 → 700 (Lik)

2nd Gen.

- D2 → 300 (Unl)

3rd Gen.

- D3

**“Multiplied step” pathway likelihoods**

1st Gen.

- D1
  - 500

2nd Gen.

- D2
  - 500

3rd Gen.

- D3
  - 105 [0.35 x 0.30]

- D2
  - 350 [0.50 x 0.70 = 0.35]

- D1
  - 500
## Excipients

<table>
<thead>
<tr>
<th>Excipients &amp; Counterions</th>
<th>Contaminants</th>
</tr>
</thead>
<tbody>
<tr>
<td>(-)-Perillaldehyde</td>
<td>--</td>
</tr>
<tr>
<td>(+)-Carvone</td>
<td>--</td>
</tr>
<tr>
<td>(+)-Pulegones</td>
<td>--</td>
</tr>
<tr>
<td>3-Propanolamine</td>
<td>--</td>
</tr>
<tr>
<td>5'-Sulfosalicylic acid</td>
<td>--</td>
</tr>
<tr>
<td>Acetamidone</td>
<td>--</td>
</tr>
<tr>
<td>Acetic acid</td>
<td>--</td>
</tr>
<tr>
<td>Adipic acid</td>
<td>--</td>
</tr>
<tr>
<td>Ammonia</td>
<td>--</td>
</tr>
<tr>
<td>Ammonium glycyrhizinate</td>
<td>✓ 1</td>
</tr>
<tr>
<td>* Only contaminants will be processed</td>
<td></td>
</tr>
<tr>
<td>Aspartame</td>
<td>✓ 1</td>
</tr>
<tr>
<td>Benzoaldehyde</td>
<td>✓ 1</td>
</tr>
<tr>
<td>Benzathine</td>
<td>--</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Excipients &amp; Counterions</th>
<th>Contaminants</th>
</tr>
</thead>
<tbody>
<tr>
<td>D-Fructose</td>
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<tr>
<td>Fructose</td>
<td></td>
</tr>
<tr>
<td>D-Galactose</td>
<td>✓ 4</td>
</tr>
<tr>
<td>Galactose</td>
<td></td>
</tr>
<tr>
<td>D-Glucose</td>
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<tr>
<td>Glucose</td>
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</tr>
<tr>
<td>D-Lactose</td>
<td>✓ 6</td>
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<tr>
<td>Lactose</td>
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</tr>
<tr>
<td>D-Mannose</td>
<td>✓ 4</td>
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<tr>
<td>Sucrose</td>
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</tr>
<tr>
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<tr>
<td>D-Saccharose</td>
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<tr>
<td>Saccharose</td>
<td></td>
</tr>
<tr>
<td>Sugar</td>
<td></td>
</tr>
</tbody>
</table>
Building the knowledge base

- External requests (members)
  - provide data for a reaction
  - proprietary data via data sharing initiatives

- Group discussion with members
  - discuss proposals for new reactions
  - provide feedback on new & existing chemistry

- Internal requests, updates to existing knowledge
  - general maintenance
  - investigation of primary literature
  - specialised degradation chemistry books

- Strategic decision (e.g. cover a new reaction type)

Knowledge base

Oxidation [148]
Hydrolysis [118]
Condensation [109]
Elimination [60]
Isomerisation [28]
Photolysis [44]

New knowledge added & existing knowledge continuously maintained
New developments

- Stereochemistry
- Three-component reactions
- Intramolecular reactions
- Chemical descriptors / calculators
Stereochemistry

• Take into account stereodefinition

This transformation now operates only on carbon centres that have a defined stereocentre:

```c
if (!isDefinedStereocentre (1)) { abort(); }
```

![Chemical structures](image1)

• Nucleophilic substitutions

$S_{N2}$-type reactions exhibit inversion of configuration at a stereocentre:

```
substitutionWithInversion (3, 1, 2);
```

![Chemical structures](image2)
Three-component reactions can now be expressed and handled:

2 bidentate oxygen nucleophiles + boric acid → spiroborate anion

Code:

1. breakBond(3, 5);
2. hideStructure(5);
3. breakBond(7, 8);
4. hideStructure(8);
5. makeBond(3, 7, SINGLE);
6. captureIntermediate();
7. setIntermediateTypeObservable();
8. breakBond(4, 6);
9. hideStructure(6);
10. breakBond(7, 9);
11. hideStructure(9);
12. makeBond(4, 7, SINGLE);
13. captureIntermediate();
14. setIntermediateTypeObservable();
15. breakBond(13, 15);
16. hideStructure(15);
Intramolecular reactions

More intramolecular transformations can now be written

- **Cyclisations**
- **Cycloadditions**

Illustrated with the photochemical [2+2] addition of two alkenes
Intramolecular reactions

Altrenogest

267 - Intramolecular photochemical cycloaddition of two alkenes
700

064 - Dehydration of alcohol
300

300
Chemical descriptors / calculators

- $pK_a$
- Bond Dissociation Energy (BDE)
- Electrophilicity/Nucleophilicity
- Photochemical Reactivity
- Aromaticity
- Steric Hindrance

Reasoning Engine
Epimerisation is more likely at C1 than C4 if the isDefinedStereocentre(1) condition is met, and if the isBridgehead(1) condition is not met. The substitutionWithInversion(4, 1, 3) operation is then performed, and the hideStructure(3) command is issued. The pH and pKa are calculated as follows:

\[
\text{pH} = \text{getpH();}
\]

\[
\text{pKa} = \text{getpKa(1);}
\]

\[
\text{raw_score} = \left( \max(\text{pH}, 14 - \text{pH}) + 6 - \text{pKa} \right) / 10;
\]

if (raw_score < 0.1) { abort(); }

setScore(min(raw_score, 0.9));

The score depends on pKa as well as on pH, and epimerisation is more likely at C1 than C4.
Zeneth 8: A faster, more intuitive, degradation predictive system

Software demonstration slides

Dr Martin Ott (Head of Chemistry)
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Dr Ash Ali (Senior Scientist)
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Welcome

Projects

Start new project

Untitled
Query: PU-H71

Conditions: 
oxxygen, light, pH 11, temperature 20 °C

Pathway length: 
2 steps

Minimum score: 
600

Reaction types: 
all options off (= “no dimerisations”)

Pathway likelihood calc.: 
multiplied step
Create new query structure
Use this structure
Settings for processing
Settings

Condition Set A

- Temperature (°C): 20
- pH: 11
- Water: (on)
- Oxygen: (on)
- Metal: (off)
- Radical initiator: (off)
- Peroxide: (off)
- Light: (on)

- Add new set of conditions

Reset to default settings
APPLY
Settings

Reaction Types:

System defaults:
- Query compound reacting on its own (Q)
- Query compound reacting with excipient(s) (Q + A)
- Degradant reacting on its own (D1)
- Degradants reacting with excipient(s) (D1 + A)

User options:
- Query compound reacting with itself (Q + Q)
- Degradant reacting with itself (D1 + D1)
- Query compound reacting with degradants (Q + D1)

Numerical Settings:

- Maximum number of degradants: 400
- Maximum number of steps in a pathway: 2
- Minimum score: 600

Pathway Likelihood:
- Lowest step likelihood
- Multiplied step likelihood

Reset to default settings  APPLY
Start processing
Project screen

• Processing completed
• Click on "View results" to view tree
<table>
<thead>
<tr>
<th>Degradant</th>
<th>Parent</th>
<th>Parent 2</th>
<th>Intermediate Types</th>
<th>Duplicate</th>
<th>Score</th>
<th>Transformation ID</th>
<th>Transformation Name</th>
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<tbody>
<tr>
<td>D1</td>
<td>Q</td>
<td></td>
<td></td>
<td></td>
<td>900</td>
<td>011</td>
<td>S-Oxidation of thioether to sulfoxide</td>
</tr>
<tr>
<td>D2</td>
<td>Q</td>
<td></td>
<td></td>
<td></td>
<td>700</td>
<td>039</td>
<td>Photolytic dehalogenation of aryl bromide or iodide</td>
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<tr>
<td>D3</td>
<td>Q</td>
<td></td>
<td>1 - Mechanistic</td>
<td>D3</td>
<td>700</td>
<td>497</td>
<td>Intramolecular nucleophilic aromatic substitution of 2-heter</td>
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<td>D4</td>
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<td></td>
<td>700</td>
<td>497</td>
<td>Intramolecular nucleophilic aromatic substitution of 2-heter</td>
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<tr>
<td>D5</td>
<td>D1</td>
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<td>3 - Mechanistic</td>
<td>D3</td>
<td>810</td>
<td>499</td>
<td>Intramolecular nucleophilic aromatic substitution of 2-nitro</td>
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<tr>
<td>D6</td>
<td>D1</td>
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<td>D3</td>
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<td>499</td>
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<td>012</td>
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<td>D8</td>
<td>D1</td>
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<td>D6</td>
<td>630</td>
<td>039</td>
<td>Photolytic dehalogenation of aryl bromide or iodide</td>
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<tr>
<td>D9</td>
<td>D2</td>
<td></td>
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<td>D8</td>
<td>630</td>
<td>011</td>
<td>S-Oxidation of thioether to sulfoxide</td>
</tr>
</tbody>
</table>
Query: Adrenaline (epinephrine)

Conditions: oxygen, light, pH 11, temperature 20 °C
Pathway length: 3 steps
Minimum score: 600
Reaction types: all options off (= “no dimerisations”)
Pathway likelihood calc.: multiplied step
Processing completed

Click on "View results" to view tree.

6 degradants returned  View results
Results

• Tree view of chemical reactions and intermediates:
  - 091 - Oxidation of 1,2-dihydroquinone or 2-aminophenol
  - 316 - Intramolecular conjugate addition of heteronucleophile to quinone or related compound
  - 096 - Diels-Alder reaction with singlet oxygen
316 - Intramolecular conjugate addition of heteronucleophile to quinone or related compound

006 - Diels-Alder reaction with singlet oxygen

033 - Oxidation of 1,4-dihydroquinone or 4-aminophenol
091 - Oxidation of 1,2-dihydroquinone or 2-aminophenol
240 - Oxidative aromatisation of 2,3-dihydropyrrrole or related compound
### Results

#### Go back to project

#### Score key: Show Tree

#### Filters: Transformation groups  Score  Exact mass  Average mass

![Chemical Structure](image)

<table>
<thead>
<tr>
<th>Degradent</th>
<th>Parent</th>
<th>Parent 2</th>
<th>Intermediate Types</th>
<th>Duplicate</th>
<th>Score</th>
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<th>Transformation Name</th>
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<tbody>
<tr>
<td>D1</td>
<td>Q</td>
<td></td>
<td></td>
<td></td>
<td>900</td>
<td>091</td>
<td>Oxidation of 1,2-dihydroquinone or 2-aminophenol</td>
</tr>
<tr>
<td>D2</td>
<td>D1</td>
<td></td>
<td>1 - Tautomer</td>
<td></td>
<td>810</td>
<td>316</td>
<td>Intramolecular conjugate addition of heteronucleophile to quinone</td>
</tr>
<tr>
<td>D3</td>
<td>D1</td>
<td></td>
<td></td>
<td></td>
<td>630</td>
<td>096</td>
<td>Diels-Alder reaction with singlet oxygen</td>
</tr>
<tr>
<td>D4</td>
<td>D2</td>
<td></td>
<td></td>
<td></td>
<td>729</td>
<td>033</td>
<td>Oxidation of 1,4-dihydroquinone or 4-aminophenol</td>
</tr>
<tr>
<td>D5</td>
<td>D2</td>
<td></td>
<td></td>
<td></td>
<td>729</td>
<td>091</td>
<td>Oxidation of 1,2-dihydroquinone or 2-aminophenol</td>
</tr>
<tr>
<td>D6</td>
<td>D2</td>
<td></td>
<td></td>
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<td>729</td>
<td>240</td>
<td>Oxidative aromatisation of 2,3-dihdropyrrole or related compound</td>
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</table>
Query: Boric acid

Conditions: oxygen, light, pH 11, temperature 20 °C
Pathway length: 2 steps
Minimum score: 600
Reaction types: all options off (= “no dimerisations”)
Pathway likelihood calc.: multiplied step
Excipient(s): Glycerol
Query structure with added excipient

A - Excipient: Glycerol
Project screen

- Processing completed
- Click on “View results” to view tree

A - Excipient: Glycerol

ADD EXCIPIENTS
Results

A - Excipient: Glycerol

505 - Condensation with boric acid to spiroborate anion

700

D [1]

D [1]

[1]
Results

• Tree with intermediates
# Results

## Table

<table>
<thead>
<tr>
<th>Degradant</th>
<th>Parent</th>
<th>Parent 2</th>
<th>Intermediate Types</th>
<th>Duplicate</th>
<th>Score</th>
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<th>Transformation Name</th>
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<tbody>
<tr>
<td>D1</td>
<td>Q</td>
<td>A</td>
<td>1 - Observable, 2 - Observable, 3 - Observable</td>
<td>D1</td>
<td>700</td>
<td>505</td>
<td>Condensation with boric acid to spiroboroxine</td>
</tr>
<tr>
<td>D2</td>
<td>Q</td>
<td>A</td>
<td>4 - Observable, 5 - Observable, 6 - Observable</td>
<td>D1</td>
<td>700</td>
<td>505</td>
<td>Condensation with boric acid to spiroboroxine</td>
</tr>
<tr>
<td>D3</td>
<td>Q</td>
<td>A</td>
<td>7 - Observable, 8 - Observable, 9 - Observable</td>
<td>D1</td>
<td>700</td>
<td>505</td>
<td>Condensation with boric acid to spiroboroxine</td>
</tr>
</tbody>
</table>

## Diagrams

- **A - Excipient: Glycerol**

![Diagram of a complex molecule](image)

- ![Diagram of another complex molecule](image)
Query: Altrenogest

Conditions: oxygen, light, pH 11, temperature 20 °C
Pathway length: 2 steps
Minimum score: 600
Reaction types: all options off (= “no dimerisations”)
Pathway likelihood calc.: multiplied step
Project screen

- Processing completed
- Click on "View results" to view tree
Results

- 077 - Ene reaction with singlet oxygen
- 267 - Intramolecular photochemical cycloaddition of two alkenes
- 216 - Tautomerisation to arenol, arenethiol or arenamine
- 032 - Oxidation of aldehyde
- 153 - Cyclisation to hemiaminal, hemiacetal or hemimercaptal
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<thead>
<tr>
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<th>Parent 2</th>
<th>Intermediate Types</th>
<th>Duplicate</th>
<th>Score</th>
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<th>Transformation Name</th>
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</thead>
<tbody>
<tr>
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<td>Q</td>
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<td>1 - Observable</td>
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<td>Q</td>
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<td>700</td>
<td>077</td>
<td>Ene reaction with singlet oxygen</td>
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<tr>
<td>D3</td>
<td>Q</td>
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<td>3 - Observable</td>
<td></td>
<td>700</td>
<td>077</td>
<td>Ene reaction with singlet oxygen</td>
</tr>
<tr>
<td>D4</td>
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<td>700</td>
<td>077</td>
<td>Ene reaction with singlet oxygen</td>
</tr>
<tr>
<td>D5</td>
<td>Q</td>
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<td>700</td>
<td>267</td>
<td>Intramolecular photochemical cycloaddition of two alkenes</td>
</tr>
<tr>
<td>D6</td>
<td>D1</td>
<td></td>
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<td>630</td>
<td>153</td>
<td>Cyclisation to hemiaminal, hemiacetal or hemimercaptal</td>
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<tr>
<td>D7</td>
<td>D2</td>
<td></td>
<td></td>
<td></td>
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<td>215</td>
<td>Tautomerisation to arenol, arenethiol or arenamine</td>
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<tr>
<td>D8</td>
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<td>032</td>
<td>Oxidation of aldehyde</td>
</tr>
<tr>
<td>D9</td>
<td>D4</td>
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<td></td>
<td>630</td>
<td>153</td>
<td>Cyclisation to hemiaminal, hemiacetal or hemimercaptal</td>
</tr>
</tbody>
</table>
Epimerisation / pK$_a$

Conditions: oxygen, light, pH 7 or 11, temperature 20 °C
Pathway length: 2 steps
Minimum score: 600
Reaction types: all options off (= “no dimerisations”)
Pathway likelihood calc.: multiplied step
Results

- Tree

045 - Epimerisation alpha to electron-withdrawing group

715
Results

Conditions

- Temperature: 20
- pH: 11
- Water: OFF
- Oxygen: ON
- Metal: OFF
- Radical initiator: OFF
- Peroxide: OFF
- Lights: ON

Condition Set A

Score key: [Green, Yellow, Orange, Red]

Show Table

Filters: Transformation groups, Score, Exact mass, Average mass

Intermediates

045 - Epimerisation alpha to electron-withdrawing group

900

045 - Epimerisation alpha to electron-withdrawing group

881

045 - Epimerisation alpha to electron-withdrawing group
Stereochemistry / S\textsubscript{N2}

Conditions: oxygen, light, pH 11, temperature 20 °C
Pathway length: 2 steps
Minimum score: 600
Reaction types: all options off (= “no dimerisations”)
Pathway likelihood calc.: multiplied step
Results

055 - Epoxide formation from halohycrin

700
Timing experiment
Comparison with Zeneth 7

Vary between \( \geq 400 \) (\( \geq \) equivocal) and \( \geq 600 \) (\( \geq \) likely)

Vary between “lowest step” and “multiplied step”
<table>
<thead>
<tr>
<th>Settings</th>
<th>Pathway likelihood calc.</th>
<th></th>
<th>Settings</th>
<th>Pathway likelihood calc.</th>
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<td>Multiplied step</td>
<td>Score threshold</td>
<td>Lowest step</td>
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<tr>
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<td>288 degs</td>
<td>≥ 400</td>
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<td></td>
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<td>455 sec</td>
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<td>57 sec</td>
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<tr>
<td>≥ likely</td>
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<td></td>
<td>208 sec</td>
<td>65 sec</td>
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</tbody>
</table>

*: in the absence of excipients in the query.
Zeneth is an expert knowledge-based system for the prediction of forced degradation

Helps understand mechanistic pathways as well as aid degradant identification and structure elucidation

Zeneth generates predictions from its knowledge base which currently contains 507 transformations

Our members drive the development of the Zeneth program and directly influence the scientific content

Zeneth has recently undergone a complete re-design with the result of much improved usability as well as improvements to the quality and speed of predictions.

Efforts are underway to develop additional property calculators and expand/improve the knowledge base, more fully exploiting the added functionality
Thank you for your attention!