Comparative assessment of an alternative route to (5-benzylfuran-3-yl)methanol (Elliott's alcohol), a key intermediate for the industrial production of resmethrins.

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Electronic Supporting Information

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Substances' data used for EATOS calculations[a]

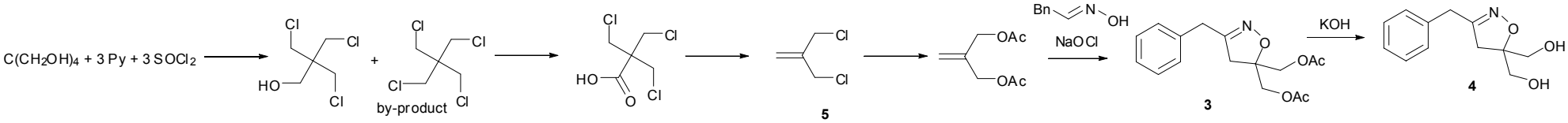
Name	Price €	Size	Risk phrases	TWA	Hazard	Acute tox.	Type	Chronic tox	WGK	LC50	BCF/logP
$C(CH_2OH)_4$	23.50	1 kg		4 mg/m^3		19500 mg/kg	Oral rat		1	50000 mg/l	.6
$SOCl_2$	22.60	1 l	14-20/22-29-35	1 ppm		324 mg/kg	Oral rat		1	1100 mg/l	
Pyridine	181.00	2 l	11-20/21/22	5 ppm	Xn	891 mg/kg	Oral rat	C3	2	93 mg/l fs	/0.65
$HOCH2C(CH_2Cl)_3$	95.5	1 g	41					M			/1.57
SO_2			23-34	5 ppm	T	2520 mg/kg	Inhl rat	C3	1	1 mg/ml f	
HCl	21.90	2.5 l	34-37	5 ppm		3124 mg/kg	Inhl rat		1	282 mg/l f	
$C(CH_2Cl)_4$	67.00	25 g			Xn			M	3		
HNO_3	95.4	10 l	35	2 ppm		0.8 mg/l	Ihl rat		1	72 mg/l f	
NaOH	85.00	2.5 kg	35	2 mg/m3		1350 mg/kg	Dermal rat		1	125 mg/l f	
CH_2Cl_2	52.10	2.5 l	40	100 ppm	Xn	1600 mg/kg	Oral rat	C3	2	193 mg/l f	/1.25
$MgSO_4$	81.40	1 kg	22-24/25			1029 mg/kg	Intrap rat		1	2820 mg/l f	
$HOOCC(CH_2Cl)_3$								M3			
NOx			26-34	3 ppm	T+	105 mg/m^3	Inhl rat	M T	1		
CH2=C(CH2Cl)2	45.10	5 ml	10-25-36/37/38		T	150 mg/kg	Oral rat	M3	3		
CO2				5000 ppm							
AcONa	24.40	1 kg				3530 mg/kg	Oral rat		1	1000 mg/l d	
TBAHS	322.00	1 kg	22-36/37/38		Xn				3		
CH_3CN	77.00	2 l	11-20/21/22-36	40 ppm	Xn	2640 mg kg	Oral rat		2	1640	/-0.34
$CH_2=C(CH_2OAc)_2$											
NaCl						3000 mg/kg	Oral rat		1	9675 mg/l f	
Oxime											
NaOCl 10%	20.10	2.5 l	31-34	3 mg/m^3		5800 mg/kg	Oral rat	C3	2	0.22 mg/l f	
Diacetoxyisox											
KOH	67.00	5 kg	22-35	2 mg/m^3		273 mg/kg	Oral rat		1	80 mg/l f	
EtOH	77.80	10 l	11-52/53	1000 mg/		7060 mg/kg	Oral rat		1	10400 mg/l f	
Diolisox											
AcOK	28.80	1 kg				3250 mg/kg	Oral rat		1	6800 mg/l f	

[a] Taken from the 2007 Aldrich catalogue, the TOXNET Hazardous Substance DataBank (HSDB), the European Chemical Bureau (ECB), and the OSIRIS tool @ www.organic-chemstry.org

Name	Price €	Size	Risk phrases	TWA	Hazard	Acute tox.	Type	Chronic tox	WGK	LC50	BCF/logP
TEPA	95.80	500 ml	51/53						3		
$(CH_2O)_n$	101.00	5 kg	20/22-37/38-40-41-43		Xn	592 mg/kg	Oral rat	C1	2	42 mg/l D	
K_2CO_3	69.40	5 kg	22-36/37/38	10 mg/m^3	Xn	1870 mg/kg	Oral rat		1	510 mg/l F	
H_3PO_4	44.80	2.5 l	34	1 mg/m^3		1350 mg/kg	Oral rat		1		
Et_2O	73.00	4 l	12-19-22-66-67	100 ppm	Xn	1215 mg/kg	Oral rat		1	2560 mg/l F	
Na_2SO_4	61.20	2.5 kg		6 mg/m^3		5989 mgkg	Oral rat		1	56 mg/l F	
Hydroxymethylacrl	232.85	5 g	36/37/38								
$KHCO_3$	62.60	5 kg		6 mg/m^3		2000 mg/kg	Oral rat		1		
KH_2PO_4	87.60	5 kg		10 mg/m^3		1700 mg/kg	Oral rat		2		
Carbethoxyisox											
$NaBH_4$	149.50	0.5 kg	15-24/25-34	.5 mg/m^3	T	162 mg/kg	Oral rat		2	5600 mg/l F	
H_3BO_3	37.10	2.5 kg				2660 mg/kg	Oral rat		1		
$PhCH_2CHO$	94.40	0.5 l	22-36/37/38		Xn	1550 mg/kg	Oral rat		1		
$NH_2OH \cdot HCl$	72.70	1 kg	22-36/38-43-48/22-50			141 mg/kg	Oral rat		3	1 mg/l F	
Na_2CO_3	43.30	5 kg	36	10 mg/m^3	Xi	4090 mg/kg	Oral rat		1	300 mg/l F	

EATOS Output

Route A. Existing route (EP 0 187 345, 1986)



Atom Selectivity (AS) of Route A

Route A:

step 6 (Route A):
AS (of the following synthesis):53.0%, AS (of the synthesis sequence):14.0%
1 Diacetoxyisoxazoline + 2 Potassium hydroxide 85% ---> 1 Isoxazoline diol + 2 Potassium acetate

step 5 (Route A 5):
AS (of the following synthesis):80.0%, AS (of the synthesis sequence):20.9%
1 Diacetoxyisobutene + 1 Oxime + 1 NaOCl 10% ---> 1 Diacetoxyisoxazoline + 1 NaCl + 1 Water

further syntheses appendant to step 5:
appendant to Oxime (Substrate):
AS (of the following synthesis):55.7%, AS (of the synthesis sequence):55.7%
2 Phenylacetaldehyde + 2 Hydroxylamine Hydrochloride + 1 Sodium carbonate ---> 2 Oxime + 1 Carbon dioxide + 2 Sodium chloride + 3 Water

step 4 (Route A 4):
AS (of the following synthesis):59.6%, AS (of the synthesis sequence):15.0%
1 3-Chloro-2-chloromethyl-1-propene + 2 Sodium acetate ---> 1 Diacetoxyisobutene + 2 NaCl

step 3 (Route A 3):
AS (of the following synthesis):60.8%, AS (of the synthesis sequence):12.7%
1 Trichloroacid ---> 1 3-Chloro-2-chloromethyl-1-propene + 1 CO2 + 1 Hydrogen chloride

step 2 (Route A 2):
AS (of the following synthesis):46.3%, AS (of the synthesis sequence):20.9%
1 Tricloro + 4 Nitric acid 65% ---> 1 Trichloroacid + 2 NOx + 3 Water

step 1 (Route A 1):
AS (of the following synthesis):26.2%, AS (of the synthesis sequence):26.2%
1 Pentaerythritol + 3 Thionyl chloride + 3 Pyridine ---> 1 Tricloro + 3 Pyridine + 3 Sulfur dioxide + 3 Hydrogen chloride

E-factor of Route A: 183.1 kg waste/kg product

```
According to synthetic step:
step 6                    ( 19.47 (10.64%) of 183.1)
step 5                    ( 80.80 (44.13%) of 183.1)
step 4                    (  3.18 ( 1.74%) of 183.1)
step 3                    (  0.71 ( 0.39%) of 183.1)
step 2                    ( 55.33 (30.22%) of 183.1)
step 1                    ( 23.61 (12.89%) of 183.1)

According to substance category:
Sewage/Water              ( 76.07 (41.55%) of 183.1)
Auxiliaries (isolation)   ( 52.17 (28.49%) of 183.1)
Solvents                  ( 31.42 (17.16%) of 183.1)
Substrates                (  3.83 ( 2.09%) of 183.1)
By-products               (  8.16 ( 4.45%) of 183.1)
Coupled products          ( 11.19 ( 6.11%) of 183.1)
```

E/Route A:
Sewage/Water (76.07 (41.55%) of 183.1):

```
step 6 (Route A):
    out of solvent EtOH
        Water
            Mass:                           2.42

    out of auxiliary material Hydrochloric acid (37%aq)
        Water
            Mass:                           0.61

step 5 (Route A 5):
    out of substrate NaOCl 10%
        Water
            Mass:                            18.29

    out of auxiliary material NaCl; Sodium chloride (aq, conc.)
        Water
            Mass:                             6.10

further syntheses appendant to step 5:
    appendant to Oxime (Substrate):
        out of auxiliary material Washing water (as Water separately)
```

Water
Mass: 5.35

step 2 (Route A 2):
out of substrate Nitric acid 65%
Water
Mass: 2.11

out of auxiliary material Washing water (as Water separately)
Water
Mass: 12.12

out of auxiliary material NaOH 1M
Water
Mass: 16.00

out of auxiliary material Hydrochloric acid (37%aq)
Water
Mass: 1.14

step 1 (Route A 1):
out of auxiliary material Washing water (as Water separately)
Water
Mass: 11.96

E/Route A:
Auxiliaries (isolation) (52.17 (28.49%) of 183.1):
step 6 (Route A):
Hydrochloric acid (37%aq)
Loss: 0.36

Dichloromethane
Loss: 11.49
Recoverable thereof: 9.19

step 5 (Route A 5):
Dichloromethane
Loss: 17.95
Recoverable thereof: 14.36

NaCl; Sodium chloride (aq, conc.)
Loss: 2.03

Magnesium sulfate
Loss: 0.68

further syntheses appendant to step 5:
appendant to Oxime (Substrate):
Washing water (as Water separately)
Loss: 0.00

step 2 (Route A 2):
Washing water (as Water separately)
Loss: 0.00

NaOH 1M
Loss: 0.67

Hydrochloric acid (37%aq)
Loss: 0.67

Dichloromethane
Loss: 18.06
Recoverable thereof: 14.45

Magnesium sulfate
Loss: 0.27

step 1 (Route A 1):
Washing water (as Water separately)
Loss: 0.00

E/Route A:
Solvents(31.42(17.16%) of 183.1):
step 6 (Route A):
Water
Loss: 2.31

EtOH

Loss: 1.21
Recoverable thereof: 0.97

step 5 (Route A 5):
Dichloromethane
Loss: 20.19
Recoverable thereof: 16.15

further syntheses appendant to step 5:
appendant to Oxime (Substrate):
Ethanol
Loss: 1.87

Water
Loss: 3.72

step 4 (Route A 4):
Acetonitrile
Loss: 2.12
Recoverable thereof: 1.70

E/Route A:
Substrates(3.83(2.09%) of 183.1):
step 6 (Route A):
Potassium hydroxide 85%
Excess: 0.05
(*Utilized mass (pure): 0.57*)
(*Converted mass: 0.52*)

step 5 (Route A 5):
Oxime
Excess: 0.46
(*Utilized mass (pure): 1.37*)
(*Converted mass: 0.91*)

NaOCl 10%
Excess: 1.53
(*Utilized mass (pure): 2.03*)
(*Converted mass: 0.50*)

further syntheses appendant to step 5:

```
    appendant to Oxime (Substrate):
        Hydroxylamine Hydrochloride
            Excess:                          0.15
          (*Utilized mass (pure):            0.89*)
          (*Converted mass:                  0.74*)

        Sodium carbonate
            Excess:                          0.11
          (*Utilized mass (pure):            0.68*)
          (*Converted mass:                  0.57*)

step 4 (Route A 4):
    Sodium acetate
        Excess:                          0.11
      (*Utilized mass (pure):            1.30*)
      (*Converted mass:                  1.18*)

step 2 (Route A 2):
    Nitric acid 65%
        Excess:                          1.28
      (*Utilized mass (pure):            3.91*)
      (*Converted mass:                  2.63*)

step 1 (Route A 1):
    Thionyl chloride
        Excess:                          0.11
      (*Utilized mass (pure):            6.65*)
      (*Converted mass:                  6.54*)

    Pyridine
        Excess:                          0.02
      (*Utilized mass (pure):            4.37*)
      (*Converted mass:                  4.35*)


E/Route A:
By-products( 8.16(4.45%) of 183.1 ):
step 6 (Route A):
    Unknown by-products:
        Loss:                          0.03
```

```
step 5 (Route A 5):
    Unknown by-products:
        Loss:                           0.83

further syntheses appendant to step 5:
    appendant to Oxime (Substrate):
        Unknown by-products:
            Loss:                           0.13

step 4 (Route A 4):
    Unknown by-products:
        Loss:                           0.13

step 3 (Route A 3):
    Unknown by-products:
        Loss:                           0.13

step 2 (Route A 2):
    Unknown by-products:
        Loss:                           1.16

step 1 (Route A 1):
    Pentaerythrityl tetrachloride
        Loss:                           0.78

    Unknown by-products:
        Loss:                           4.97


E/Route A:
Coupled products( 11.19(6.11%) of 183.1 ):
step 6 (Route A):
    Potassium acetate
        Loss:                         0.89
      (*Total mass:                   0.89*)

step 5 (Route A 5):
    NaCl
        Loss:                           0.27
```

```
      (*Total mass:                       0.27*)

    Water
        Loss:                             0.08
      (*Total mass:                       0.08*)

further syntheses appendant to step 5:
    appendant to Oxime (Substrate):
        Carbon dioxide
            Loss:                             0.22
          (*Total mass:                       0.22*)

        Sodium chloride
            Loss:                             0.59
          (*Total mass:                       0.59*)

        Water
            Loss:                             0.27
          (*Total mass:                       0.27*)

step 4 (Route A 4):
    NaCl
        Loss:                             0.79
      (*Total mass:                       0.79*)

step 3 (Route A 3):
    CO2
        Loss:                             0.32
      (*Total mass:                       0.32*)

    Hydrogen chloride
        Loss:                             0.26
      (*Total mass:                       0.26*)

step 2 (Route A 2):
    NOx
        Loss:                             1.44
      (*Total mass:                       1.44*)

    Water
        Loss:                             0.42
```

```
      (*Total mass:                       0.42*)

step 1 (Route A 1):
    Pyridine
        Loss:                             2.48
      (*Total mass:                       2.48*)

    Sulfur dioxide
        Loss:                             2.01
      (*Total mass:                       2.01*)

    Hydrogen chloride
        Loss:                             1.14
      (*Total mass:                       1.14*)
```

Environmental Impact of Waste (EI_out) of Route A: 696.65 PEI units/kg product

```
According to synthetic step:
step 6                    ( 90.50 (12.99%) of 696.65)
step 5                    (319.41 (45.85%) of 696.65)
step 4                    ( 15.16 ( 2.18%) of 696.65)
step 3                    (  2.92 ( 0.42%) of 696.65)
step 2                    (183.85 (26.39%) of 696.65)
step 1                    ( 84.80 (12.17%) of 696.65)

According to substance category:
Sewage/Water              ( 76.07 (10.92%) of 696.65)
Auxiliaries (isolation)   (333.38 (47.85%) of 696.65)
Solvents                  (161.54 (23.19%) of 696.65)
Substrates                ( 21.64 ( 3.11%) of 696.65)
By-products               ( 47.90 ( 6.88%) of 696.65)
Coupled products          ( 54.70 ( 7.85%) of 696.65)
```

EI_out/Route A:
Sewage/Water(76.07(10.92%) of 696.65):

```
step 6 (Route A):
    out of solvent EtOH
        Water
            (Q=1)
            Mass:                           2.42 -->   2.42

    out of auxiliary material Hydrochloric acid (37%aq)
        Water
            (Q=1)
            Mass:                           0.61 -->   0.61

step 5 (Route A 5):
    out of substrate NaOCl 10%
        Water
            (Q=1)
            Mass:                            18.29 -->    18.29

    out of auxiliary material NaCl; Sodium chloride (aq, conc.)
        Water
            (Q=1)
            Mass:                              6.10 -->     6.10
```

```
further syntheses appendant to step 5:
    appendant to Oxime (Substrate):
        out of auxiliary material Washing water (as Water separately)
            Water
                (Q=1)
                Mass:                            5.35 -->     5.35

step 2 (Route A 2):
    out of substrate Nitric acid 65%
        Water
            (Q=1)
            Mass:                             2.11 -->     2.11

    out of auxiliary material Washing water (as Water separately)
        Water
            (Q=1)
            Mass:                            12.12 -->    12.12

    out of auxiliary material NaOH 1M
        Water
            (Q=1)
            Mass:                            16.00 -->    16.00

    out of auxiliary material Hydrochloric acid (37%aq)
        Water
            (Q=1)
            Mass:                             1.14 -->     1.14

step 1 (Route A 1):
    out of auxiliary material Washing water (as Water separately)
        Water
            (Q=1)
            Mass:                            11.96 -->    11.96
```

EI_out/Route A:
Auxiliaries (isolation)(333.38(47.85%) of 696.65):

```
step 6 (Route A):
    Hydrochloric acid (37%aq)
        (Q=5.0; Q_human tox.(50.0%)=6; Q_ecotox.(50.0%)=4)
        Loss:                           0.36 -->   1.79
```

```
    Dichloromethane
        (Q=6.7; Q_human tox.(33.3%)=3; Q_chron. tox.(33.3%)=10;
        Q_ecotox.(33.3%)=7)
        Loss:                          11.49 -->  76.59
        Recoverable thereof:            9.19 -->  61.27

step 5 (Route A 5):
    Dichloromethane
        (Q=6.7; Q_human tox.(33.3%)=3; Q_chron. tox.(33.3%)=10;
        Q_ecotox.(33.3%)=7)
        Loss:                            17.95 -->   119.64
        Recoverable thereof:             14.36 -->    95.72

    NaCl; Sodium chloride (aq, conc.)
        (Q=2.5; Q_human tox.(50.0%)=1; Q_ecotox.(50.0%)=4)
        Loss:                              2.03 -->     5.08

    Magnesium sulfate
        (Q=3.0; Q_human tox.(50.0%)=2; Q_ecotox.(50.0%)=4)
        Loss:                              0.68 -->     2.03

further syntheses appendant to step 5:
    appendant to Oxime (Substrate):
        Washing water (as Water separately)
            (Q=1)
            Loss:                              0.00 -->     0.00

step 2 (Route A 2):
    Washing water (as Water separately)
        (Q=1)
        Loss:                              0.00 -->     0.00

    NaOH 1M
        (Q=5.5; Q_human tox.(50.0%)=7; Q_ecotox.(50.0%)=4)
        Loss:                              0.67 -->     3.67

    Hydrochloric acid (37%aq)
        (Q=5.0; Q_human tox.(50.0%)=6; Q_ecotox.(50.0%)=4)
        Loss:                              0.67 -->     3.33
```

```
    Dichloromethane
        (Q=6.7; Q_human tox.(33.3%)=3; Q_chron. tox.(33.3%)=10;
        Q_ecotox.(33.3%)=7)
        Loss:                           18.06 -->   120.42
        Recoverable thereof:            14.45 -->    96.34

    Magnesium sulfate
        (Q=3.0; Q_human tox.(50.0%)=2; Q_ecotox.(50.0%)=4)
        Loss:                            0.27 -->     0.82

step 1 (Route A 1):
    Washing water (as Water separately)
        (Q=1)
        Loss:                            0.00 -->     0.00
```

EI_out/Route A:
Solvents(161.54(23.19%) of 696.65):

```
step 6 (Route A):
    Water
        (Q=1)
        Loss:                           2.31 -->   2.31

    EtOH
        (Q=3.0; Q_human tox.(50.0%)=2; Q_ecotox.(50.0%)=4)
        Loss:                           1.21 -->   3.63
        Recoverable thereof:            0.97 -->   2.90

step 5 (Route A 5):
    Dichloromethane
        (Q=6.7; Q_human tox.(33.3%)=3; Q_chron. tox.(33.3%)=10;
        Q_ecotox.(33.3%)=7)
        Loss:                           20.19 -->   134.60
        Recoverable thereof:            16.15 -->   107.68

further syntheses appendant to step 5:
    appendant to Oxime (Substrate):
        Ethanol
            (Q=3.0; Q_human tox.(50.0%)=2; Q_ecotox.(50.0%)=4)
            Loss:                            1.87 -->     5.60

        Water
```

```
            (Q=1)
            Loss:                            3.72 -->     3.72

step 4 (Route A 4):
    Acetonitrile
        (Q=5.5; Q_human tox.(50.0%)=4; Q_ecotox.(50.0%)=7)
        Loss:                             2.12 -->    11.68
        Recoverable thereof:              1.70 -->     9.34
```
EI_out/Route A:
Substrates(21.64(3.11%) of 696.65):
```
step 6 (Route A):
    Potassium hydroxide 85%
        (Q=5.5; Q_human tox.(50.0%)=7; Q_ecotox.(50.0%)=4)
        Excess:                         0.05 -->   0.30

step 5 (Route A 5):
    Oxime
        (Q=1)
        Excess:                           0.46 -->     0.46

    NaOCl 10%
        (Q=7.7; Q_human tox.(33.3%)=6; Q_chron. tox.(33.3%)=10;
        Q_ecotox.(33.3%)=7)
        Excess:                           1.53 -->    11.72

further syntheses appendant to step 5:
    appendant to Oxime (Substrate):
        Hydroxylamine Hydrochloride
            (Q=7.0; Q_human tox.(50.0%)=4; Q_ecotox.(50.0%)=10)
            Excess:                           0.15 -->     1.05

        Sodium carbonate
            (Q=4.5; Q_human tox.(50.0%)=5; Q_ecotox.(50.0%)=4)
            Excess:                           0.11 -->     0.51

step 4 (Route A 4):
    Sodium acetate
        (Q=4.5; Q_human tox.(50.0%)=5; Q_ecotox.(50.0%)=4)
        Excess:                           0.11 -->     0.52

step 2 (Route A 2):
```

```
    Nitric acid 65%
        (Q=5.0; Q_human tox.(50.0%)=6; Q_ecotox.(50.0%)=4)
        Excess:                          1.28 -->     6.41

step 1 (Route A 1):
    Thionyl chloride
        (Q=5.0; Q_human tox.(50.0%)=6; Q_ecotox.(50.0%)=4)
        Excess:                          0.11 -->     0.54

    Pyridine
        (Q=7.3; Q_human tox.(33.3%)=5; Q_chron. tox.(33.3%)=10;
        Q_ecotox.(33.3%)=7)
        Excess:                          0.02 -->     0.14
```

EI_out/Route A:
By-products(47.9(6.88%) of 696.65):

```
step 6 (Route A):
    Unknown by-products:
        (Q=2.2 Calculated from the weightings of the substrates)
        Loss:                          0.03 -->   0.07

step 5 (Route A 5):
    Unknown by-products:
        (Q=2.3 Calculated from the weightings of the substrates)
        Loss:                          0.83 -->     1.90

further syntheses appendant to step 5:
    appendant to Oxime (Substrate):
        Unknown by-products:
            (Q=5.0 Calculated from the weightings of the substrates)
            Loss:                              0.13 -->     0.64

step 4 (Route A 4):
    Unknown by-products:
        (Q=6.4 Calculated from the weightings of the substrates)
        Loss:                          0.13 -->     0.82

step 3 (Route A 3):
    Unknown by-products:
        (Q=10.0 Calculated from the weightings of the substrates)
        Loss:                          0.13 -->     1.29
```

```
step 2 (Route A 2):
    Unknown by-products:
        (Q=7.2 Calculated from the weightings of the substrates)
        Loss:                            1.16 -->     8.29

step 1 (Route A 1):
    Pentaerythrityl tetrachloride
        (Q=8.0; Q_human tox.(33.3%)=4; Q_chron. tox.(33.3%)=10;
        Q_ecotox.(33.3%)=10)
        Loss:                            0.78 -->     6.27

    Unknown by-products:
        (Q=5.8 Calculated from the weightings of the substrates)
        Loss:                            4.97 -->    28.62
```

EI_out/Route A:
Coupled products(54.7(7.85%) of 696.65):

```
step 6 (Route A):
    Potassium acetate
        (Q=2.5; Q_human tox.(50.0%)=1; Q_ecotox.(50.0%)=4)
        Loss:                           0.89 -->   2.22

step 5 (Route A 5):
    NaCl
        (Q=2.5; Q_human tox.(50.0%)=1; Q_ecotox.(50.0%)=4)
        Loss:                            0.27 -->     0.67

    Water
        (Q=1)
        Loss:                            0.08 -->     0.08

further syntheses appendant to step 5:
    appendant to Oxime (Substrate):
        Carbon dioxide
            (Q=1.0; Q_human tox.(100.0%)=1)
            Loss:                            0.22 -->     0.22

        Sodium chloride
            (Q=2.5; Q_human tox.(50.0%)=1; Q_ecotox.(50.0%)=4)
            Loss:                            0.59 -->     1.48
```

```
        Water
            (Q=1)
            Loss:                            0.27 -->     0.27

step 4 (Route A 4):
    NaCl
        (Q=2.5; Q_human tox.(50.0%)=1; Q_ecotox.(50.0%)=4)
        Loss:                            0.79 -->     1.98

step 3 (Route A 3):
    CO2
        (Q=1.0; Q_human tox.(100.0%)=1)
        Loss:                            0.32 -->     0.32

    Hydrogen chloride
        (Q=5.0; Q_human tox.(50.0%)=6; Q_ecotox.(50.0%)=4)
        Loss:                            0.26 -->     1.31

step 2 (Route A 2):
    NOx
        (Q=6.3; Q_human tox.(33.3%)=5; Q_chron. tox.(33.3%)=10;
        Q_ecotox.(33.3%)=4)
        Loss:                            1.44 -->     9.13

    Water
        (Q=1)
        Loss:                            0.42 -->     0.42

step 1 (Route A 1):
    Pyridine
        (Q=7.3; Q_human tox.(33.3%)=5; Q_chron. tox.(33.3%)=10;
        Q_ecotox.(33.3%)=7)
        Loss:                            2.48 -->    18.17

    Sulfur dioxide
        (Q=6.3; Q_human tox.(33.3%)=5; Q_chron. tox.(33.3%)=10;
        Q_ecotox.(33.3%)=4)
        Loss:                            2.01 -->    12.71

    Hydrogen chloride
```

```
(Q=5.0; Q_human tox.(50.0%)=6; Q_ecotox.(50.0%)=4)
Loss:                                1.14 -->     5.71
```

Environmental Impact of Feedstock (EI_in) of Route A: 248.49 PEI units/kg product

```
According to synthetic step:
step 6                    ( 32.19 (10.79%) of 298.49)
step 5                    (126.33 (42.32%) of 298.49)
step 4                    (  7.73 ( 2.59%) of 298.49)
step 3                    less than 0.1%
step 2                    ( 78.53 (26.31%) of 298.49)
step 1                    ( 53.71 (17.99%) of 298.49)

According to substance category:
Sewage/Water              ( 76.07 (25.49%) of 298.49)
Auxiliaries (isolation)   (102.31 (34.28%) of 298.49)
Solvents                  ( 57.39 (19.23%) of 298.49)
Substrates                ( 61.83 (20.72%) of 298.49)
```

Route A/EI_in:

Sewage/Water(76.07(25.49%) of 298.49):

```
step 6 (Route A):
    out of solvent EtOH
        Water
            (Q=1.0; Q_claiming of ressources(100.0%)=1)
            Mass:                           2.42 -->   2.42

    out of auxiliary material Hydrochloric acid (37%aq)
        Water
            (Q=1.0; Q_claiming of ressources(100.0%)=1)
            Mass:                           0.61 -->   0.61

step 5 (Route A 5):
    out of substrate NaOCl 10%
        Water
            (Q=1.0; Q_claiming of ressources(100.0%)=1)
            Mass:                            18.29 -->    18.29

    out of auxiliary material NaCl; Sodium chloride (aq, conc.)
        Water
            (Q=1.0; Q_claiming of ressources(100.0%)=1)
            Mass:                             6.10 -->     6.10

further syntheses appendant to step 5:
```

```
    appendant to Oxime (Substrate):
        out of auxiliary material Washing water (as Water separately)
            Water
                (Q=1.0; Q_claiming of ressources(100.0%)=1)
                Mass:                            5.35 -->     5.35

step 2 (Route A 2):
    out of substrate Nitric acid 65%
        Water
            (Q=1.0; Q_claiming of ressources(100.0%)=1)
            Mass:                             2.11 -->     2.11

    out of auxiliary material Washing water (as Water separately)
        Water
            (Q=1.0; Q_claiming of ressources(100.0%)=1)
            Mass:                            12.12 -->    12.12

    out of auxiliary material NaOH 1M
        Water
            (Q=1.0; Q_claiming of ressources(100.0%)=1)
            Mass:                            16.00 -->    16.00

    out of auxiliary material Hydrochloric acid (37%aq)
        Water
            (Q=1.0; Q_claiming of ressources(100.0%)=1)
            Mass:                             1.14 -->     1.14

step 1 (Route A 1):
    out of auxiliary material Washing water (as Water separately)
        Water
            (Q=1.0; Q_claiming of ressources(100.0%)=1)
            Mass:                            11.96 -->    11.96
```

Route A/EI_in:
Auxiliaries (isolation)(102.31(34.28%) of 298.49):

```
step 6 (Route A):
    Hydrochloric acid (37%aq)
        (Q=2.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=3)
        Mass:                           0.36 -->   0.72

    Dichloromethane
```

```
        (Q=2.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=3)
        Mass:                          11.49 -->  22.98
        Recoverable thereof:            9.19 -->  18.38

step 5 (Route A 5):
    Dichloromethane
        (Q=2.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=3)
        Mass:                           17.95 -->    35.89
        Recoverable thereof:            14.36 -->    28.71

    NaCl; Sodium chloride (aq, conc.)
        (Q=1.0; Q_claiming of ressources(100.0%)=1)
        Mass:                            2.03 -->     2.03

    Magnesium sulfate
        (Q=2.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=3)
        Mass:                            0.68 -->     1.35

further syntheses appendant to step 5:
    appendant to Oxime (Substrate):
        Washing water (as Water separately)
            (Q=1.0; Q_claiming of ressources(100.0%)=1)
            Mass:                            0.00 -->     0.00

step 2 (Route A 2):
    Washing water (as Water separately)
        (Q=1.0; Q_claiming of ressources(100.0%)=1)
        Mass:                            0.00 -->     0.00

    NaOH 1M
        (Q=2.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=3)
        Mass:                            0.67 -->     1.33

    Hydrochloric acid (37%aq)
        (Q=2.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=3)
        Mass:                            0.67 -->     1.33

    Dichloromethane
        (Q=2.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=3)
        Mass:                           18.06 -->    36.13
        Recoverable thereof:            14.45 -->    28.90
```

```
    Magnesium sulfate
        (Q=2.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=3)
        Mass:                            0.27 -->     0.55

step 1 (Route A 1):
    Washing water (as Water separately)
        (Q=1.0; Q_claiming of ressources(100.0%)=1)
        Mass:                            0.00 -->     0.00
```

Route A/EI_in:
Solvents(57.39(19.23%) of 298.49):

```
step 6 (Route A):
    Water
        (Q=1.0; Q_claiming of ressources(100.0%)=1)
        Mass:                          2.31 -->   2.31

    EtOH
        (Q=1.5; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=2)
        Mass:                          1.21 -->   1.81
        Recoverable thereof:           0.97 -->   1.45

step 5 (Route A 5):
    Dichloromethane
        (Q=2.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=3)
        Mass:                           20.19 -->    40.38
        Recoverable thereof:            16.15 -->    32.30

further syntheses appendant to step 5:
    appendant to Oxime (Substrate):
        Ethanol
            (Q=1.5; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=2)
            Mass:                            1.87 -->     2.80

        Water
            (Q=1.0; Q_claiming of ressources(100.0%)=1)
            Mass:                            3.72 -->     3.72

step 4 (Route A 4):
    Acetonitrile
        (Q=3.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=5)
```

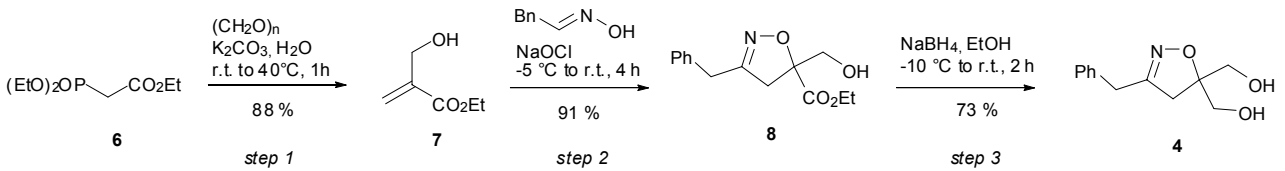
```
        Mass:                             2.12 -->     6.37
        Recoverable thereof:              1.70 -->     5.10
```

Route A/EI_in:
Substrates(61.83(20.72%) of 298.49):

```
step 6 (Route A):
    Diacetoxyisoxazoline imported from Route A 5
        The substrate is imported. Appropriate quantities are attributed
to the precedent syntheses: see there.

    Potassium hydroxide 85%
        (Q=2.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=3)
        Mass:                           0.57 -->   1.14

step 5 (Route A 5):
    Diacetoxyisobutene imported from Route A 4
        The substrate is imported. Appropriate quantities are attributed
to the precedent syntheses: see there.

    Oxime imported from Oxime
        The substrate is imported. Appropriate quantities are attributed
to the precedent syntheses: see there.

    NaOCl 10%
        (Q=2.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=3)
        Mass:                             2.03 -->     4.06

further syntheses appendant to step 5:
    appendant to Oxime (Substrate):
        Phenylacetaldehyde
            (Q=2.0; Q_claiming of ressources(50.0%)=2; Q_risk(50.0%)=2)
            Mass:                           1.28 -->     2.57

        Hydroxylamine Hydrochloride
            (Q=3.5; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=6)
            Mass:                           0.89 -->     3.12

        Sodium carbonate
            (Q=1.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=1)
            Mass:                           0.68 -->     0.68
```

```
step 4 (Route A 4):
    3-Chloro-2-chloromethyl-1-propene imported from Route A 3
        The substrate is imported. Appropriate quantities are attributed
to the precedent syntheses: see there.

    Sodium acetate
        (Q=1.0; Q_claiming of ressources(100.0%)=1)
        Mass:                            1.30 -->     1.30

step 3 (Route A 3):
    Trichloroacid imported from Route A 2
        The substrate is imported. Appropriate quantities are attributed
to the precedent syntheses: see there.

step 2 (Route A 2):
    Tricloro imported from Route A 1
        The substrate is imported. Appropriate quantities are attributed
to the precedent syntheses: see there.

    Nitric acid 65%
        (Q=2.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=3)
        Mass:                            3.91 -->     7.83

step 1 (Route A 1):
    Pentaerythritol
        (Q=1.0; Q_claiming of ressources(100.0%)=1)
        Mass:                            2.49 -->     2.49

    Thionyl chloride
        (Q=4.5; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=8)
        Mass:                            6.65 -->    29.91

    Pyridine
        (Q=2.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=3)
        Mass:                            4.37 -->     8.73
```

Route B. Alternative route (this paper)



Atom Selectivity (AS) of Route B

Route B:

step 3 (Route B):

AS (of the following synthesis):56.5%, AS (of the synthesis sequence):24.5%

1 Isoxazoline carbethoxy + 1 NaBH4 + 1 Hydrochloric acid (37%aq) + 3 Water ---> 1 Isoxazoline diol + 1 Boric acid + 1 NaCl + 2 Hydrogen + 1 EtOH

step 2 (Route B 2):

AS (of the following synthesis):77.5%, AS (of the synthesis sequence):33.9%

1 Hydroxymethylacrylate + 1 Oxime + 1 NaOCl 10% ---> 1 Isoxazoline carbethoxy + 1 NaCl + 1 Water

further syntheses appendant to step 2:

appendant to Oxime (Substrate):

AS (of the following synthesis):55.7%, AS (of the synthesis sequence):55.7%

2 Phenylacetaldehyde + 2 Hydroxylamine Hydrochloride + 1 Sodium carbonate ---> 2 Oxime + 1 Carbon dioxide + 2 Sodium chloride + 3 Water

step 1 (Route B 1):

AS (of the following synthesis):28.4%, AS (of the synthesis sequence):28.4%

1 (EtO)2POCH2COOEt + 2 (CH2O)n + 1 K2CO3 + 2 Water ---> 1 Hydroxymethylacrylate + 1 KHCO3 + 1 KH2PO4 + 2 EtOH

E-factor of Route B: 101.98 kg waste/kg product

```
According to synthetic step:
step 3                    (15.90 (15.59%) of 101.98)
step 2                    (59.18 (58.03%) of 101.98)
step 1                    (26.90 (26.38%) of 101.98)

According to substance category:
Sewage/Water              (25.48 (24.98%) of 101.98)
Auxiliaries (isolation)   (41.49 (40.68%) of 101.98)
Solvents                  (26.29 (25.77%) of 101.98)
Substrates                ( 3.09 ( 3.03%) of 101.98)
By-products               ( 1.38 ( 1.35%) of 101.98)
Coupled products          ( 4.23 ( 4.15%) of 101.98)
```

Route B/E:
Sewage/Water(25.48(24.98%) of 101.98):

```
step 3 (Route B):
    out of substrate Hydrochloric acid (37%aq)
        Water
            Mass:                           0.14

    out of solvent EtOH
        Water
            Mass:                           6.52

step 2 (Route B 2):
    out of substrate NaOCl 10%
        Water
            Mass:                             8.76

    out of auxiliary material Washing water (as Water separately)
        Water
            Mass:                             4.54

    out of auxiliary material NaCl; Sodium chloride (aq, conc.)
        Water
            Mass:                             0.82

further syntheses appendant to step 2:
    appendant to Oxime (Substrate):
```

out of auxiliary material Washing water (as Water separately)
Water
Mass: 3.72

step 1 (Route B 1):
out of catalyst H3PO4 1N
Water
Mass: 0.22

out of auxiliary material NaCl; Sodium chloride (aq, conc.)
Water
Mass: 0.77

Route B/E:
Auxiliaries (isolation)(41.49(40.68%) of 101.98):
step 3 (Route B):
Dichloromethane
Loss: 4.51
Recoverable thereof: 3.61

step 2 (Route B 2):
Dichloromethane
Loss: 22.55
Recoverable thereof: 18.04

Washing water (as Water separately)
Loss: 0.00

NaCl; Sodium chloride (aq, conc.)
Loss: 0.27

Magnesium sulfate
Loss: 0.41

further syntheses appendant to step 2:
appendant to Oxime (Substrate):
Washing water (as Water separately)
Loss: 0.00

step 1 (Route B 1):
Et2O

```
        Loss:                            13.06
        Recoverable thereof:             10.45

    NaCl; Sodium chloride (aq, conc.)
        Loss:                             0.26

    Na2SO4
        Loss:                             0.43
```

Route B/E:
Solvents(26.29(25.77%) of 101.98):

```
step 3 (Route B):
    EtOH
        Loss:                         3.26
        Recoverable thereof:          2.61

step 2 (Route B 2):
    Dichloromethane
        Loss:                            12.03
        Recoverable thereof:              9.62

further syntheses appendant to step 2:
    appendant to Oxime (Substrate):
        Ethanol
            Loss:                             1.30

        Water
            Loss:                             2.58

step 1 (Route B 1):
    Water
        Loss:                             7.12
```

Route B/E:
Substrates(3.09(3.03%) of 101.98):

```
step 3 (Route B):
    NaBH4
        Excess:                       0.00
      (*Utilized mass (pure):         0.23*)
      (*Converted mass:               0.23*)
```

```
    Hydrochloric acid (37%aq)
        Excess:                          0.00
      (*Utilized mass (pure):            0.23*)
      (*Converted mass:                  0.22*)

    Water
        Excess:                          0.03
      (*Utilized mass (pure):            0.37*)
      (*Converted mass:                  0.33*)

step 2 (Route B 2):
    Oxime
        Excess:                            0.03
      (*Utilized mass (pure):              0.95*)
      (*Converted mass:                    0.92*)

    NaOCl 10%
        Excess:                            0.47
      (*Utilized mass (pure):              0.97*)
      (*Converted mass:                    0.51*)

further syntheses appendant to step 2:
    appendant to Oxime (Substrate):
        Hydroxylamine Hydrochloride
            Excess:                            0.10
          (*Utilized mass (pure):              0.62*)
          (*Converted mass:                    0.52*)

        Sodium carbonate
            Excess:                            0.08
          (*Utilized mass (pure):              0.47*)
          (*Converted mass:                    0.39*)

step 1 (Route B 1):
    (CH2O)n
        Excess:                            2.27
      (*Utilized mass (pure):              2.73*)
      (*Converted mass:                    0.46*)

    K2CO3
        Excess:                            0.10
```

```
      (*Utilized mass (pure):             1.17*)
      (*Converted mass:                   1.07*)

    Water
        Excess:                           0.01
      (*Utilized mass (pure):             0.28*)
      (*Converted mass:                   0.28*)
```

Route B/E:
By-products(1.38(1.35%) of 101.98):

```
step 3 (Route B):
    Unknown by-products:
        Loss:                           0.64

step 2 (Route B 2):
    Unknown by-products:
        Loss:                             0.22

further syntheses appendant to step 2:
    appendant to Oxime (Substrate):
        Unknown by-products:
            Loss:                             0.09

step 1 (Route B 1):
    Unknown by-products:
        Loss:                             0.43
```

Route B/E:
Coupled products(4.23(4.15%) of 101.98):

```
step 3 (Route B):
    Boric acid
        Loss:                           0.28
      (*Total mass:                     0.28*)

    NaCl
        Loss:                           0.26
      (*Total mass:                     0.26*)

    Hydrogen
        Loss:                           0.02
      (*Total mass:                     0.02*)
```

```
    EtOH
        Loss:                           0.21
      (*Total mass:                     0.21*)

step 2 (Route B 2):
    NaCl
        Loss:                             0.36
      (*Total mass:                       0.36*)

    Water
        Loss:                             0.11
      (*Total mass:                       0.11*)

further syntheses appendant to step 2:
    appendant to Oxime (Substrate):
        Carbon dioxide
            Loss:                             0.16
          (*Total mass:                       0.16*)

        Sodium chloride
            Loss:                             0.41
          (*Total mass:                       0.41*)

        Water
            Loss:                             0.19
          (*Total mass:                       0.19*)

step 1 (Route B 1):
    KHCO3
        Loss:                             0.68
      (*Total mass:                       0.68*)

    KH2PO4
        Loss:                             0.93
      (*Total mass:                       0.93*)

    EtOH
        Loss:                             0.63
      (*Total mass:                       0.63*)
```

Environmental Impact of Waste (EI_out) of Route B: 401.63 PEI units/kg product

```
According to synthetic step:
step 3                    ( 49.88 (12.42%) of 401.63)
step 2                    (264.77 (65.92%) of 401.63)
step 1                    ( 86.98 (21.66%) of 401.63)

According to substance category:
Sewage/Water              ( 25.48 ( 6.34%) of 401.63)
Auxiliaries (isolation)   (230.79 (57.46%) of 401.63)
Solvents                  (103.56 (25.78%) of 401.63)
Substrates                ( 21.07 ( 5.25%) of 401.63)
By By-products            (  5.35 ( 1.33%) of 401.63)
Coupled products          ( 15.23 ( 3.79%) of 401.63)
```

Route B/EI_out:
Sewage/Water(25.48(6.34%) of 401.63):

```
step 3 (Route B):
    out of substrate Hydrochloric acid (37%aq)
        Water
            (Q=1)
            Mass:                           0.14 -->   0.14

    out of solvent EtOH
        Water
            (Q=1)
            Mass:                           6.52 -->   6.52

step 2 (Route B 2):
    out of substrate NaOCl 10%
        Water
            (Q=1)
            Mass:                             8.76 -->     8.76

    out of auxiliary material Washing water (as Water separately)
        Water
            (Q=1)
            Mass:                             4.54 -->     4.54

    out of auxiliary material NaCl; Sodium chloride (aq, conc.)
        Water
```

```
            (Q=1)
            Mass:                            0.82 -->     0.82

further syntheses appendant to step 2:
    appendant to Oxime (Substrate):
        out of auxiliary material Washing water (as Water separately)
            Water
                (Q=1)
                Mass:                            3.72 -->     3.72

step 1 (Route B 1):
    out of catalyst H3PO4 1N
        Water
            (Q=1)
            Mass:                            0.22 -->     0.22

    out of auxiliary material NaCl; Sodium chloride (aq, conc.)
        Water
            (Q=1)
            Mass:                            0.77 -->     0.77
```

Route B/EI_out:
Auxiliaries (isolation)(230.79(57.46%) of 401.63):

```
step 3 (Route B):
    Dichloromethane
        (Q=6.7; Q_human tox.(33.3%)=3; Q_chron. tox.(33.3%)=10;
        Q_ecotox.(33.3%)=7)
        Loss:                           4.51 -->  30.07
        Recoverable thereof:            3.61 -->  24.05

step 2 (Route B 2):
    Dichloromethane
        (Q=6.7; Q_human tox.(33.3%)=3; Q_chron. tox.(33.3%)=10;
        Q_ecotox.(33.3%)=7)
        Loss:                            22.55 -->   150.33
        Recoverable thereof:             18.04 -->   120.26

    Washing water (as Water separately)
        (Q=1)
        Loss:                             0.00 -->     0.00
```

```
    NaCl; Sodium chloride (aq, conc.)
        (Q=2.5; Q_human tox.(50.0%)=1; Q_ecotox.(50.0%)=4)
        Loss:                              0.27 -->     0.68

    Magnesium sulfate
        (Q=3.0; Q_human tox.(50.0%)=2; Q_ecotox.(50.0%)=4)
        Loss:                              0.41 -->     1.23

further syntheses appendant to step 2:
    appendant to Oxime (Substrate):
        Washing water (as Water separately)
            (Q=1)
            Loss:                              0.00 -->     0.00

step 1 (Route B 1):
    Et2O
        (Q=3.5; Q_human tox.(50.0%)=3; Q_ecotox.(50.0%)=4)
        Loss:                             13.06 -->    45.72
        Recoverable thereof:              10.45 -->    36.57

    NaCl; Sodium chloride (aq, conc.)
        (Q=2.5; Q_human tox.(50.0%)=1; Q_ecotox.(50.0%)=4)
        Loss:                              0.26 -->     0.64

    Na2SO4
        (Q=5.0; Q_human tox.(50.0%)=6; Q_ecotox.(50.0%)=4)
        Loss:                              0.43 -->     2.13
```

Route B/EI_out:
Solvents(103.56(25.78%) of 401.63):

```
step 3 (Route B):
    EtOH
        (Q=3.0; Q_human tox.(50.0%)=2; Q_ecotox.(50.0%)=4)
        Loss:                             3.26 -->   9.79
        Recoverable thereof:              2.61 -->   7.83

step 2 (Route B 2):
    Dichloromethane
        (Q=6.7; Q_human tox.(33.3%)=3; Q_chron. tox.(33.3%)=10;
```

```
        Q_ecotox.(33.3%)=7)
        Loss:                           12.03 -->    80.18
        Recoverable thereof:             9.62 -->    64.14

further syntheses appendant to step 2:
    appendant to Oxime (Substrate):
        Ethanol
            (Q=3.0; Q_human tox.(50.0%)=2; Q_ecotox.(50.0%)=4)
            Loss:                            1.30 -->     3.89

        Water
            (Q=1)
            Loss:                            2.58 -->     2.58

step 1 (Route B 1):
    Water
        (Q=1)
        Loss:                            7.12 -->     7.12
```

Route B/EI_out:
Substrates(21.07(5.25%) of 401.63):

```
step 3 (Route B):
    NaBH4
        (Q=7.5; Q_human tox.(50.0%)=8; Q_ecotox.(50.0%)=7)
        Excess:                         0.00 -->   0.00

    Hydrochloric acid (37%aq)
        (Q=5.0; Q_human tox.(50.0%)=6; Q_ecotox.(50.0%)=4)
        Excess:                         0.00 -->   0.00

    Water
        (Q=1)
        Excess:                         0.03 -->   0.03

step 2 (Route B 2):
    Oxime
        (Q=1)
        Excess:                          0.03 -->     0.03

    NaOCl 10%
```

```
        (Q=7.7; Q_human tox.(33.3%)=6; Q_chron. tox.(33.3%)=10;
        Q_ecotox.(33.3%)=7)
        Excess:                          0.47 -->     3.58

further syntheses appendant to step 2:
    appendant to Oxime (Substrate):
        Hydroxylamine Hydrochloride
            (Q=7.0; Q_human tox.(50.0%)=4; Q_ecotox.(50.0%)=10)
            Excess:                          0.10 -->     0.73

        Sodium carbonate
            (Q=4.5; Q_human tox.(50.0%)=5; Q_ecotox.(50.0%)=4)
            Excess:                          0.08 -->     0.36

step 1 (Route B 1):
    (CH2O)n
        (Q=7.0; Q_human tox.(33.3%)=4; Q_chron. tox.(33.3%)=10;
        Q_ecotox.(33.3%)=7)
        Excess:                          2.27 -->    15.88

    K2CO3
        (Q=4.5; Q_human tox.(50.0%)=5; Q_ecotox.(50.0%)=4)
        Excess:                          0.10 -->     0.45

    Water
        (Q=1)
```

Route B/EI_out:
By-products(5.35(1.33%) of 401.63):

```
step 3 (Route B):
    Unknown by-products:
        (Q=2.0 Calculated from the weightings of the substrates)
        Loss:                          0.64 -->   1.29

step 2 (Route B 2):
    Unknown by-products:
        (Q=2.5 Calculated from the weightings of the substrates)
        Loss:                          0.22 -->     0.53

further syntheses appendant to step 2:
```

```
    appendant to Oxime (Substrate):
        Unknown by-products:
            (Q=5.0 Calculated from the weightings of the substrates)
            Loss:                              0.09 -->     0.45

step 1 (Route B 1):
    Unknown by-products:
        (Q=7.2 Calculated from the weightings of the substrates)
        Loss:                              0.43 -->     3.08
```

Route B/EI_out:
Coupled products(15.23(3.79%) of 401.63):

```
step 3 (Route B):
    Boric acid
        (Q=2.5; Q_human tox.(50.0%)=1; Q_ecotox.(50.0%)=4)
        Loss:                           0.28 -->   0.70

    NaCl
        (Q=2.5; Q_human tox.(50.0%)=1; Q_ecotox.(50.0%)=4)
        Loss:                           0.26 -->   0.66

    Hydrogen
        (Q=1)
        Loss:                           0.02 -->   0.02

    EtOH
        (Q=3.0; Q_human tox.(50.0%)=2; Q_ecotox.(50.0%)=4)
        Loss:                           0.21 -->   0.62

step 2 (Route B 2):
    NaCl
        (Q=2.5; Q_human tox.(50.0%)=1; Q_ecotox.(50.0%)=4)
        Loss:                              0.36 -->     0.90

    Water
        (Q=1)
        Loss:                              0.11 -->     0.11

further syntheses appendant to step 2:
    appendant to Oxime (Substrate):
```

```
        Carbon dioxide
            (Q=1.0; Q_human tox.(100.0%)=1)
            Loss:                             0.16 -->     0.16

        Sodium chloride
            (Q=2.5; Q_human tox.(50.0%)=1; Q_ecotox.(50.0%)=4)
            Loss:                             0.41 -->     1.03

        Water
            (Q=1)
            Loss:                             0.19 -->     0.19

step 1 (Route B 1):
    KHCO3
        (Q=5.0; Q_human tox.(50.0%)=6; Q_ecotox.(50.0%)=4)
        Loss:                             0.68 -->     3.40

    KH2PO4
        (Q=6.0; Q_human tox.(50.0%)=5; Q_ecotox.(50.0%)=7)
        Loss:                             0.93 -->     5.55

    EtOH
        (Q=3.0; Q_human tox.(50.0%)=2; Q_ecotox.(50.0%)=4)
        Loss:                             0.63 -->     1.88
```

Environmental Impact of Feedstock (EI_in) Route B: 196.38 PEI units/kg product

```
According to synthetic step:
step 3                   ( 22.35 (11.38%) of 196.38)
step 2                   ( 98.97 (50.39%) of 196.38)
step 1                   ( 75.07 (38.23%) of 196.38)

Main contributions:
Sewage/Water             ( 25.48 (12.97%) of 196.38)
Auxiliaries (isolation)  (101.61 (51.74%) of 196.38)
Solvents                 ( 40.59 (20.67%) of 196.38)
Substrates               ( 28.65 (14.59%) of 196.38)
```

Route B/EI_in:
Sewage/Water(25.48(12.97%) of 196.38):

```
step 3 (Route B):
    out of substrate Hydrochloric acid (37%aq)
        Water
            (Q=1.0; Q_claiming of ressources(100.0%)=1)
            Mass:                           0.14 -->   0.14

    out of solvent EtOH
        Water
            (Q=1.0; Q_claiming of ressources(100.0%)=1)
            Mass:                           6.52 -->   6.52

step 2 (Route B 2):
    out of substrate NaOCl 10%
        Water
            (Q=1.0; Q_claiming of ressources(100.0%)=1)
            Mass:                             8.76 -->     8.76

    out of auxiliary material Washing water (as Water separately)
        Water
            (Q=1.0; Q_claiming of ressources(100.0%)=1)
            Mass:                             4.54 -->     4.54

    out of auxiliary material NaCl; Sodium chloride (aq, conc.)
        Water
            (Q=1.0; Q_claiming of ressources(100.0%)=1)
            Mass:                             0.82 -->     0.82
```

```
further syntheses appendant to step 2:
    appendant to Oxime (Substrate):
        out of auxiliary material Washing water (as Water separately)
            Water
                (Q=1.0; Q_claiming of ressources(100.0%)=1)
                Mass:                              3.72 -->     3.72

step 1 (Route B 1):
    out of catalyst H3PO4 1N
        Water
            (Q=1.0; Q_claiming of ressources(100.0%)=1)
            Mass:                              0.22 -->     0.22

    out of auxiliary material NaCl; Sodium chloride (aq, conc.)
        Water
            (Q=1.0; Q_claiming of ressources(100.0%)=1)
            Mass:                              0.77 -->     0.77
```

Route B/EI_in:
Auxiliaries (isolation)(101.61(51.74%) of 196.38):

```
step 3 (Route B):
    Dichloromethane
        (Q=2.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=3)
        Mass:                           4.51 -->   9.02
        Recoverable thereof:            3.61 -->   7.22

step 2 (Route B 2):
    Dichloromethane
        (Q=2.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=3)
        Mass:                             22.55 -->    45.10
        Recoverable thereof:              18.04 -->    36.08

    Washing water (as Water separately)
        (Q=1.0; Q_claiming of ressources(100.0%)=1)
        Mass:                              0.00 -->     0.00

    NaCl; Sodium chloride (aq, conc.)
        (Q=1.0; Q_claiming of ressources(100.0%)=1)
        Mass:                              0.27 -->     0.27
```

```
    Magnesium sulfate
        (Q=2.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=3)
        Mass:                            0.41 -->     0.82

further syntheses appendant to step 2:
    appendant to Oxime (Substrate):
        Washing water (as Water separately)
            (Q=1.0; Q_claiming of ressources(100.0%)=1)
            Mass:                            0.00 -->     0.00

step 1 (Route B 1):
    Et2O
        (Q=3.5; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=6)
        Mass:                           13.06 -->    45.72
        Recoverable thereof:            10.45 -->    36.57

    NaCl; Sodium chloride (aq, conc.)
        (Q=1.0; Q_claiming of ressources(100.0%)=1)
        Mass:                            0.26 -->     0.26

    Na2SO4
        (Q=1.0; Q_claiming of ressources(100.0%)=1)
        Mass:                            0.43 -->     0.43
```

Route B/EI_in:
Solvents(40.59(20.67%) of 196.38):

```
step 3 (Route B):
    EtOH
        (Q=1.5; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=2)
        Mass:                           3.26 -->   4.89
        Recoverable thereof:            2.61 -->   3.91

step 2 (Route B 2):
    Dichloromethane
        (Q=2.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=3)
        Mass:                           12.03 -->    24.05
        Recoverable thereof:             9.62 -->    19.24

further syntheses appendant to step 2:
    appendant to Oxime (Substrate):
        Ethanol
```

```
            (Q=1.5; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=2)
            Mass:                             1.30 -->     1.95

        Water
            (Q=1.0; Q_claiming of ressources(100.0%)=1)
            Mass:                             2.58 -->     2.58

step 1 (Route B 1):
    Water
        (Q=1.0; Q_claiming of ressources(100.0%)=1)
        Mass:                             7.12 -->     7.12
```

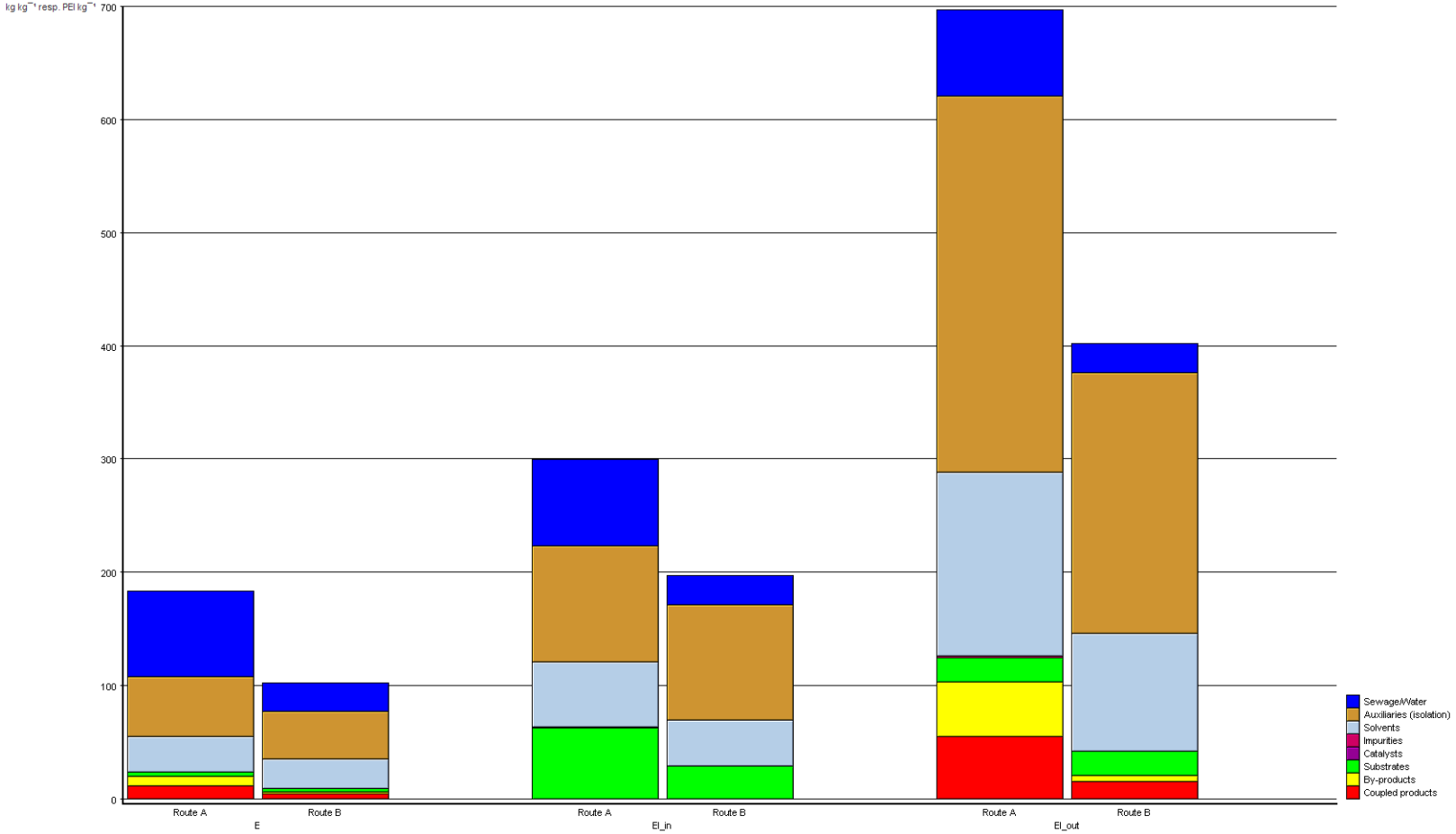
Route B/EI_in:
Substrates(28.65(14.59%) of 196.38):

```
step 3 (Route B):
    Isoxazoline carbethoxy imported from Route B 2
        The substrate is imported. Appropriate quantities are attributed
to the precedent syntheses: see there.

    NaBH4
        (Q=4.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=7)
        Mass:                           0.23 -->   0.93

    Hydrochloric acid (37%aq)
        (Q=2.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=3)
        Mass:                           0.23 -->   0.45

    Water
        (Q=1.0; Q_claiming of ressources(100.0%)=1)
        Mass:                           0.37 -->   0.37

step 2 (Route B 2):
    Hydroxymethylacrylate imported from Route B 1
        The substrate is imported. Appropriate quantities are attributed
to the precedent syntheses: see there.

    Oxime imported from Oxime
        The substrate is imported. Appropriate quantities are attributed
to the precedent syntheses: see there.

    NaOCl 10%
```

```
        (Q=2.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=3)
        Mass:                            0.97 -->     1.95

further syntheses appendant to step 2:
    appendant to Oxime (Substrate):
        Phenylacetaldehyde
            (Q=2.0; Q_claiming of ressources(50.0%)=2; Q_risk(50.0%)=2)
            Mass:                            0.89 -->     1.78

        Hydroxylamine Hydrochloride
            (Q=3.5; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=6)
            Mass:                            0.62 -->     2.17

        Sodium carbonate
            (Q=1.0; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=1)
            Mass:                            0.47 -->     0.47

step 1 (Route B 1):
    (EtO)2POCH2COOEt
        (Q=2.0; Q_claiming of ressources(100.0%)=2)
        Mass:                            1.73 -->     3.46

    (CH2O)n
        (Q=5.5; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=10)
        Mass:                            2.73 -->    15.03

    K2CO3
        (Q=1.5; Q_claiming of ressources(50.0%)=1; Q_risk(50.0%)=2)
        Mass:                            1.17 -->     1.75

    Water
        (Q=1.0; Q_claiming of ressources(100.0%)=1)
        Mass:                            0.28 -->     0.28
```

Comparisons of three indexes (E, EI_out, and EI_in) for both routes.

According to substance category



Comparisons of three indexes (E, EI_out, and EI_in) for both routes.

According to synthetic step.