Reactions of Nitric Oxide with β-Hydroxylimino Esters

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Outline

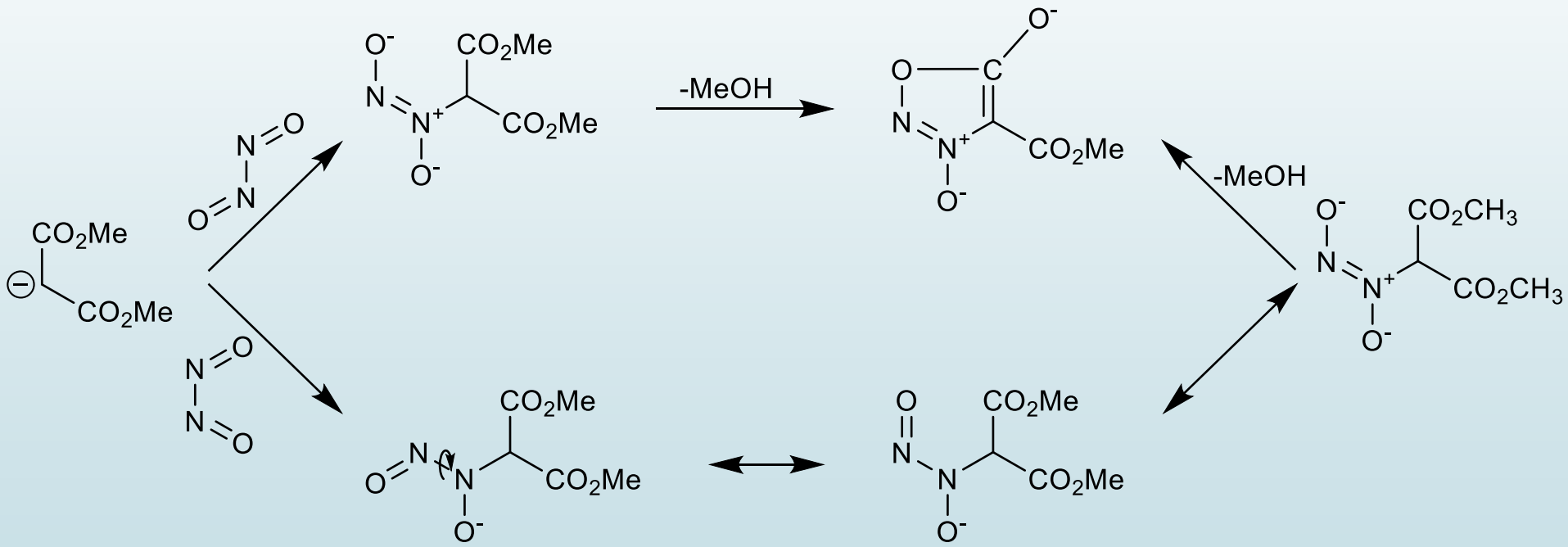
- Background and Significance
- Expected synthesis
- Results and mechanisms
- Spectra
- Further research
- Acknowledgements

Background and Significance

- Nitric oxide (NO) donor pro-drugs
- Physiological roles
  - Alcoholism deterrent (HNO)
  - Cardiovascular disease cure
- Versatile
  - NO and HNO releasing
  - Explosives
- Decomposition properties

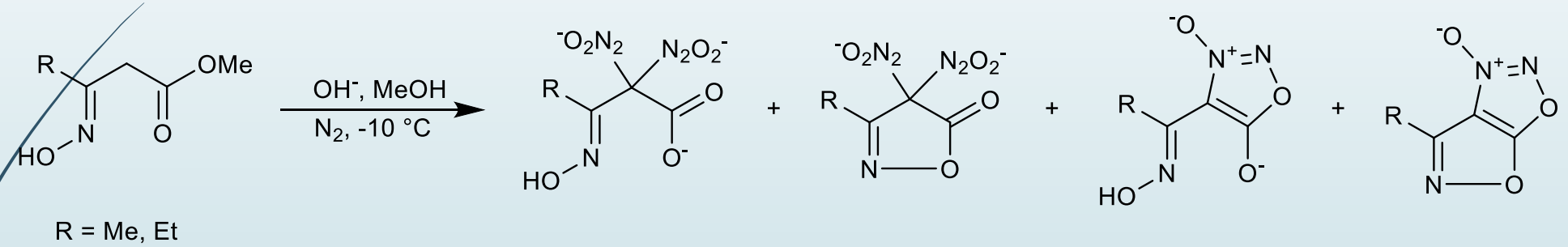
Dimeric Addition of NO

- Formation of sydnone-N-oxide and diazeniumdiolate products



Expected Products from β-Ketoximino Esters

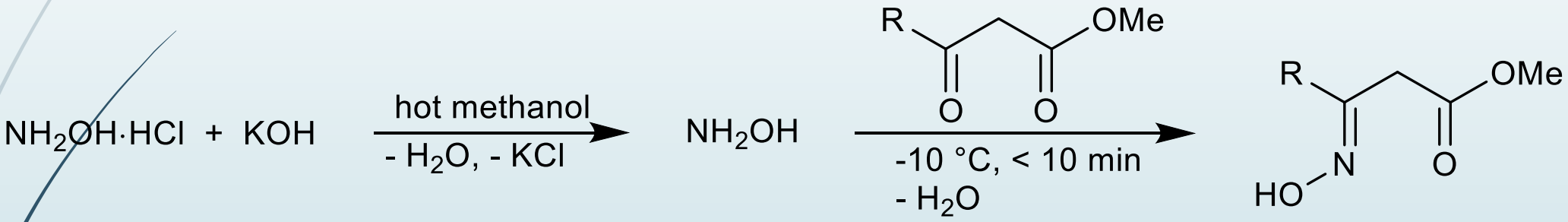
- Reaction between β-ketoxime such as methyl acetoacetoxime (R = Me) and nitric oxide



R = Me, Et

Synthesis of β-Ketoximino Esters

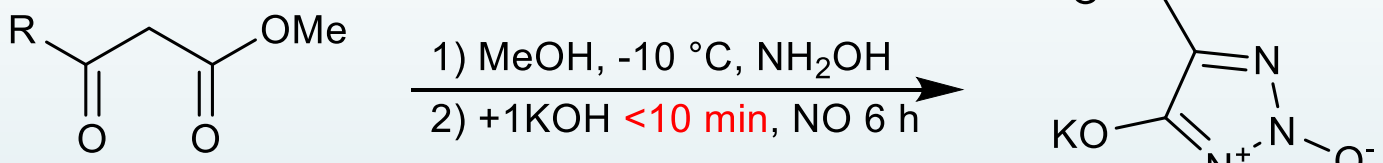
- Oxime substrates not commercially available
  - Generated in situ, not isolated



Zhao, Y.-Z.; Yang, H.-B.; Tang, X.-Y.;Shi, M., *Chem. Eur. J.*, **2015**, *21 (9)*, 3562 – 3566.

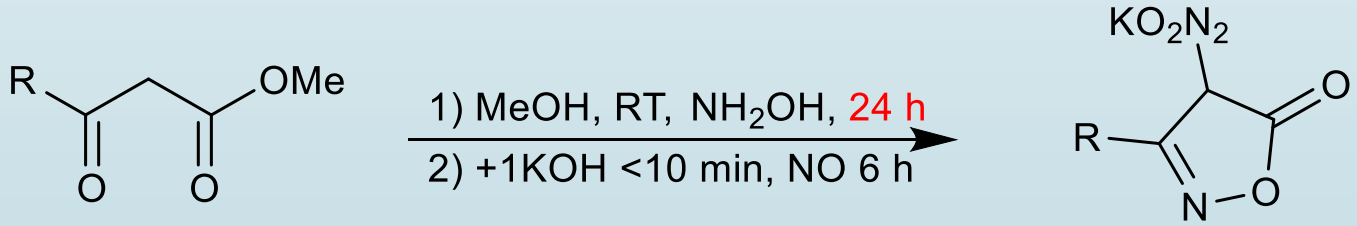
Results

- Generated β-ketoximes to form two unexpected products under two different methods



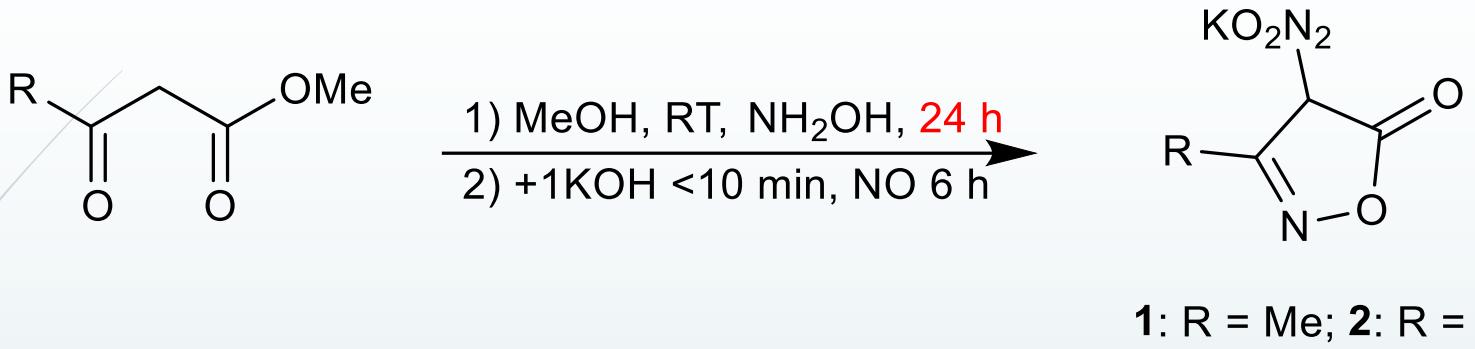
3: R = Me; **4**: R = Et

Potassium 4-acetyltriazolium-1,2,3-triolate

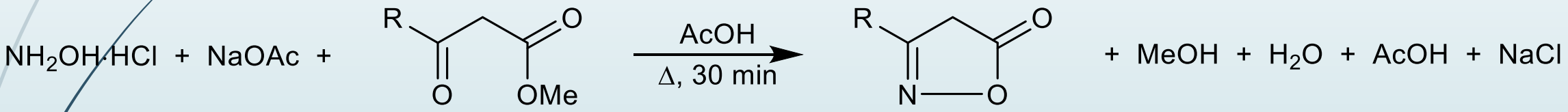


1: R = Me; **2**: R = Et

Potassium 3-ethyl-5-isoxazolone-4-diazeniumdiolate



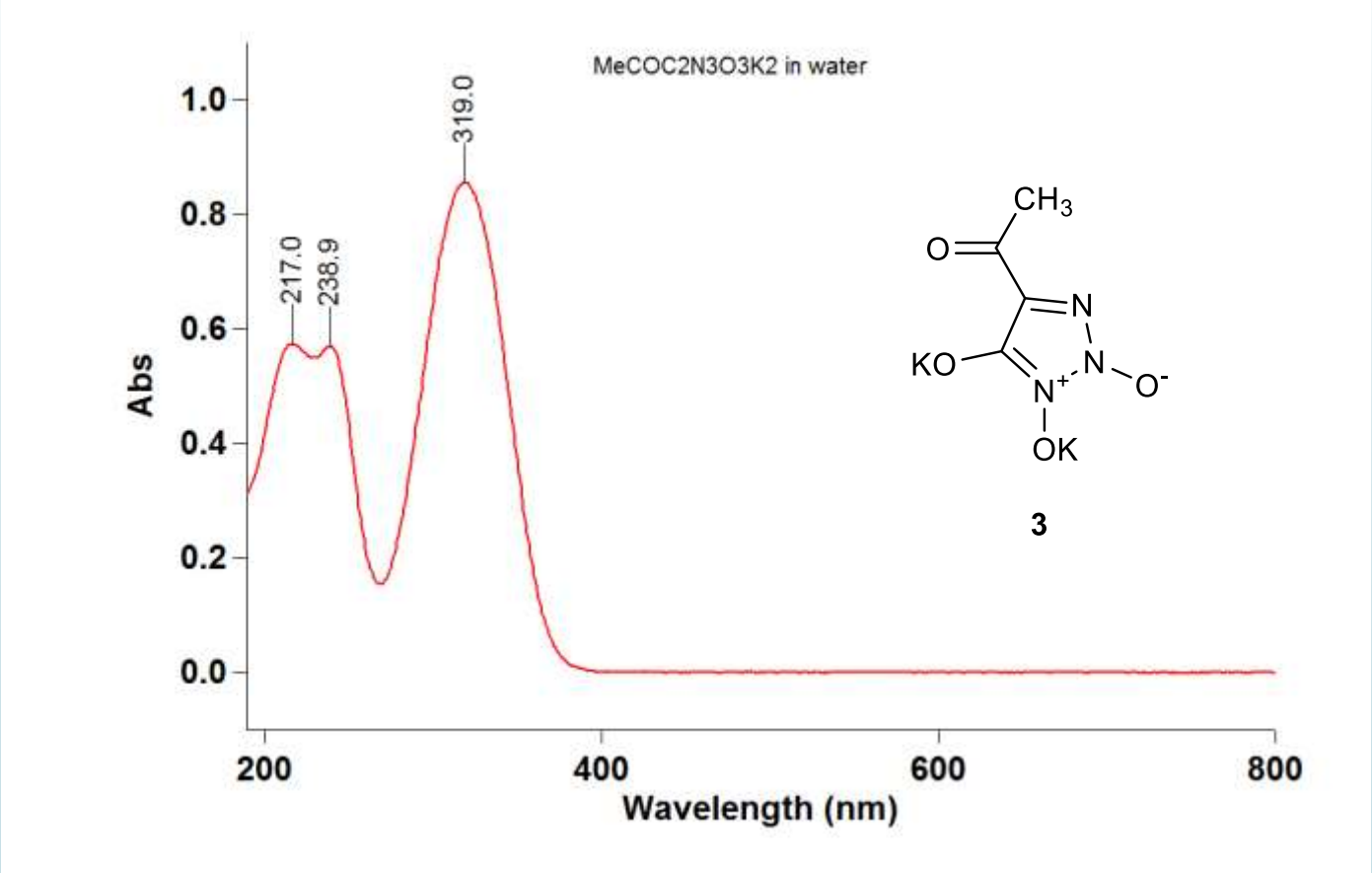
1: R = Me; **2**: R = Et



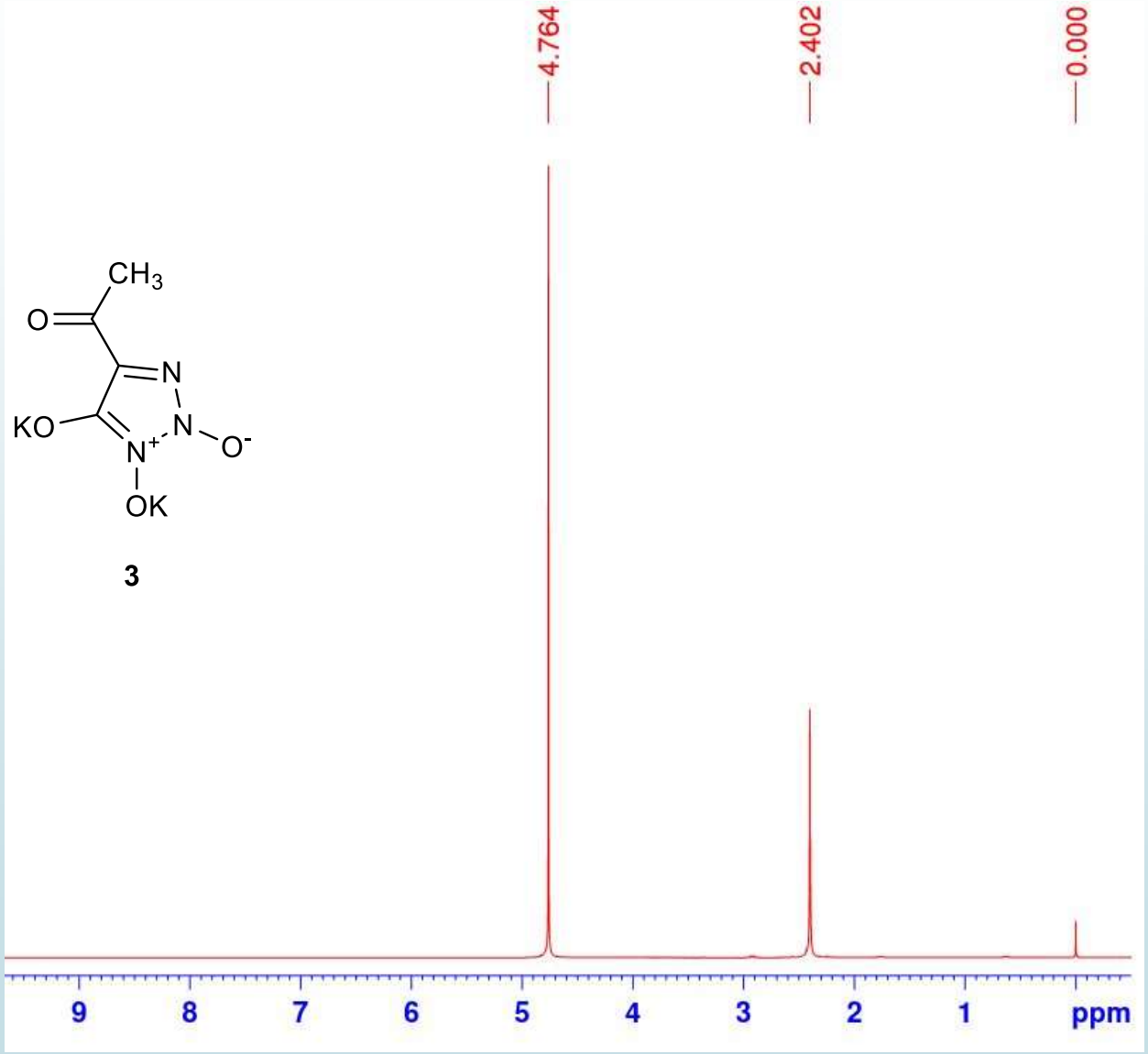
Dias-Jurburg, I.; Gagosz, F.; Zard, S. Z., *Org. Lett.*, **2010**, *12 (3)*, 416 – 419.

Product Spectra

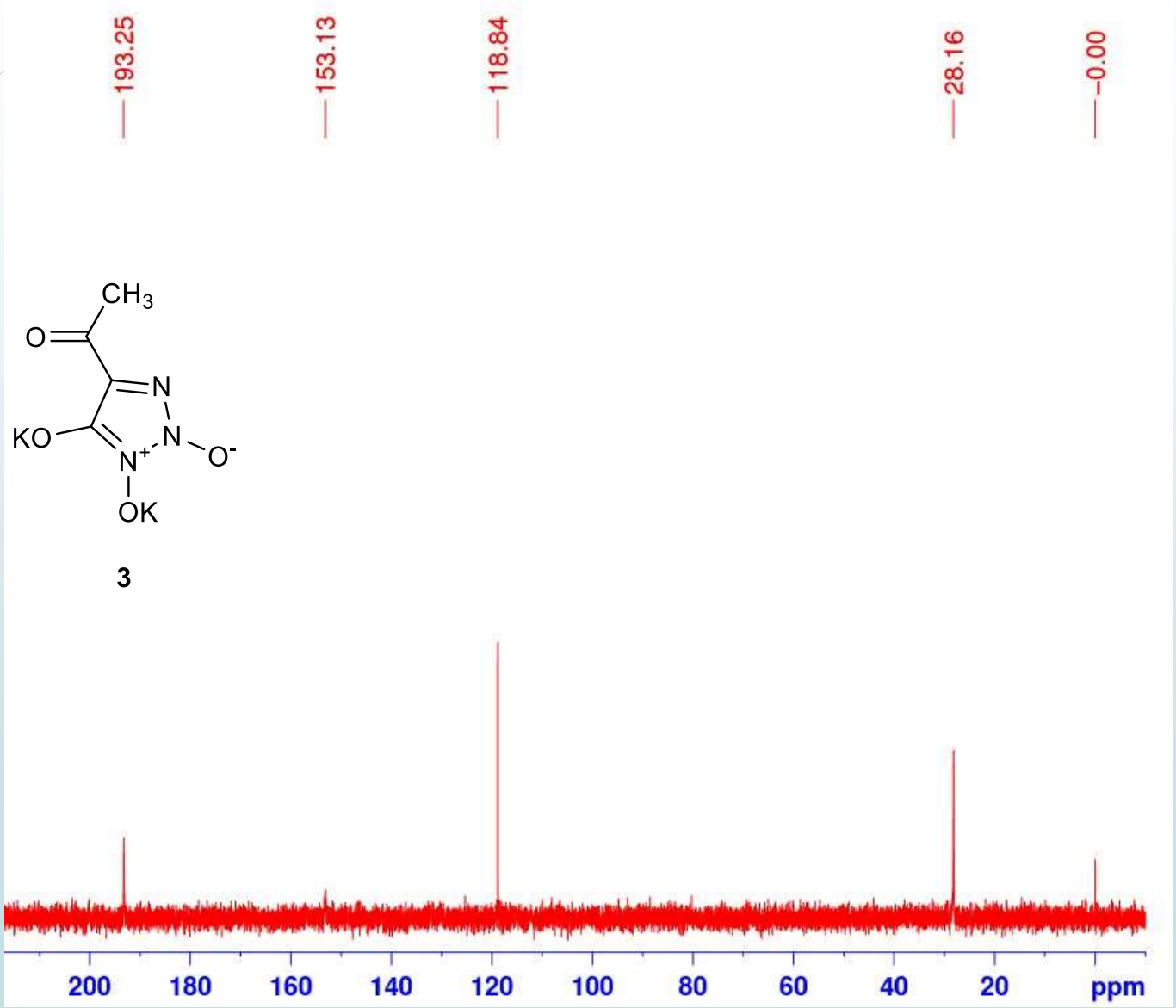
- **$MeCOC_2N_3O_3K_2$**
  - UV-Vis



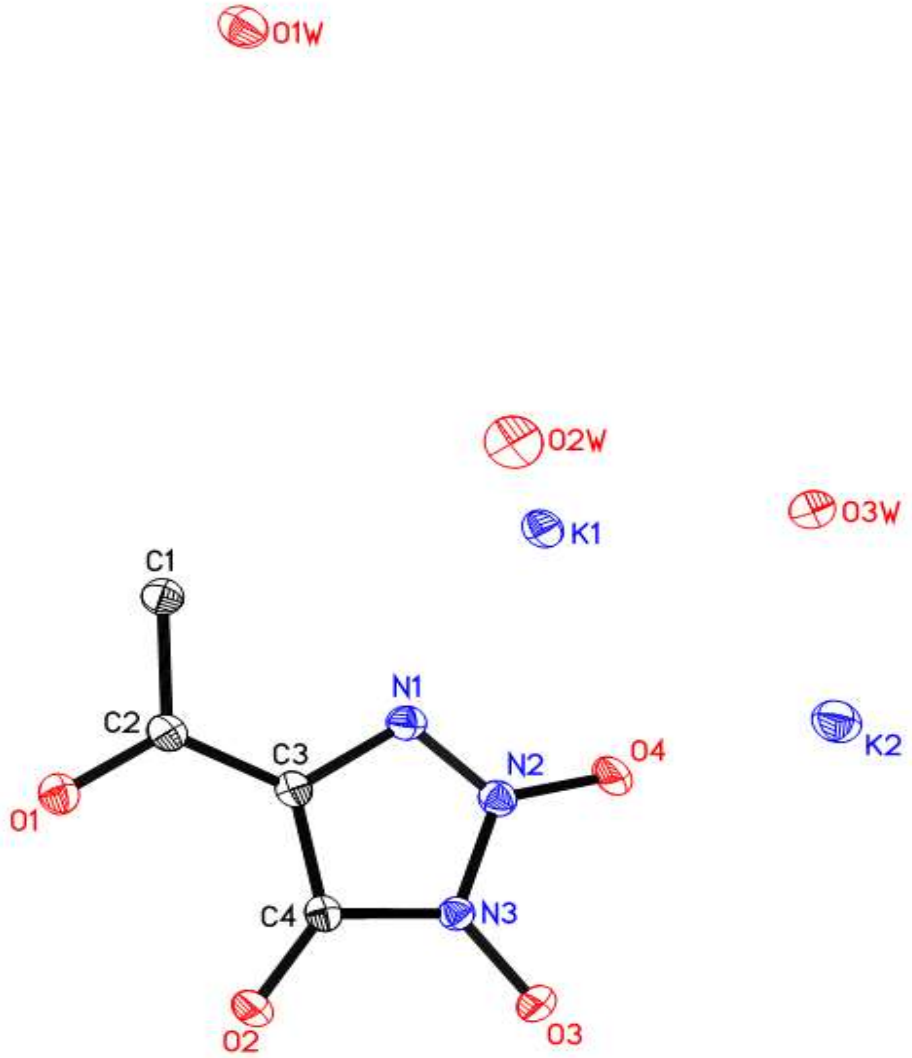
- $MeCOC_2N_3O_3K_2$ H1 NMR in D_2O/DSS



- $MeCOC_2N_3O_3K_2$ C13 NMR in D_2O/DSS



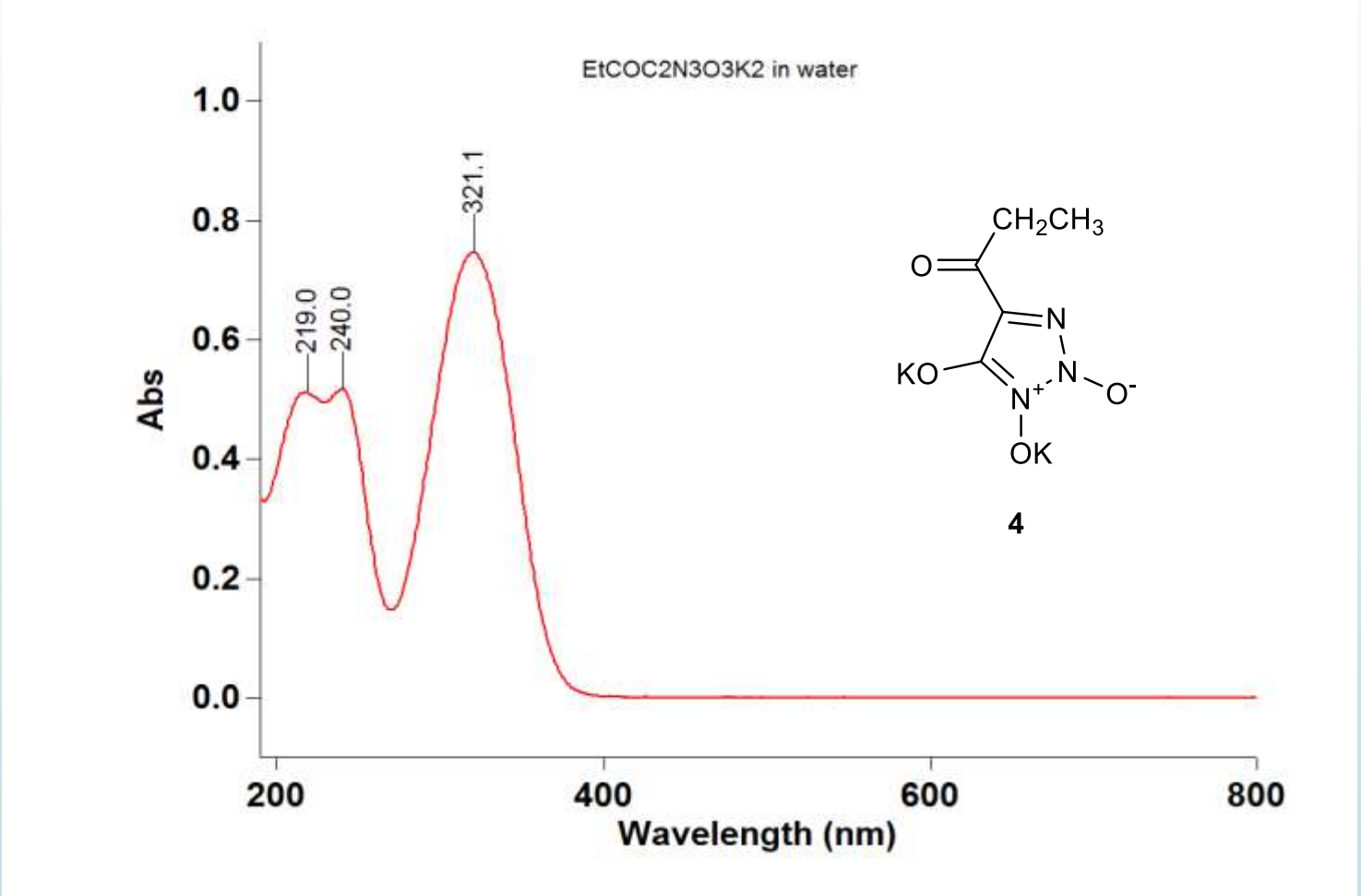
- $MeCOC_2N_3O_3K_2$ X-ray structure



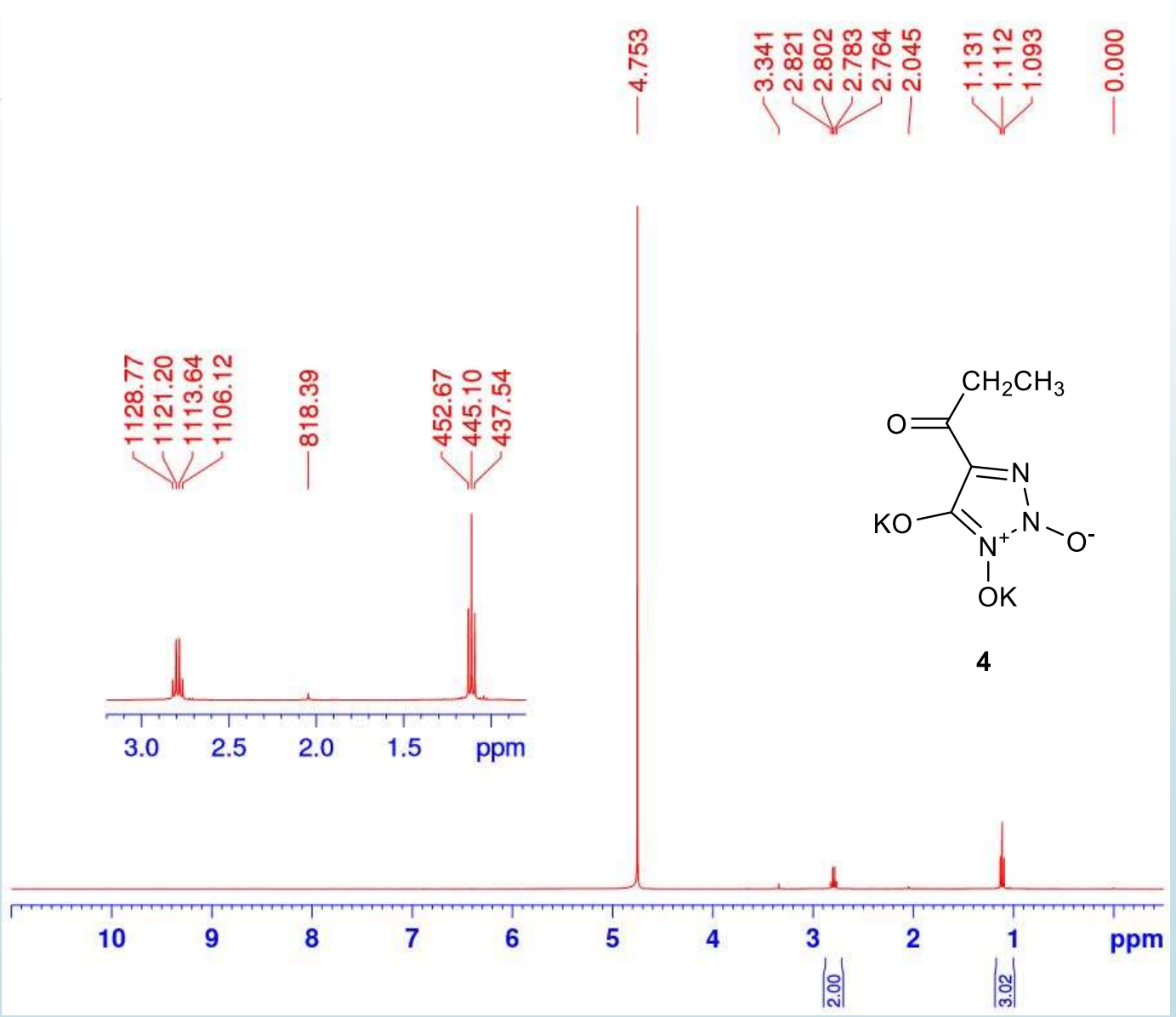
Bond Distances (Å)

C(3)-N(1)	1.387(7)
C(3)-C(4)	1.418(8)
N(1)-N(2)	1.285(7)
N(2)-O(4)	1.284(6)
N(2)-N(3)	1.370(6)
N(3)-O(3)	1.334(6)
N(3)-C(4)	1.374(7)
C(4)-O(2)	1.253(6)

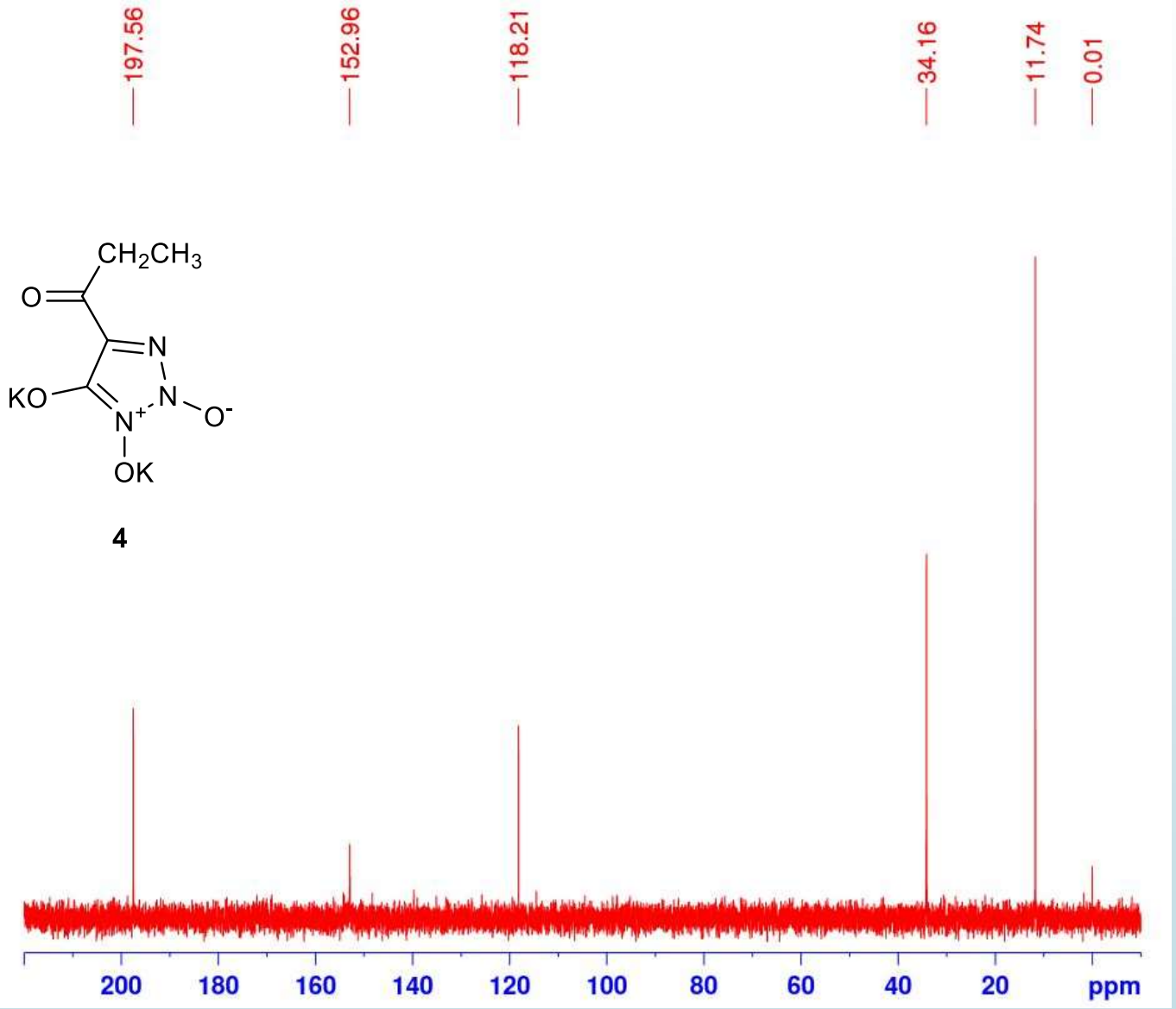
- **$EtCOC_2N_3O_3K_2$**
  - UV-Vis



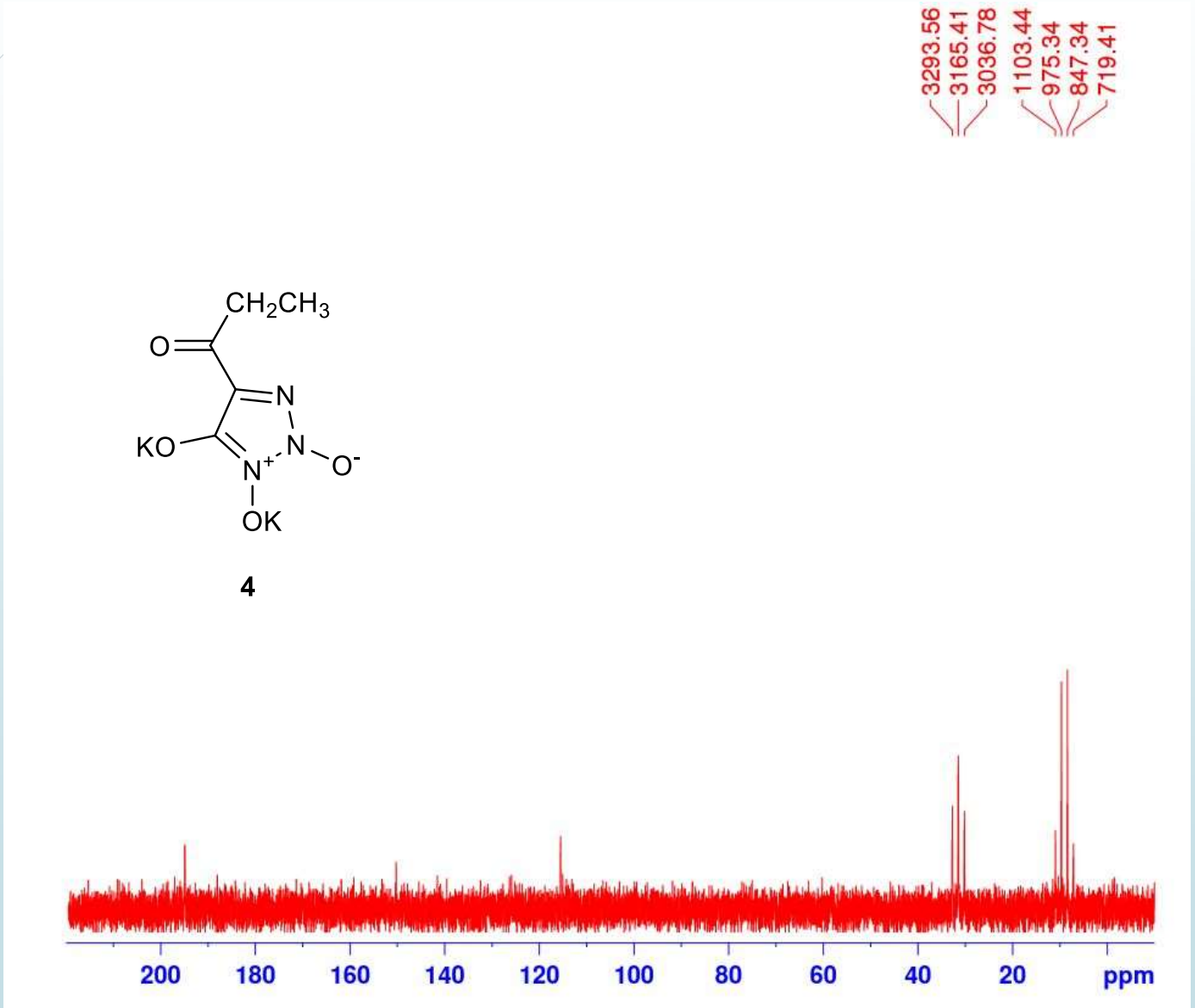
- $EtCOC_2N_3O_3K_2$ H1 NMR in D_2O/DSS



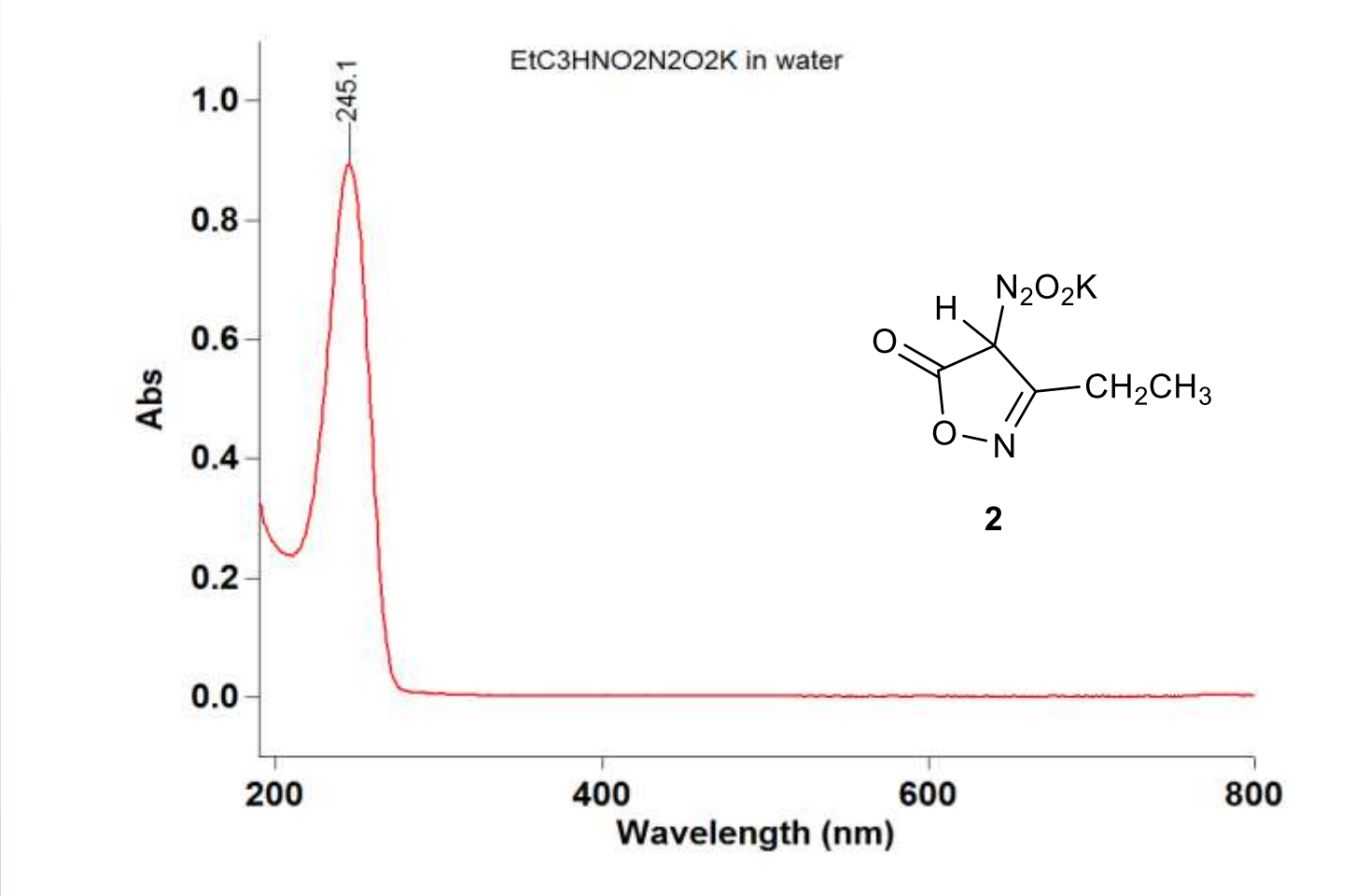
- $EtCOC_2N_3O_3K_2$ C13 NMR in D_2O/DSS



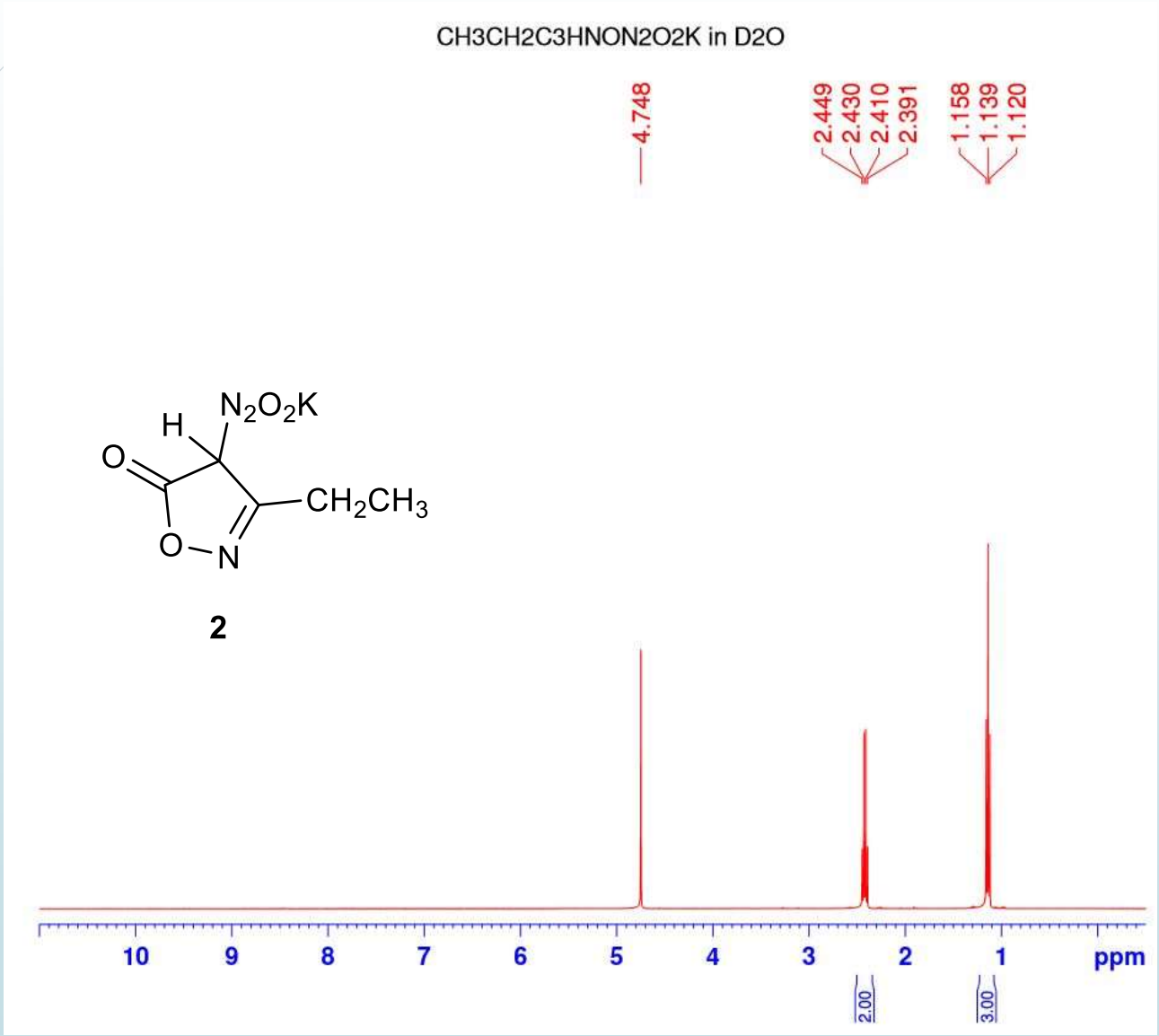
- $EtCOC_2N_3O_3K_2$ H coupled C13 NMR



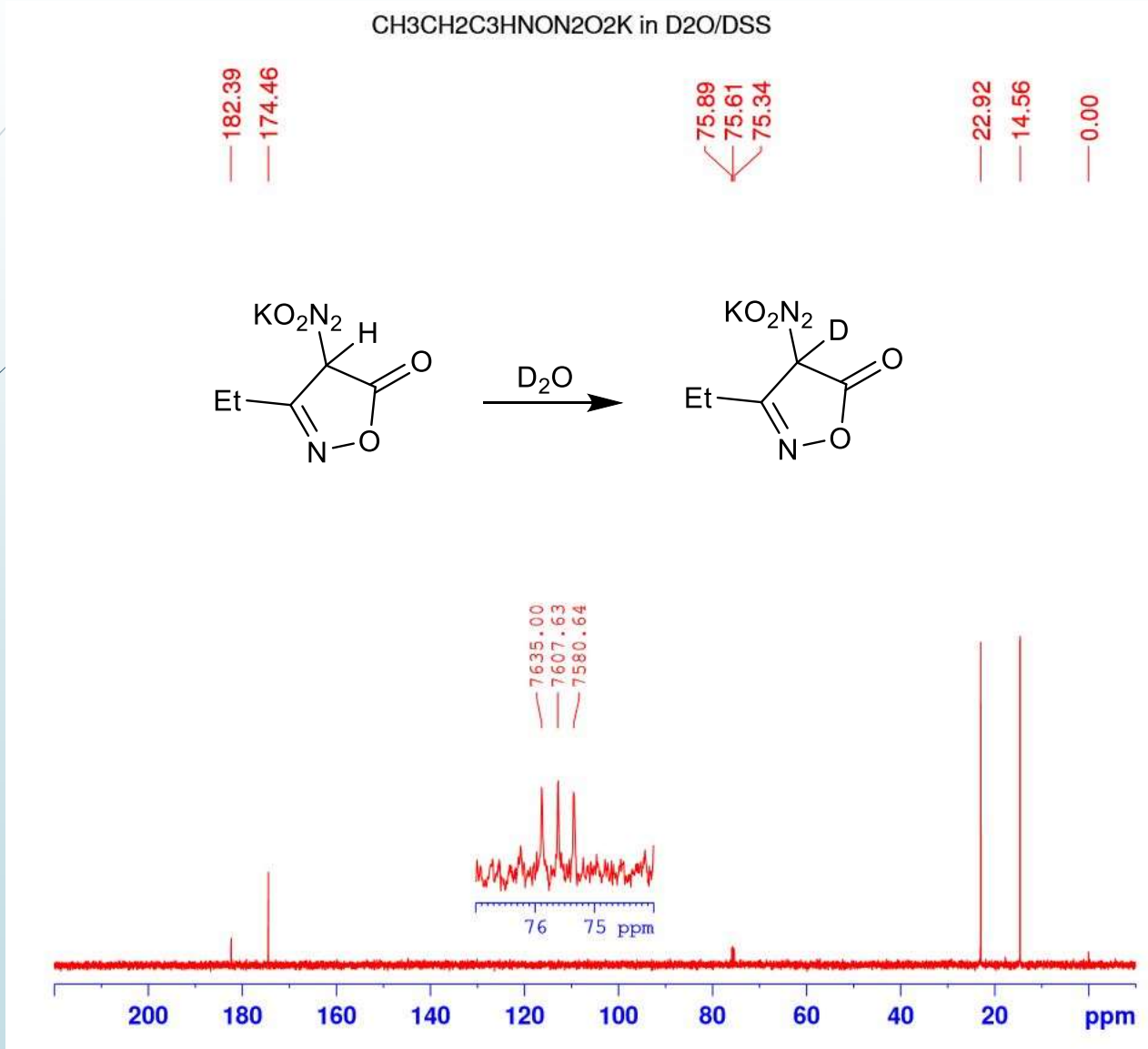
- **$EtC_3HNO_2N_2O_2K$**
  - UV-Vis



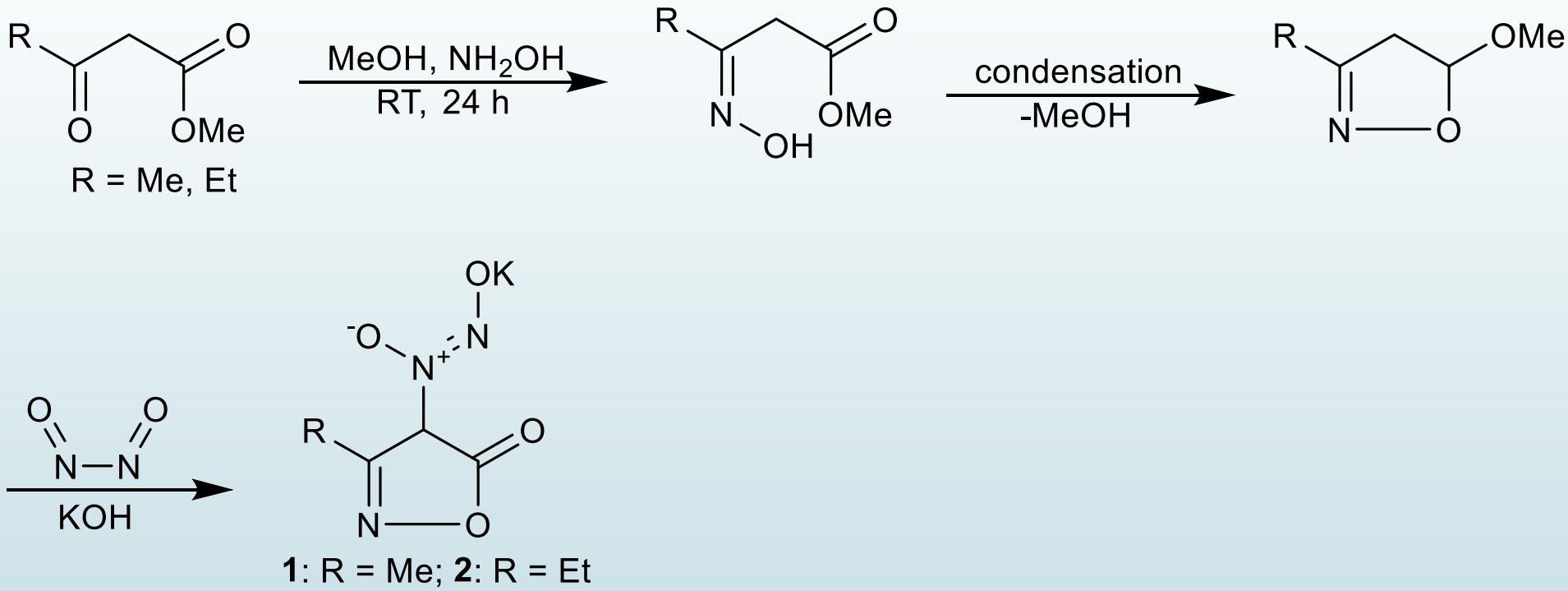
- $EtC_3HNO_2N_2O_2K$ H1 in D_2O/DSS



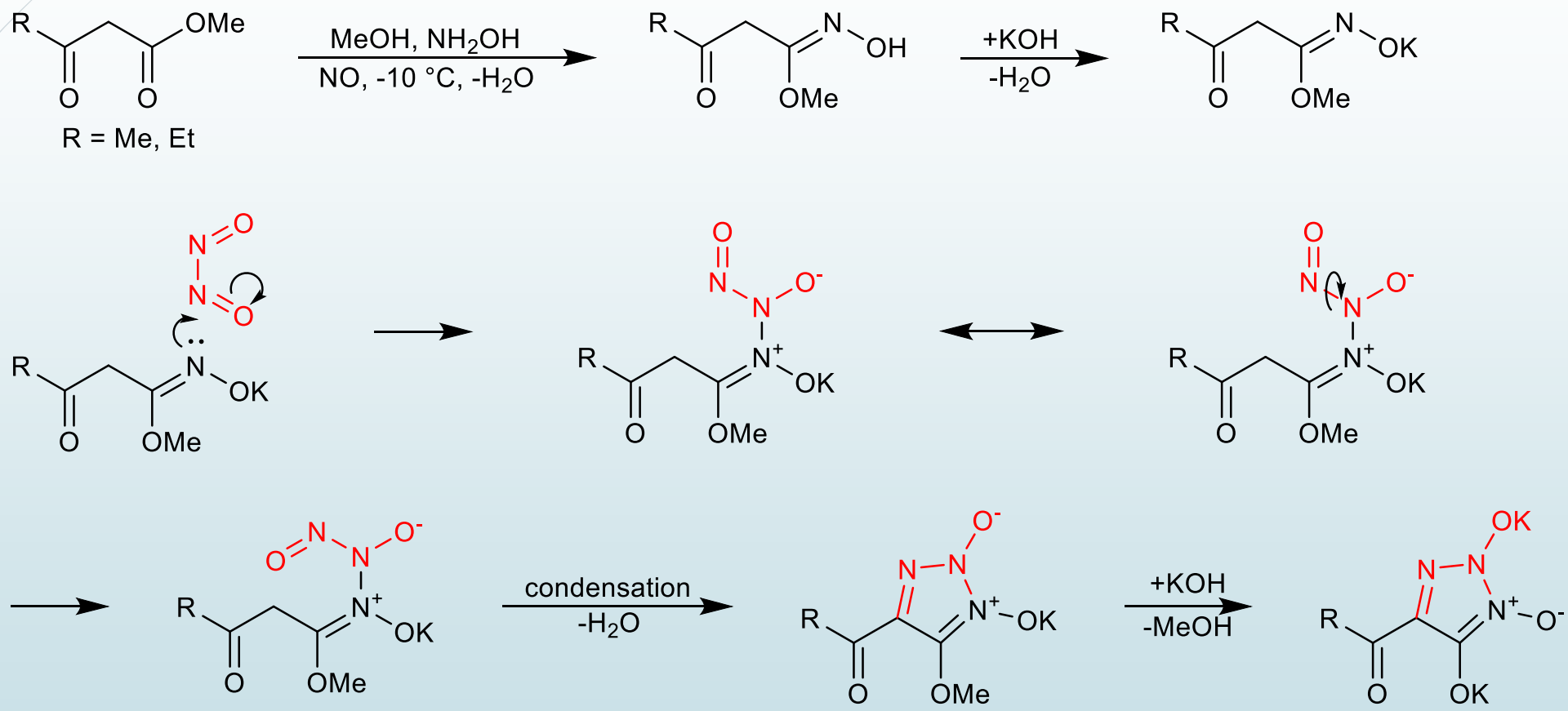
- $EtC_3HNO_2N_2O_2K$ C13 in D_2O/DSS



Mechanism


R
O
O
OMe
R = Me, Et
MeOH, NH2OH
RT, 24 h
R
O
N
OH
OMe
condensation
-MeOH
R
OMe
N
O
O
O
N—N
KOH
OK
-O
N+
N
R
O
N
O
1: R = Me; 2: R = Et

Mechanism


R
OMe
O
O
R = Me, Et
MeOH, NH2OH
NO, -10 °C, -H2O
N
OH
+KOH
-H2O
OK
condensation
-MeOH

Further Research

- EPR (electron paramagnetic resonance)
  - Release of NO
- TGA/DSC (Thermogravimetric and Differential Scanning Calorimetry)
  - Thermal decomposition properties
  - Decomposition mechanism

Acknowledgements

- Honors Program, University of Wyoming
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