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SYNTHESIS OF FUNCTIONALIZED CYCLOPROPANES FROM UNSATURATED FATTY ESTERS

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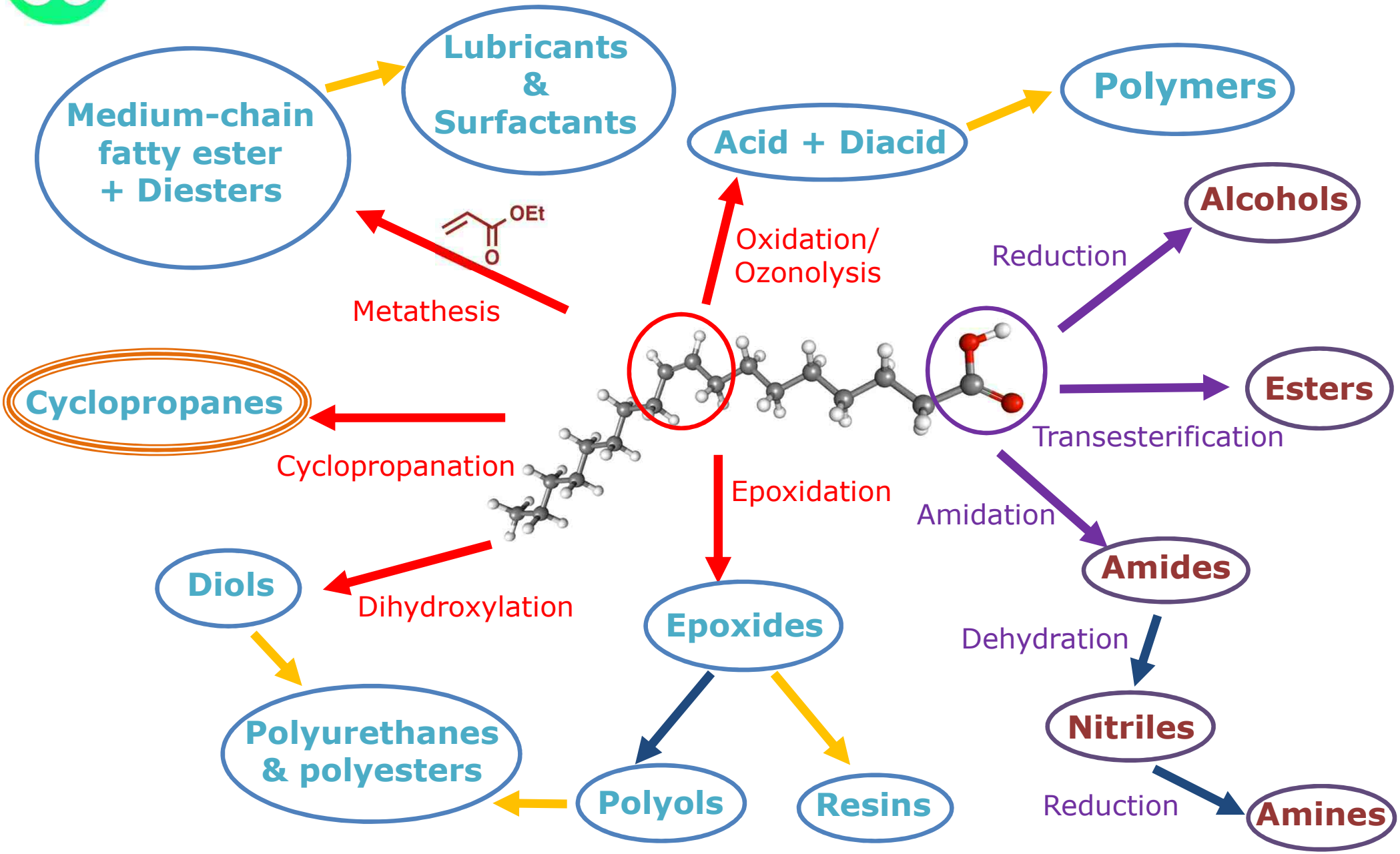
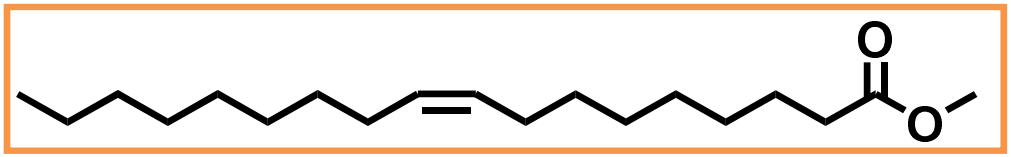
CSIC Consejo Superior de Investigaciones Científicas

FATTY ESTERS MODIFICATIONS

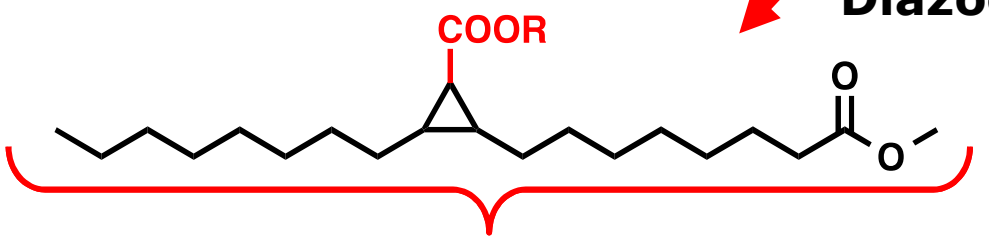


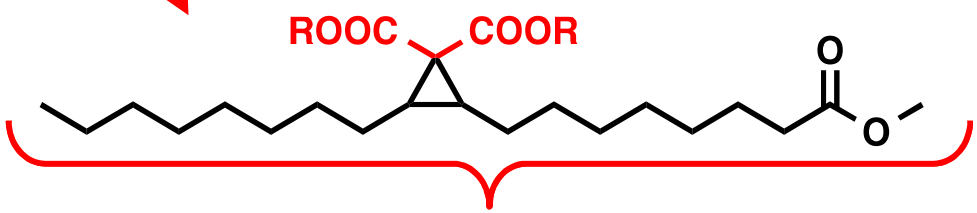
CYCLOPROPANATION REACTION



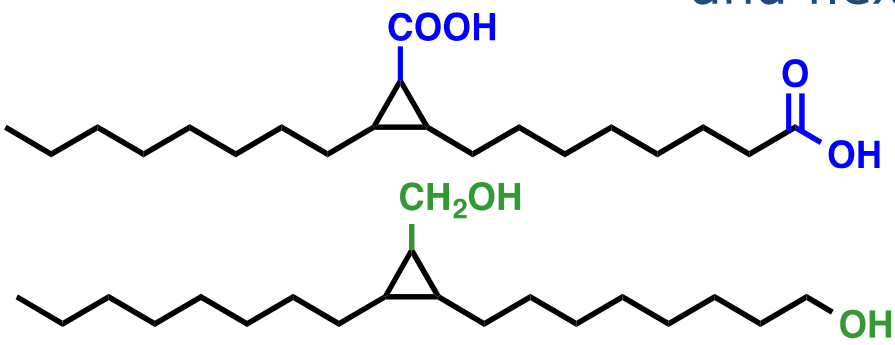
One step functionalization

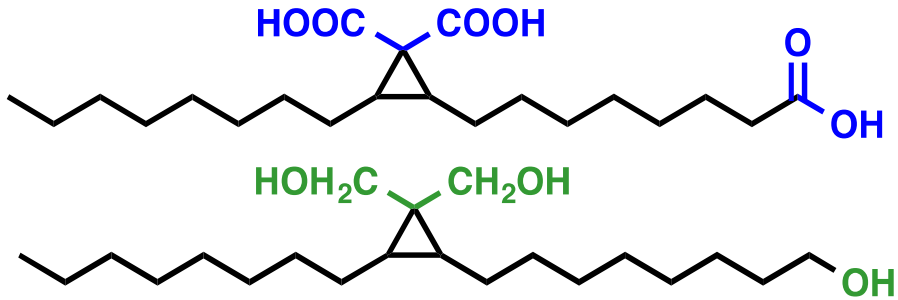
Diazoesters





Rigid cyclopropane core and flexible chains





Useful reagents for **polymerization reactions** (Monomers, cross-linkers)

Polyesters, polyamides, polyurethanes...

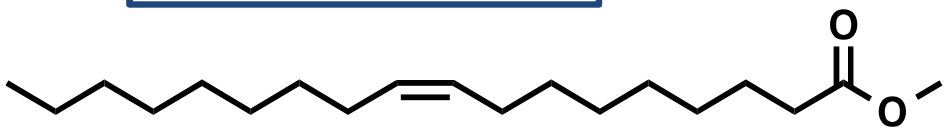
$N_2CHCOOEt$
Cu powder (13% mol)

K. U. M. Prasad et al. *Indian J. Chem.* **1969**, *7*, 460.

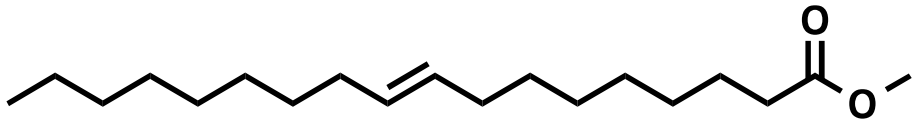
78% yield
Lack of separation and characterization

REAGENTS AND CATALYSTS

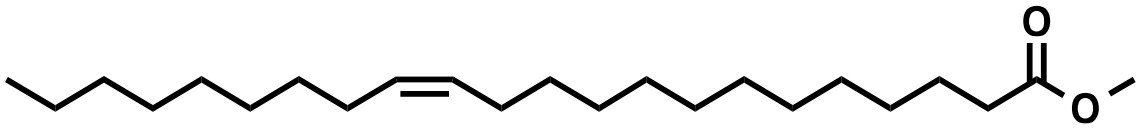
SUBSTRATES



Methyl oleate (C18:1 *cis* Δ^9)

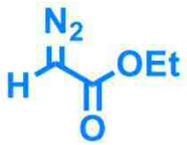


Methyl elaidate (C18:1 *trans* Δ^9)

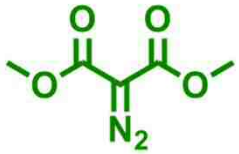


Methyl erucate (C22:1 *cis* Δ^{13})

DIAZOCOMPOUNDS



Ethyl diazoacetate (EDA)

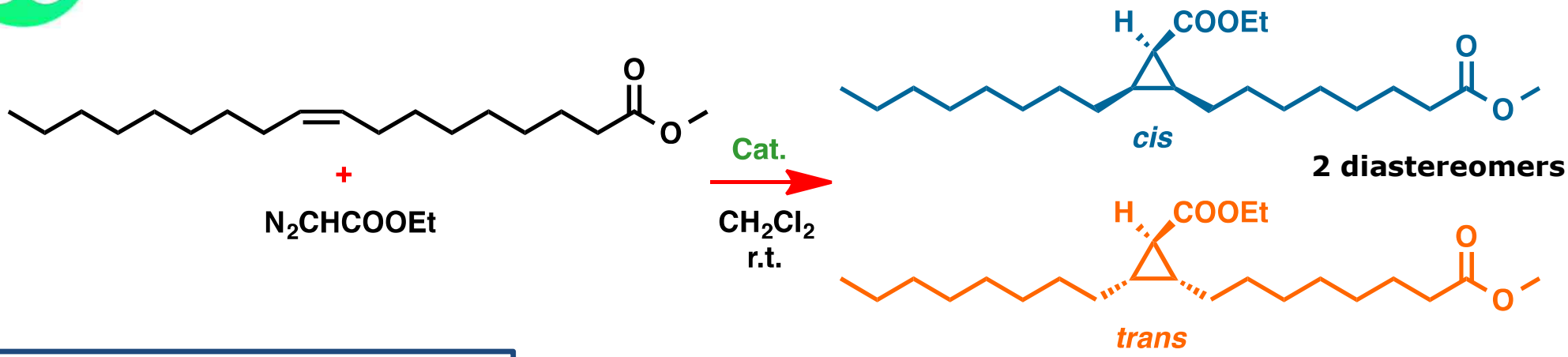


Dimethyl diazomalonate (MDM)

CATALYSTS

$Cu(OTf)_2$ $Rh_2(OAc)_4$

EXPERIMENTAL CONDITIONS

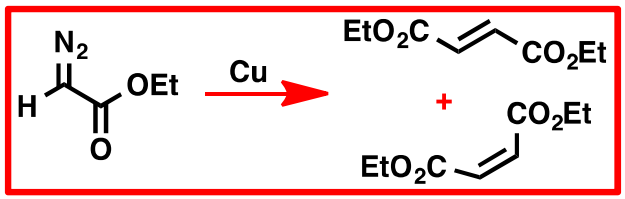


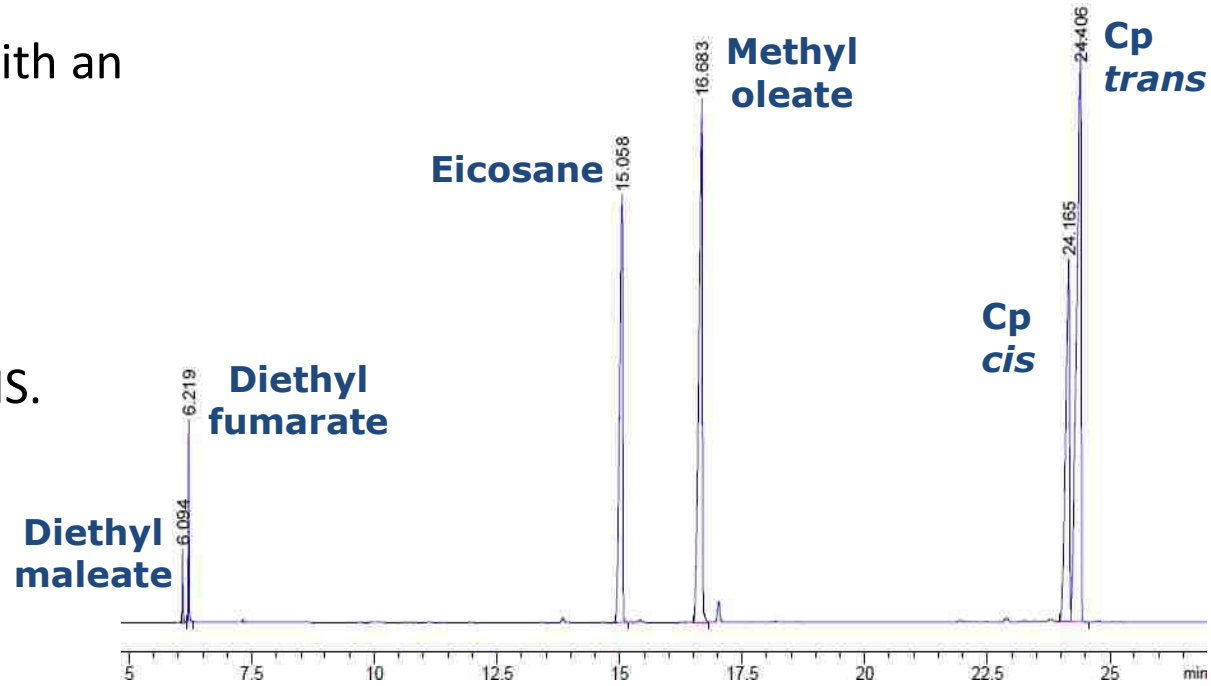
Determination of results

Reaction yield: Gas Chromatography with an internal standard.

Purification: Liquid Chromatography (column and medium pressure)

Product characterization: NMR y HR-MS.





Typical GC chromatogram

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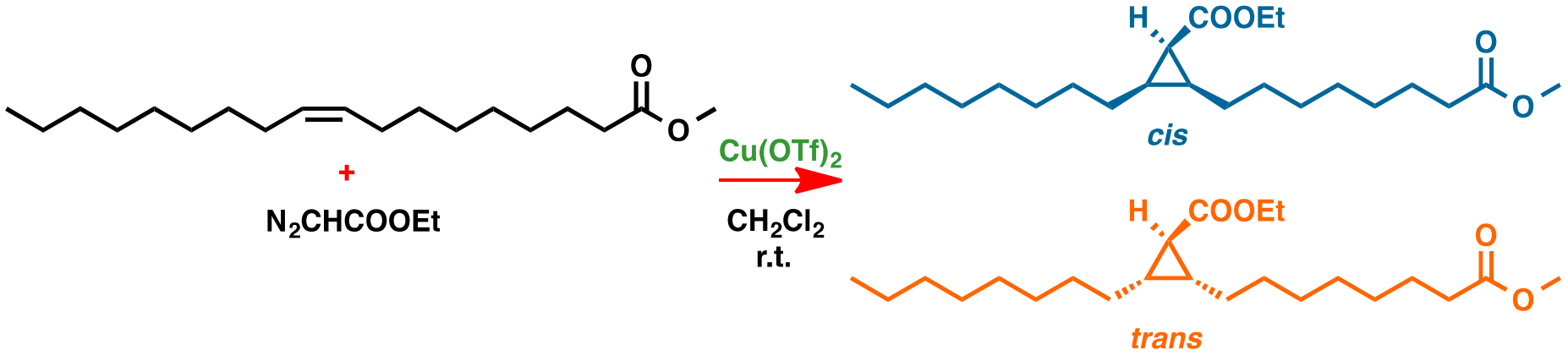
Cyclopropanation with EDA

Reaction with methyl oleate



Optimization:

- % catalyst
- Solvent
- Temperature
- Reaction time
- Methyl oleate/EDA

Optimal conditions:

- 1% $Cu(OTf)_2$
- CH_2Cl_2
- r.t.
- 15h
- Methyl oleate/EDA =1:3

>99% yield

***trans/cis* = 68/32**

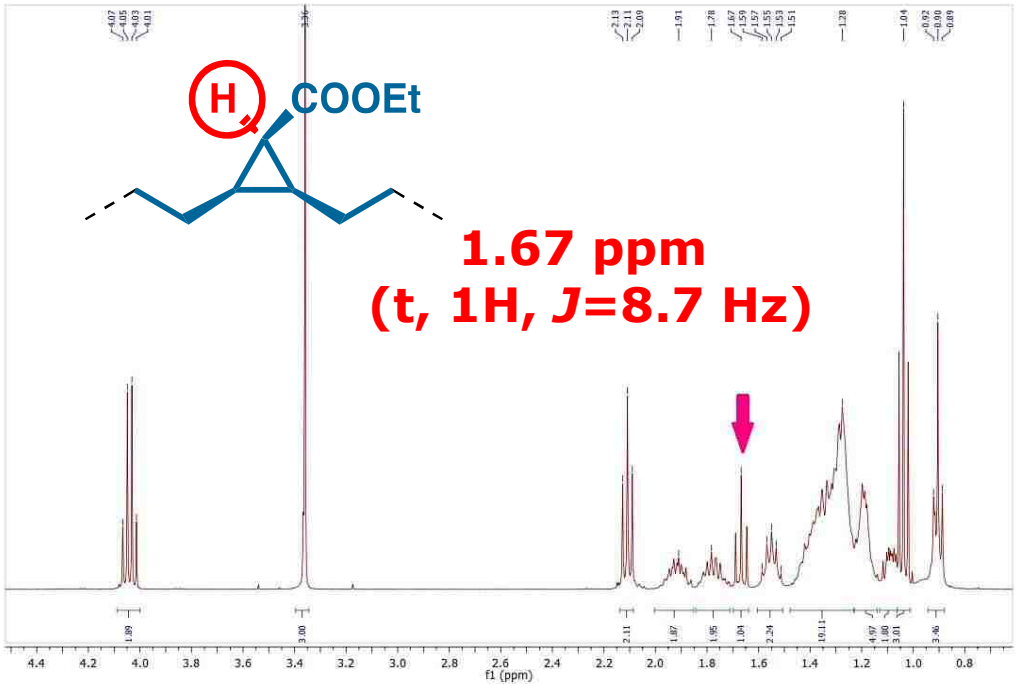
Characterization of the isomers? → **NMR**

- **^{1}H-NMR**
- **APT**
- **COSY**
- **NOESY**
- **HSQC**
- **HMBC**

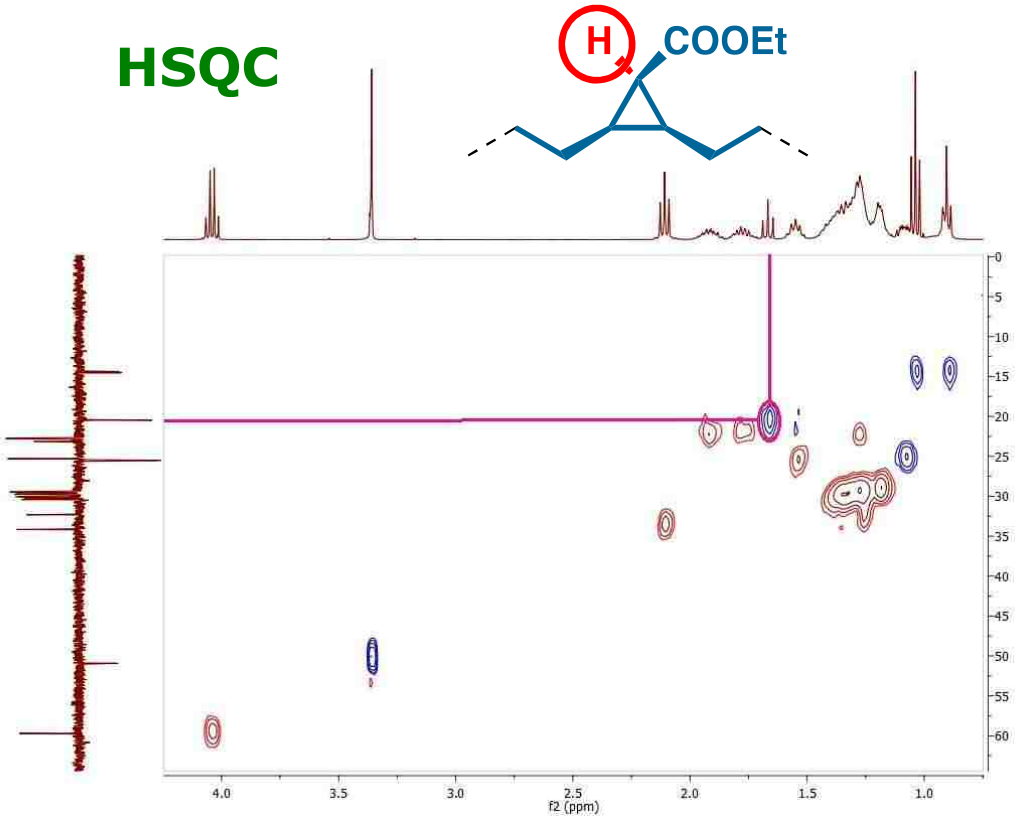
Cyclopropanation with EDA

cis cyclopropane (C_6D_6)

^{1}H-NMR



HSQC



^{1}H-NMR in **C_6D_6** allows us to establish the coupling constant (*J*) of the H in α to the ester group in the cyclopropane ring for one of the diastereomers.
The value of **8.7 Hz** is according to a ***cis* cyclopropane**.

HSQC experiments **confirm the assignment** of the H.

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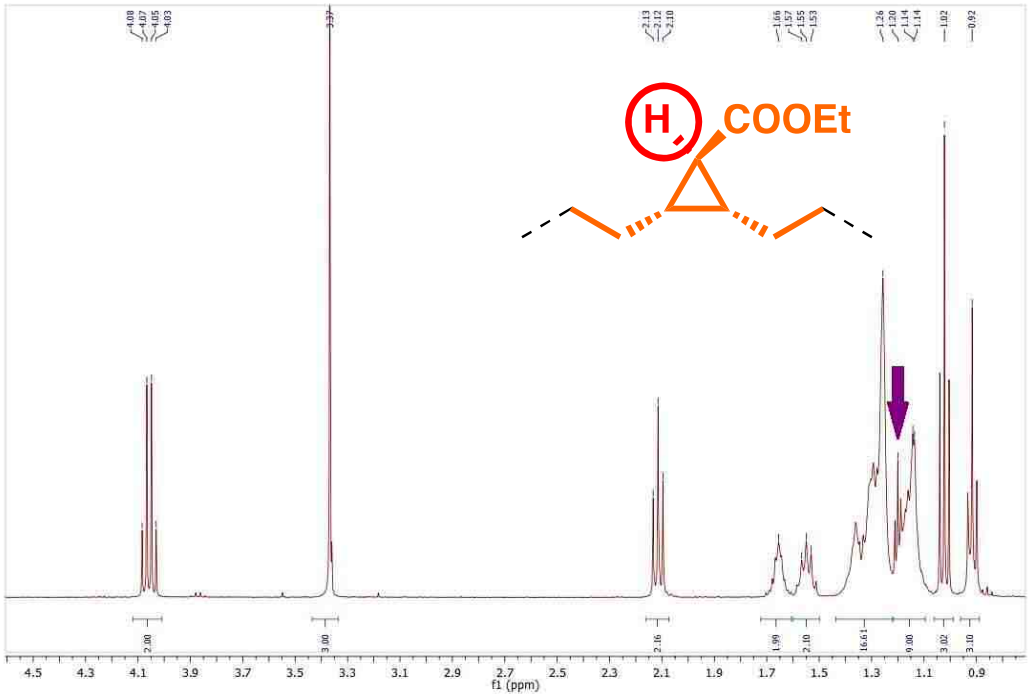
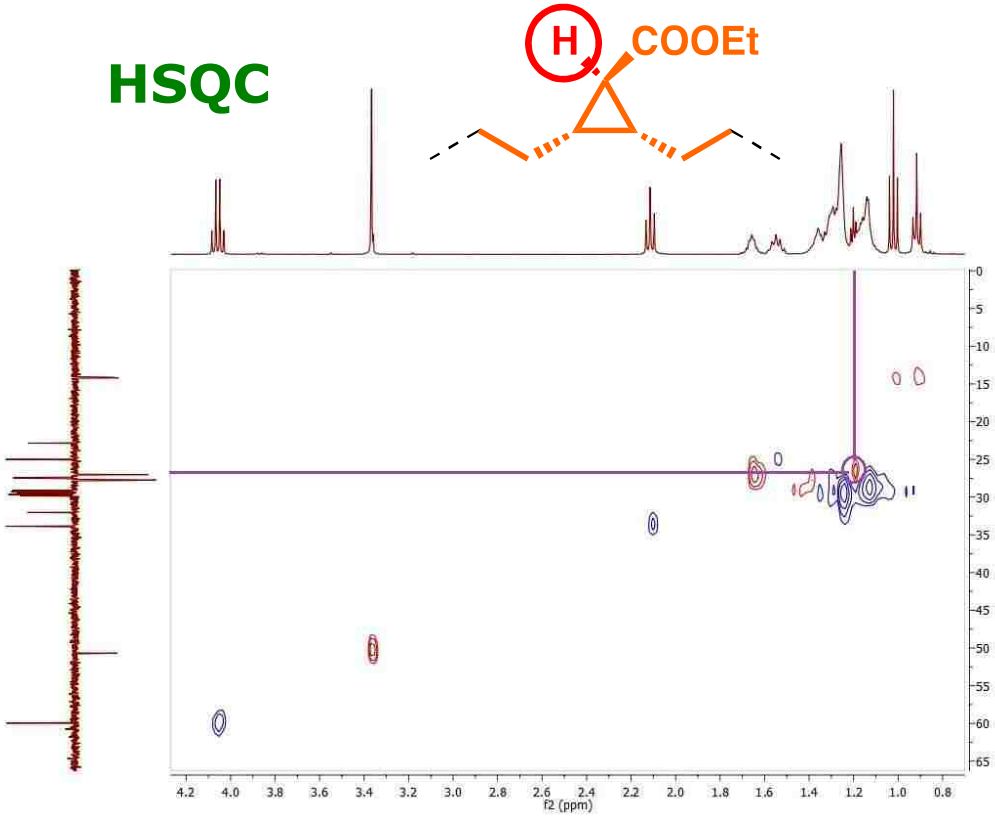
Cyclopropanation with EDA

trans cyclopropane (C_6D_6)

^{1}H-NMR



HSQC

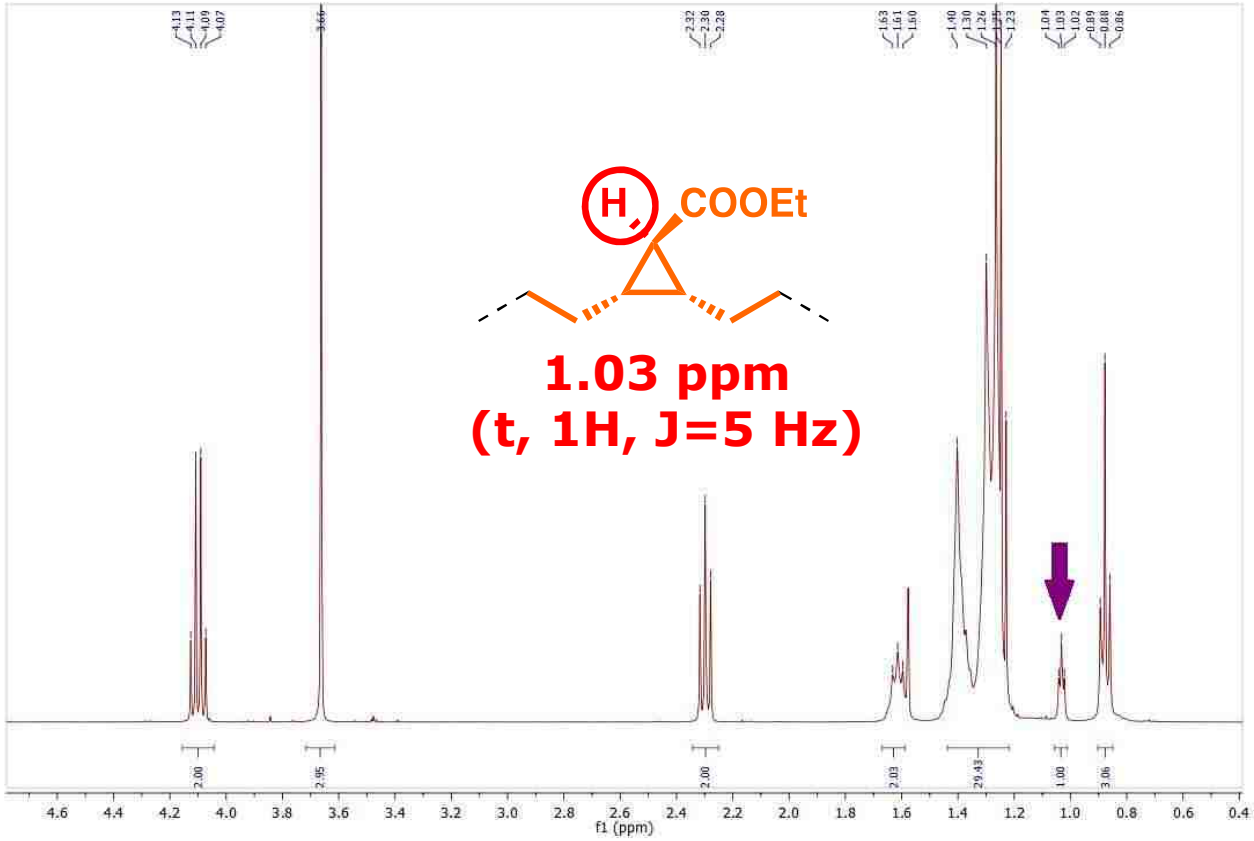


In the case of the ***trans* isomer**, it was not possible to determine the coupling constant (*J*) because of an **overlapping of signals** in the same region of the spectrum.

Cyclopropanation with EDA

trans cyclopropane ($CDCl_3$)

^{1}H-NMR



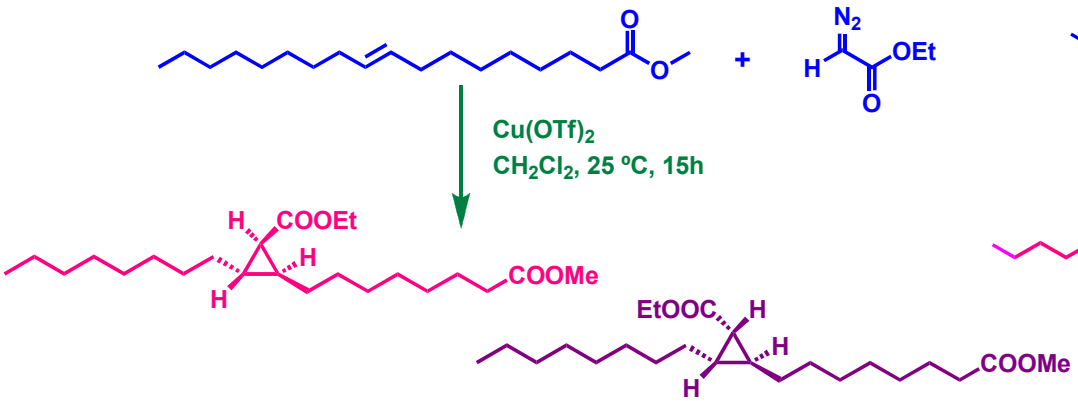
^{1}H-NMR spectra in **$CDCl_3$** complement those obtained in C_6D_6 and they allow us to determine the coupling constant (*J*) of the H in α to the ester group for the *trans* diastereomer.

The value of **5 Hz** is according to a ***trans* cyclopropane**.

HSQC experiments in **$CDCl_3$** also confirm the assignment.

Cyclopropanation with EDA

Reaction with methyl elaidate



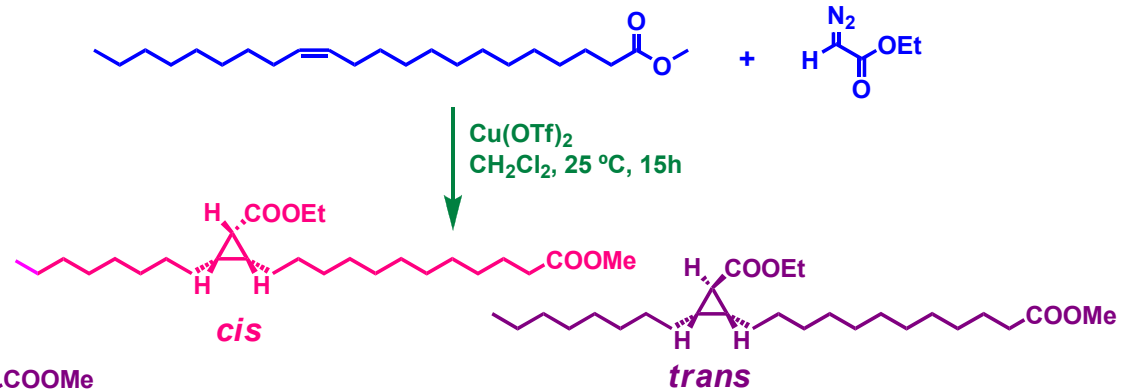
Optimal conditions:

- 1% $Cu(OTf)_2$
- CH_2Cl_2
- r.t.
- 15h
- Methyl elaidate/EDA = **1:4**

>99% yield

***trans/cis* = 50/50**

Reaction with methyl erucate



Optimal conditions:

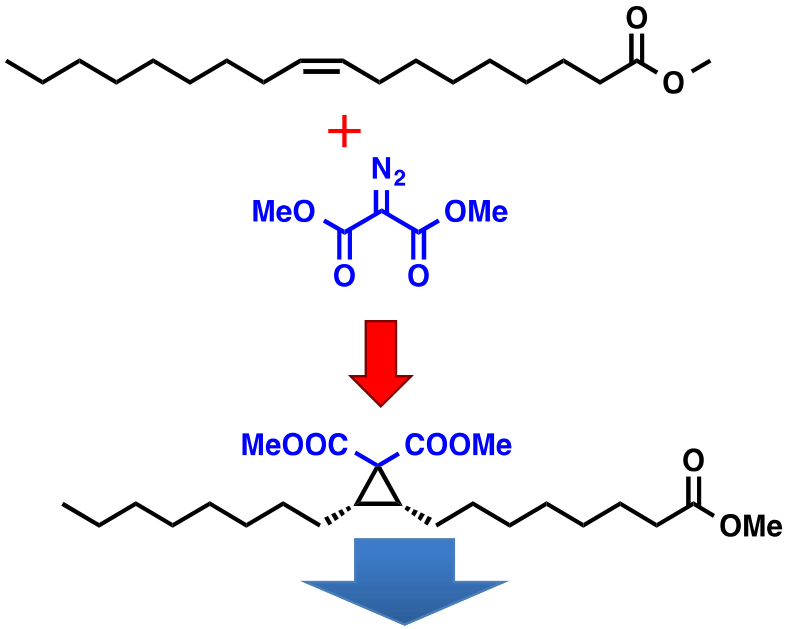
- 1% $Cu(OTf)_2$
- CH_2Cl_2
- r.t.
- 15h
- Methyl erucate/EDA =1:3

>99% yield

***trans/cis* = 69/31**

Cyclopropanation with MDM

Reaction with methyl oleate



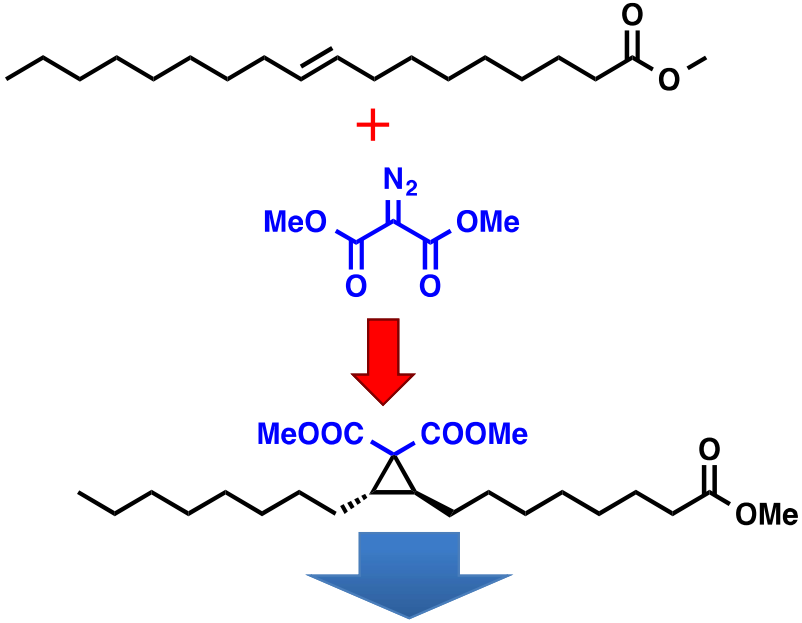
Optimal conditions:

- **2%** $Cu(OTf)_2$
- **1,2-dichloroethane**
- **Reflux**
- **24h**
- Methyl oleate/MDM = **1:6**

>99% yield

MDM is **less reactive** than EDA

Reaction with methyl elaidate



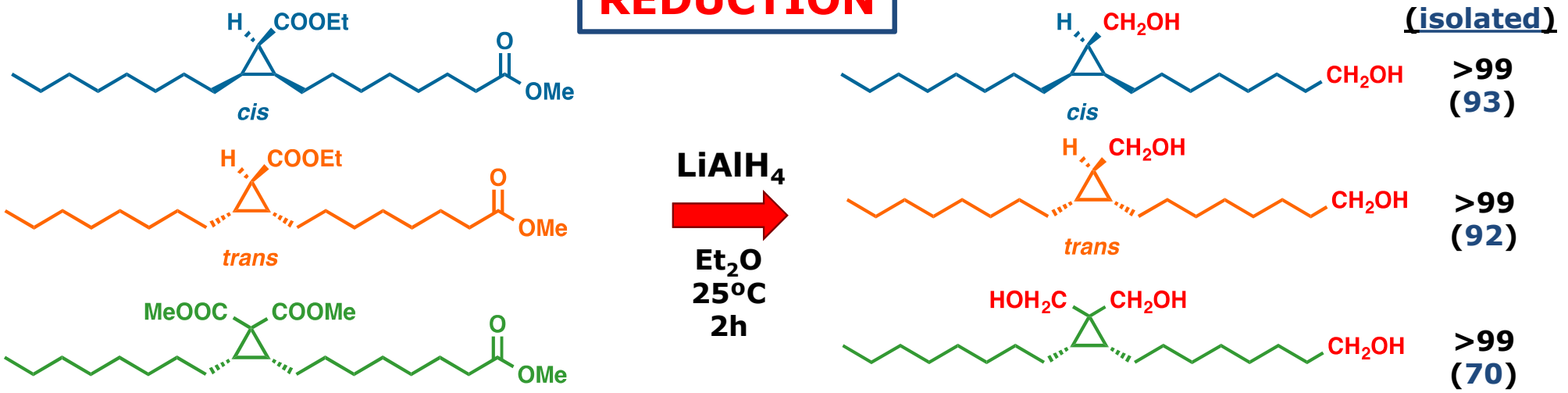
Optimal conditions:

- **4%** $Cu(OTf)_2$
- **1,2-dichloroethane**
- **Reflux**
- **48h**
- Methyl elaidate/MDM = **1:7**

55% yield

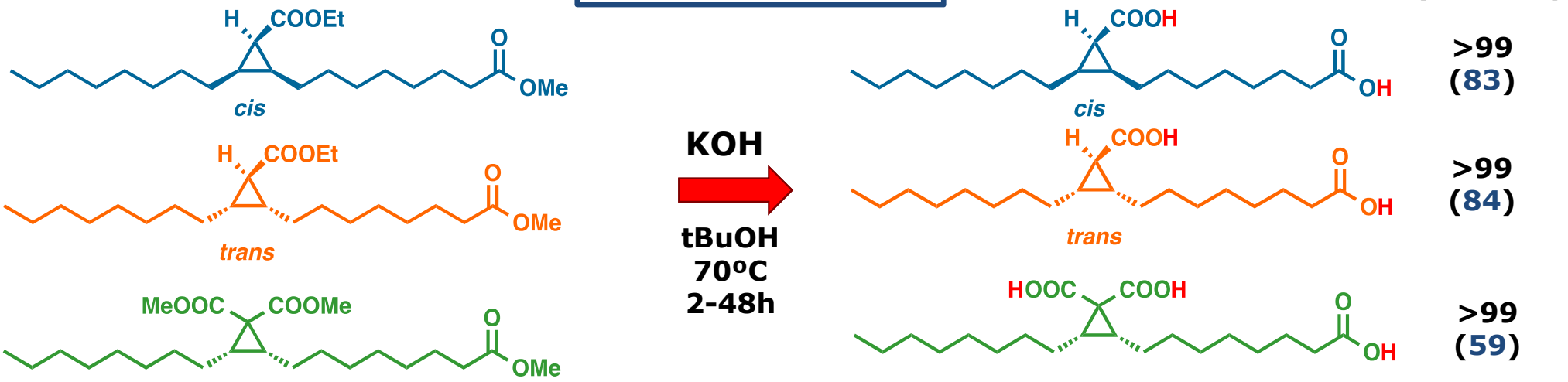
REDUCTION & HYDROLYSIS REACTIONS

REDUCTION



% Yield (isolated)
>99 (93)
>99 (92)
>99 (70)

HYDROLYSIS



% Yield (isolated)
>99 (83)
>99 (84)
>99 (59)

CONCLUSIONS

- It has been possible to carry out the cyclopropanation reaction between different fatty esters and ethyl diazoacetate (**EDA**) in **only one step** with **quantitative yields**, using **1% of catalyst** ($Cu(OTf)_2$) and **mild conditions**.

- The cyclopropanation with methyl diazomalonate (**MDM**) needed **harsher reaction conditions** because of the lower reactivity of this reagent. Even so, we were able to obtain yields from moderate to excellent.

- The products obtained in the cyclopropanation reaction have been easily transformed into **diacids, triacids, diols and triols**. These compounds have the potential to be used as monomers or co-monomers in **polymerization reactions** for the obtaining of new materials.

ACKNOWLEDGEMENTS

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Consolidate group E11

Thanks for your attention

Research Group "HETEROGENEOUS CATALYSIS FOR SELECTIVE ORGANIC SYNTHESIS"

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