Supporting Information

Mechanistic Rationalization of Organocatalyzed Conjugate Addition of Linear Aldehydes to Nitro-Olefins

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1. Materials and General Procedures

Dry toluene was obtained by passing the previously degassed solvent through activated alumina column. Toluene-d8 was purchased from Cambridge Isotope Laboratories, Inc. (D, 99.5%) in ampoules of 1 mL. Propanal (97%) and *trans*-β-nitrostyrene (98%) were purchased from Alfa Aesar and the propanal was always carefully distilled prior to use. The (*S*)-(–)-α,α-diphenyl-2-pyrrolidinemethanol trimethylsilyl ether was purchased from Sigma-Aldrich.

NMR spectra were recorded on Bruker DRX-600 equipped with a 5 mm DCH cryoprobe, DRX-500, and AMX-400 instruments and calibrated using residual undeuterated solvent as an internal reference (toluene δ_H 2.09 ppm ^{1}H NMR, δ_C 20.4 ppm ^{13}C NMR) unless stated otherwise. The following abbreviations (or combinations thereof) were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, m = multiplet, br = broad. High-resolution mass spectra (HRMS) were recorded on Agilent ESI-TOF using ACN as a cosolvent. High performance liquid chromatography (HPLC) was performed on Hitachi L-7400 UV detector (λ = 254 nm) using Daicel Chiralpak OD-H column (0.46 x 25 cm) using hexane-^{i}PrOH 97:3 (1 mL/min). The retention times for the different stereoisomers were: t_R (2*S*,3*R*) = 41.57 min, t_R (2*R*,3*R*) = 55.47 min, t_R (2*R*,3*S*) = 63.79 min, t_R (2*S*,3*S*) = 79.09 min.

2. Procedures for calorimetry kinetics

Measurements were performed using an Omnical Insight reaction calorimeter, which allows continuous monitoring of the instantaneous heat absorbed or released by a chemical reaction occurring in the vessel. The sample vessel is a 16 mL septum-cap vial equipped with a magnetic stirring bar. The system operates as a differential scanning calorimeter by comparing the heat released or consumed in a sample vessel with that from a reference compartment at intervals of 2-6 seconds over the course of the reaction.

An energy balance around the vessel for the case of a single reaction occurring demonstrates that reaction heat flow, q, is proportional to the reaction rate, r and can be given as:

$$q = r\,\Delta H_{rxn}\,V$$

Where ΔH_{rxn} is the heat of the reaction and V is the reaction volume.

Typical experimental procedure:

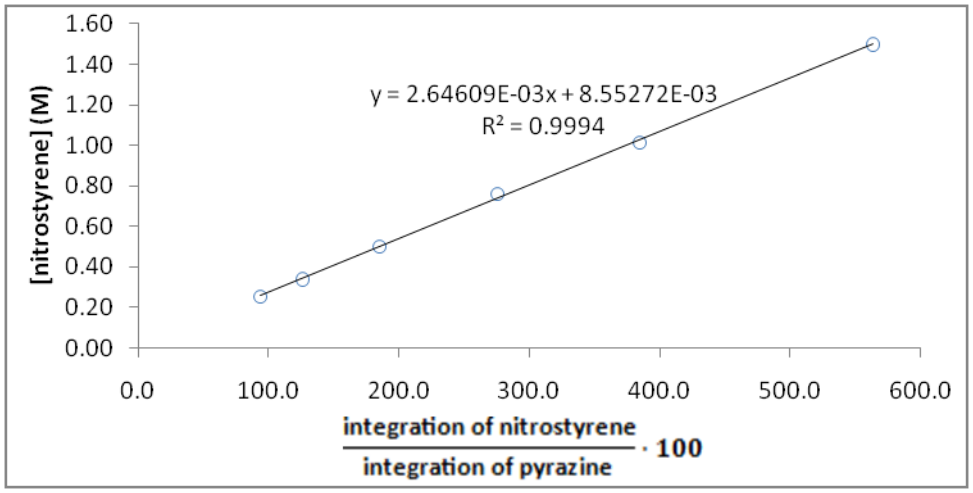
A fresh prepared stock solution of nitrostyrene and propanal (and product or water if needed) in toluene was placed in a vessel. The vessel was placed in the calorimeter and stirred until thermal equilibrium at 25 ºC was reached. A syringe containing a known amount of (*S*)-(–)-α,α-diphenyl-2-pyrrolidinemethanol trimethylsilyl ether (and acetic acid if needed) was placed in the sample injection port of the calorimeter and was as well allowed to reach thermal equilibrium (ca. 30 minutes). Once thermal equilibrium was reached, reaction was initiated by injecting the catalyst solution into the reaction mixture. At the end of the reaction a sample taken from the reaction vessel was quenched with a diluted solution of HCl and analyzed by NMR to obtain the conversion.

3. Procedures for NMR kinetics

All these experiments were performed in a Bruker DRX-500 instrument. In these experiments a capillary with pyrazine was used as a reference (pyrazine δ_H 8.34 ppm) to quantify the concentrations of the species. In order to obtain quantitative data we measured the 90 degree flip angle (**P1/4**) and the longitudinal relaxation time (**T1**) for every species. All the species minus propanal had relaxation times lower than 4.7 s (relaxation time for the pyrazine) in the standard conditions of the experiment. To assure that all signal integrations are quantitative we used 4 scans with a relaxation delay (**D1**) of 24 s.

To calibrate the capillary we used six solutions of a known concentration of nitrostyrene.

[nitrostyrene]	$\frac{\text{integration of nitrostyrene}}{\text{integration of pyrazine}} \cdot 100$
0.25	563.4
0.34	184.9
0.50	384.8
0.76	126.5
1.01	275.7
1.50	93.9



Typical experimental procedure:

0.5 mL of a fresh prepared stock solution of nitrostyrene and propanal (and product or water if it was needed) in toluene-d8 was placed in an NMR tube. 100 µL of a fresh stock solution of (*S*)-(–)-α,α-diphenyl-2-pyrrolidinemethanol trimethylsilyl ether (and acetic acid if needed) was added to the NMR tube, the solution was shaked and this time was taken as time zero of the reaction and the capillary was introduced in the NMR tube. Automatic spectra, of 4 scans with a 24 s acquisition delay (**D1**) between scans, were registered automatically every 115 seconds in average.

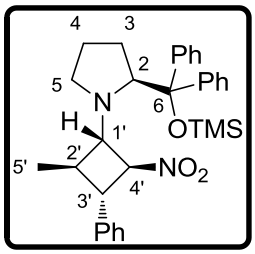
The spectra obtained were processed manually to obtain the concentration of each species during the reaction.

4. Identification and characterization of crucial intermediates

4.1. Propanal cyclobutane species (5)

It was not possible to isolate the compound **5** as a pure compound in spite of several trials. It is described in the literature that this kind of cyclobutanes with this substitution pattern and no bulky substituents cannot be isolated.[1]

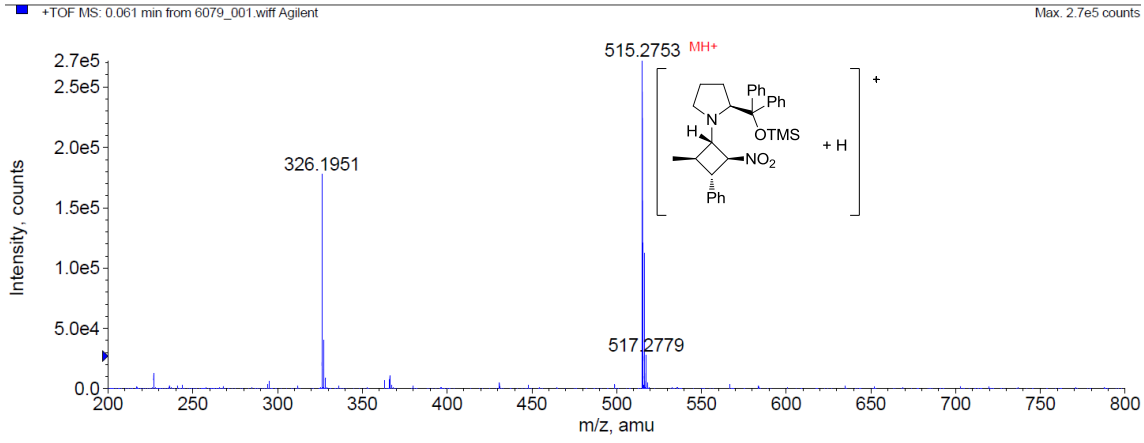
To identify and characterize the off-cycle reservoir cyclobutane species the reaction was carried out adding 100 µL (0.10 mmol) of a 1.0 M solution of (*S*)-(–)-α,α-diphenyl-2-pyrrolidinemethanol trimethylsilyl ether in toluene-d8 to 500 µL (0.05 mmol of propanal and 0.05 mmol of nitrostyrene) of a 0.1 M solution of propanal and nitrostyrene in toluene-d8 placed in a NMR tube in the presence of 4 Å molecular sieves.



(2*S*)-(diphenyl((trimethylsilyl)oxy)methyl)-1-((1'*S*,2'*R*,3'*S*,4'*S*)-2'-methyl-4'-nitro-3'-phenylcyclobutyl)pyrrolidine (5): ^{1}H-NMR (400 MHz, toluene-d8) δ –0.07 (s, 9H; OTMS), 0.48–0.63 (m, 1 H; C(4)H), 0.98–1.10 (br, 3 H; C(5')H_3), 1.11–1.21 (m, 1 H; C(4)H), 1.67–1.95 (m, 3 H; C(3)H_2, C(2')H), 2.18–2.37 (m, 2 H; C(5)H_2), 3.21 (t, 1 H, J = 9.0; C(3')H), 4.00–4.18 (br, 1 H; C(1')H), 4.36 (dd, 1 H, J = 9.5, J = 2.9; C(2)H), 4.93 (t, 1 H, J = 9.0; C(4')H); **^{13}C-NMR** (100.6 MHz, toluene-d8) δ 85.3 (C6), 82.1 (C4'), 69.7 (C1'), 68.6 (C2), 48.3 (C5), 46.2 (C3'), 37.2 (C2'), 29.3 (C3), 24.1 (C4), 18.3 (C5'), 2.1 (OTMS). **HRMS** (+ESI-TOF) calcd. for $C_{31}H_{39}N_2O_3Si$ $[M+H]^+$ 515.2724, found 515.2753.

The cyclobutane specie was prepared using an excess of catalyst in order to shift the equilibrium towards its formation. In addition, the excess of catalyst prevents the protonation of the zwitterion and therefore stabilize the cyclobutane. Molecular sieves were also used to capture the water generated in the reaction shifting the equilibrium and preventing the possible hydrolysis.

The HRMS shows a peak at 326.1951, which correspond to the free catalyst. The other only peak observed is 515.2753, which matches a compound with the molecular formula C31H39N2O3Si (calcd. 515.2724 $[M+H]^+$). This formula indicates that this compound is composed of one unit of catalyst, one unit of propanal and one unit of nitrostyrene.



[1] (a) Kuehne, M. E.; Foley, L., Reaction of Enamines with Nitro Olefins1. *The Journal of Organic Chemistry* **1965,** *30* (12), 4280-4284; (b) Felluga, F.; Nitti, P.; Pitacco, G.; Valentin, E., N-(2-Phenylprop-1-enyl)proline methyl ester: equilibrium between the enamine and the aza methine ylide form. *J. Chem. Soc., Perkin Trans. 1* **1992,** (18), 2331-5.

The proton ^{1}H-NMR and ^{13}C-NMR spectra shows a mixture of only two compounds, the new species formed and free catalyst.

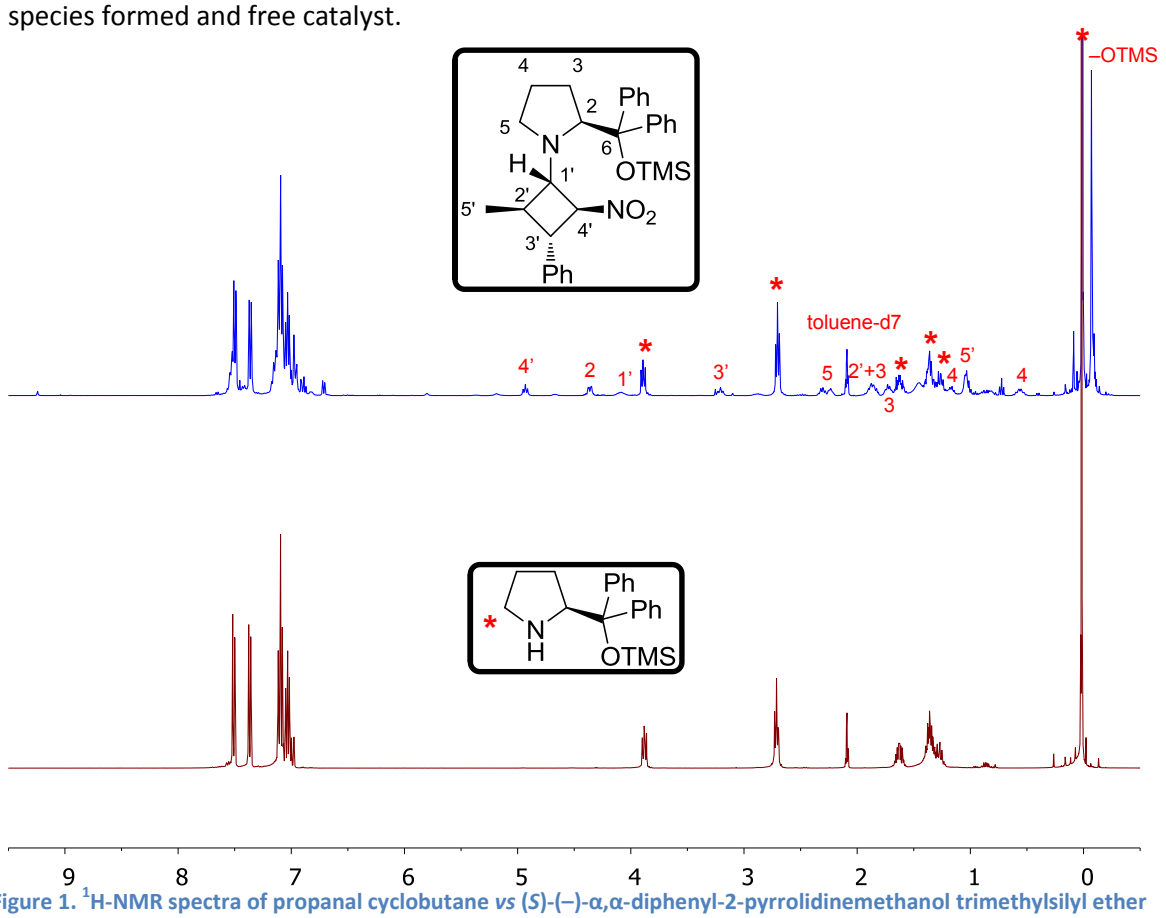


Figure 1. ^{1}H-NMR spectra of propanal cyclobutane *vs* (*S*)-(–)-α,α-diphenyl-2-pyrrolidinemethanol trimethylsilyl ether

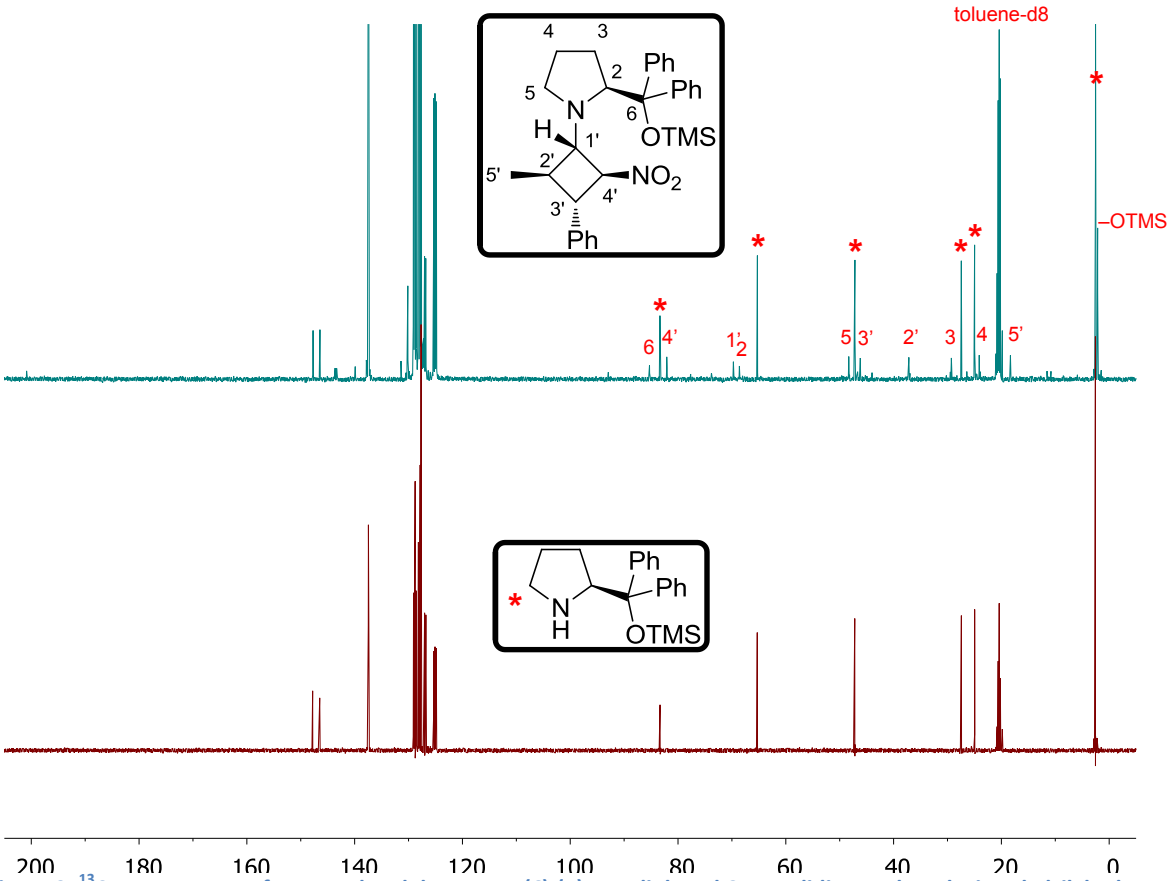


Figure 2. ^{13}C-NMR spectra of propanal cyclobutane *vs* (*S*)-(–)-α,α-diphenyl-2-pyrrolidinemethanol trimethylsilyl ether

The signal at 4.36 ppm is assigned as C(2)H because the HSQC (Figure 3) spectrum shows that it is a CH/CH_3 type signal and correlates with C(6) in the HMBC (Figure 4), that is assigned as a quaternary carbon because it does not correlate with any proton in the HSQC (Figure 3). Using the COSY (Figure 5) it is possible to assign the proton signals of the pyrrolidine ring entirely (3, 4 and 5) and this is further confirmed by the fact that these signals correspond to CH_2 type carbons in the HSCQ (Figure 3).

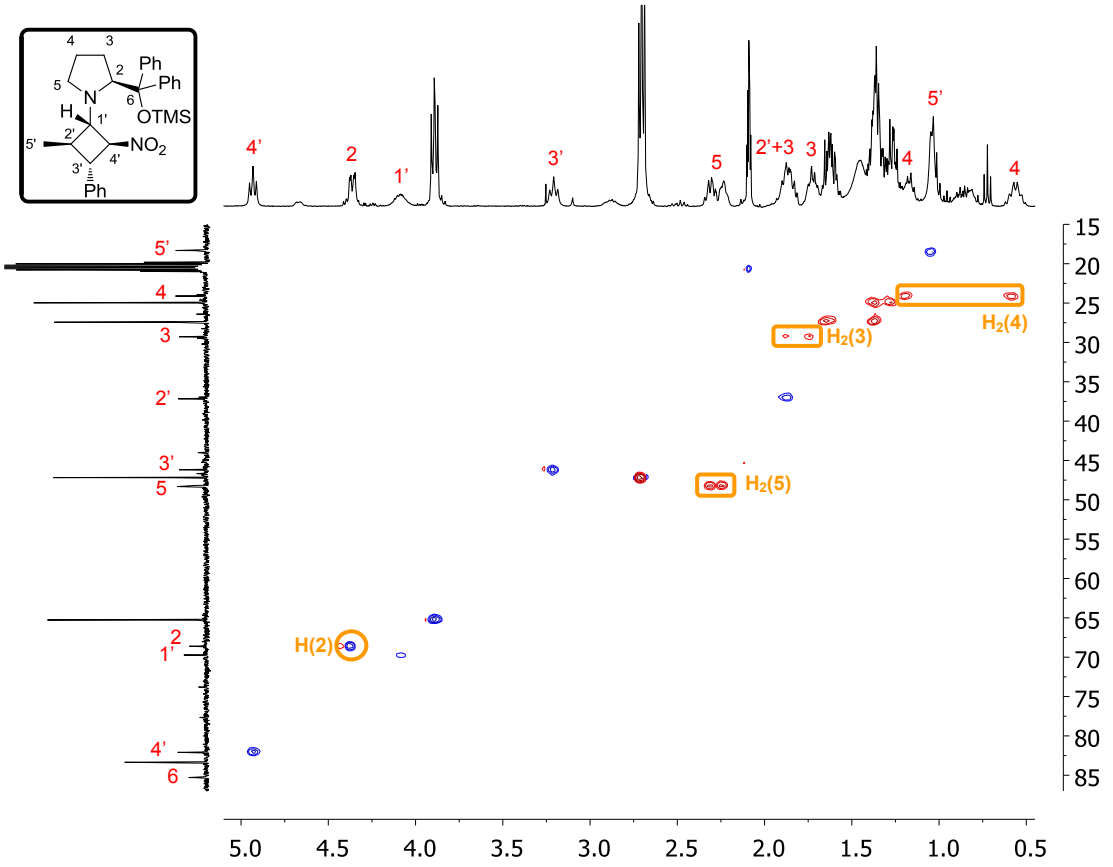


Figure 3. HSQC of propanal cyclobutane (5)

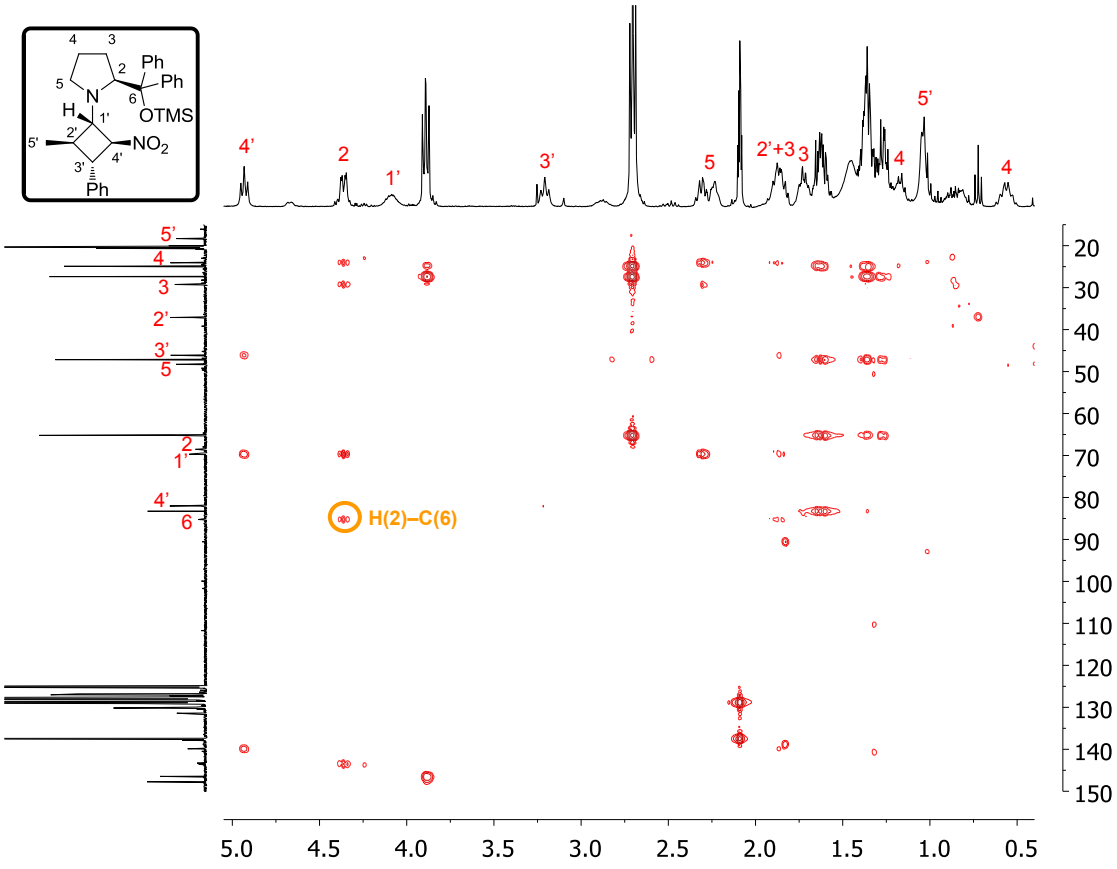


Figure 4. HMBC of propanal cyclobutane (5)

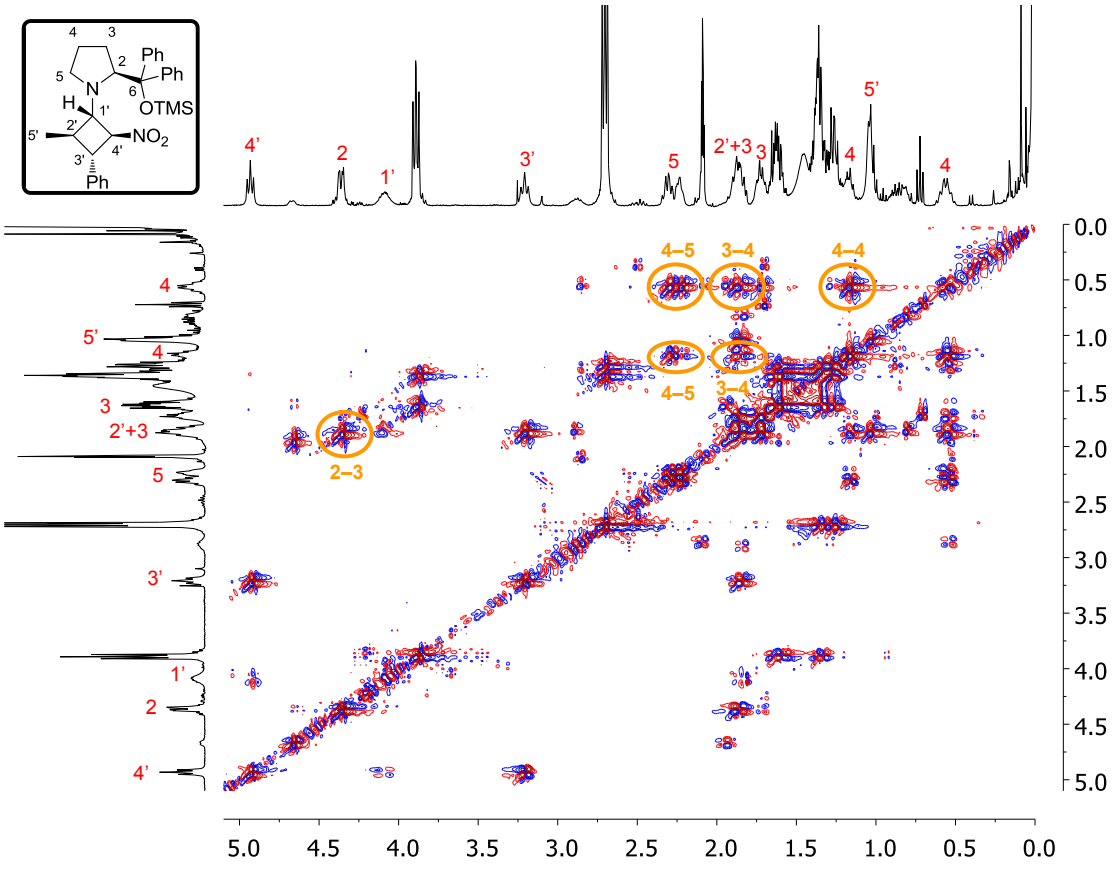


Figure 5. COSY of propanal cyclobutane (5)

HMBC (Figure 6) reveals a correlation between a carbon signal at 69.7 ppm and both H(2) and H_2(5). This new carbon center is not part of the pyrrolidine ring. Due to the chemical shift and C-H correlation the carbon signal at 69.7 ppm is as assigned to C(1').

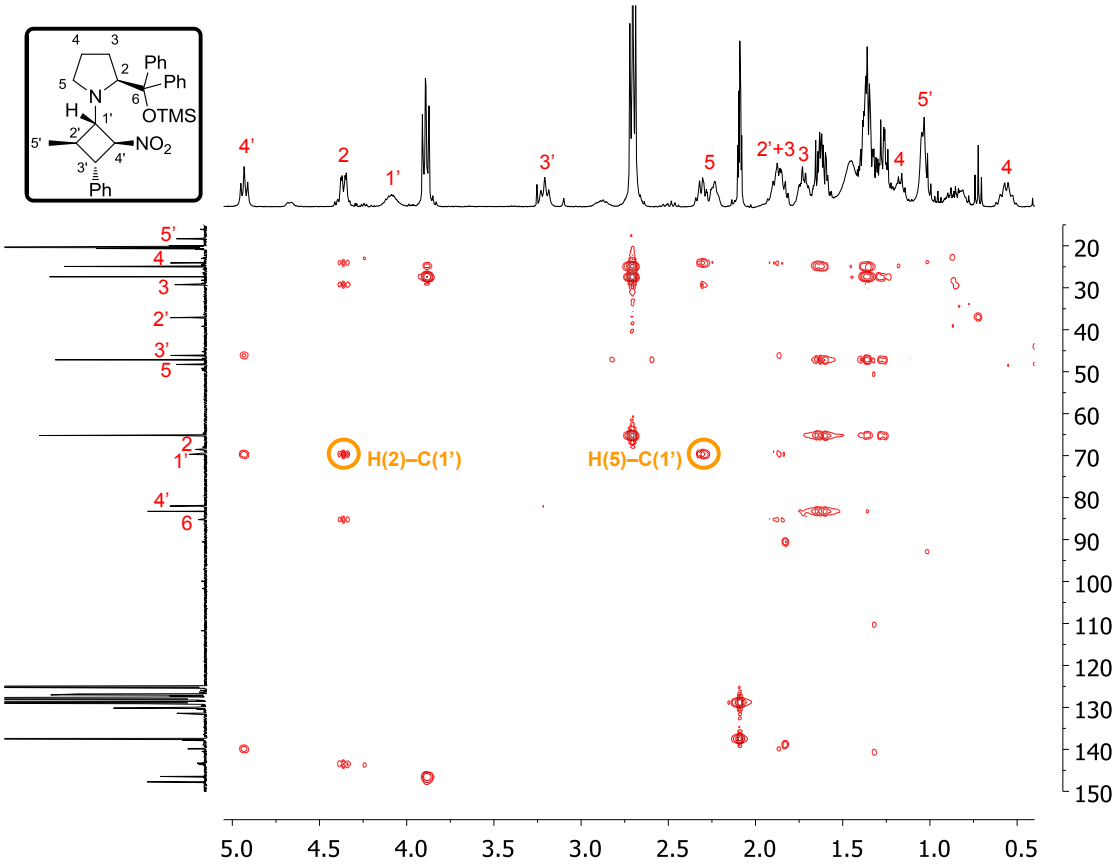
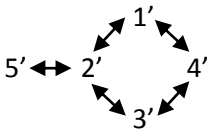


Figure 6. HMBC of propanal cyclobutane (5)

The COSY (Figure 7) clearly outlines the cyclobutane proton spin system via the correlation of H1' to H2', H2' to both H5' and H3', H3' to H4' and H4' to H1'. This last connection is key to prove the cyclobutane existence.



In addition, the HMBC (Figure 8) shows a clear signal of correlation between H4' and C1' that is not possible without the cyclobutane structure. Also, the HSCQ (Figure 9) confirms that centers C1´, C2´, C3´and C4´are CH.

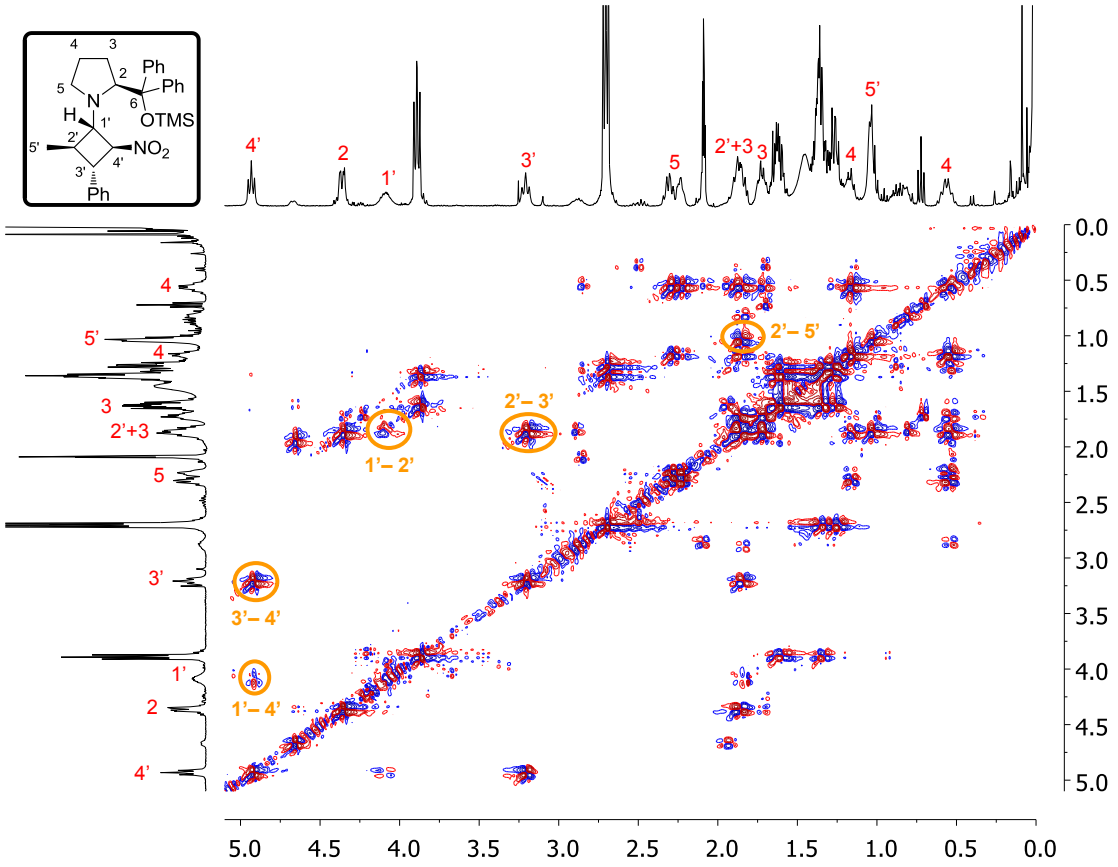


Figure 7. COSY of propanal cyclobutane (5)

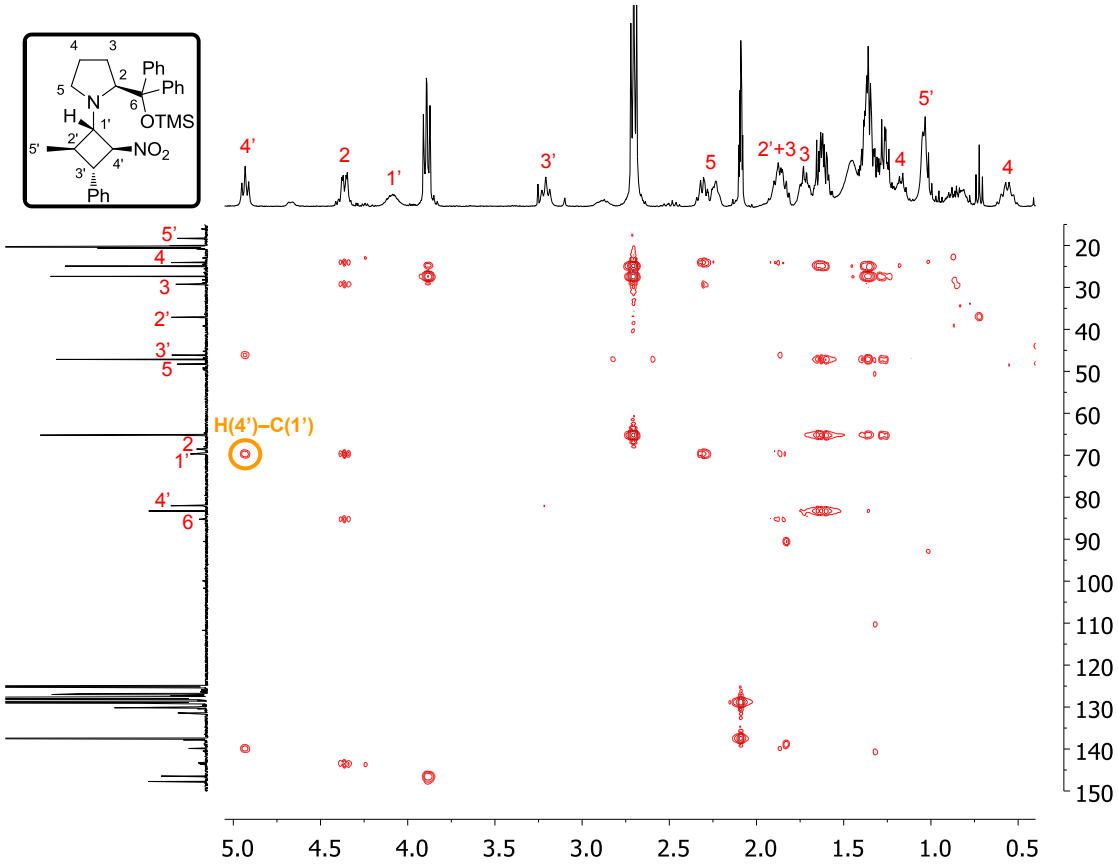


Figure 8. HMBC of propanal cyclobutane (5)

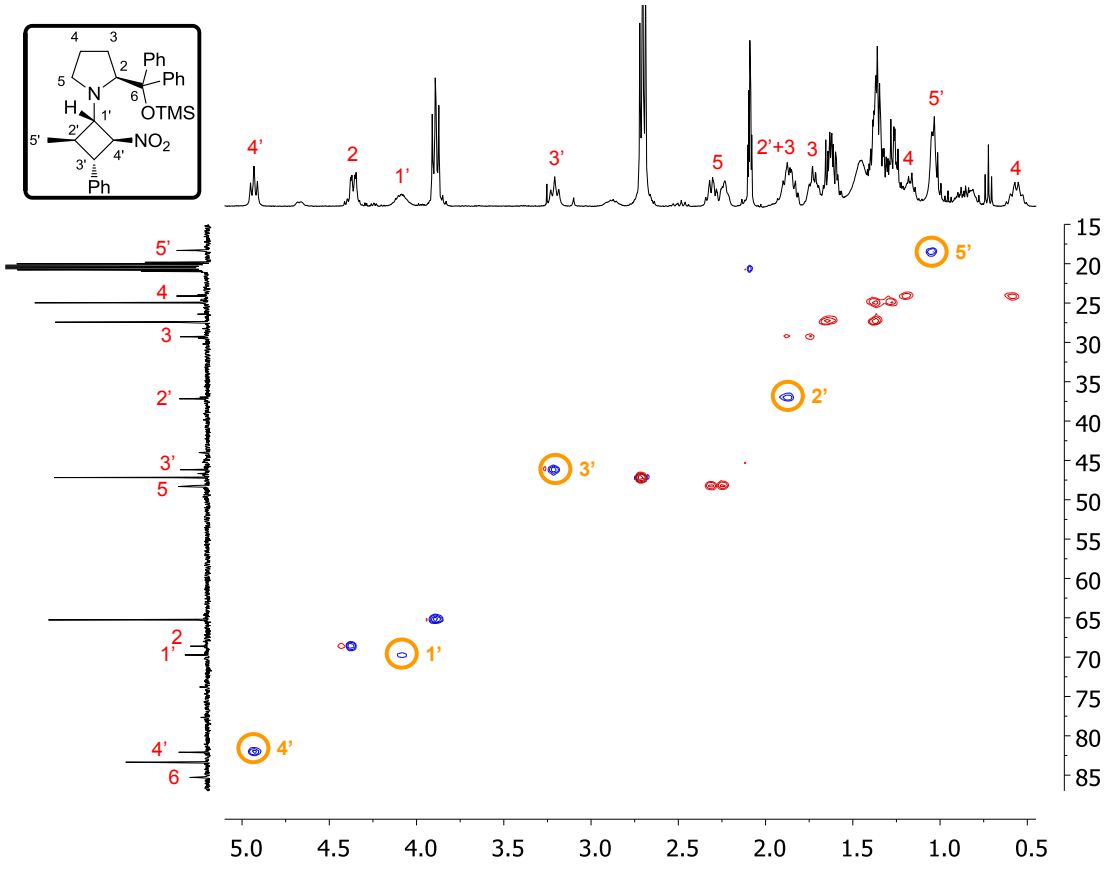


Figure 9. HSQC of propanal cyclobutane (5)

In addition, the integrations (^{1}H-NMR) and chemical shifts (^{1}H and ^{13}C-NMR) of all the assigned signals agree with the proposed cyclobutane structure.

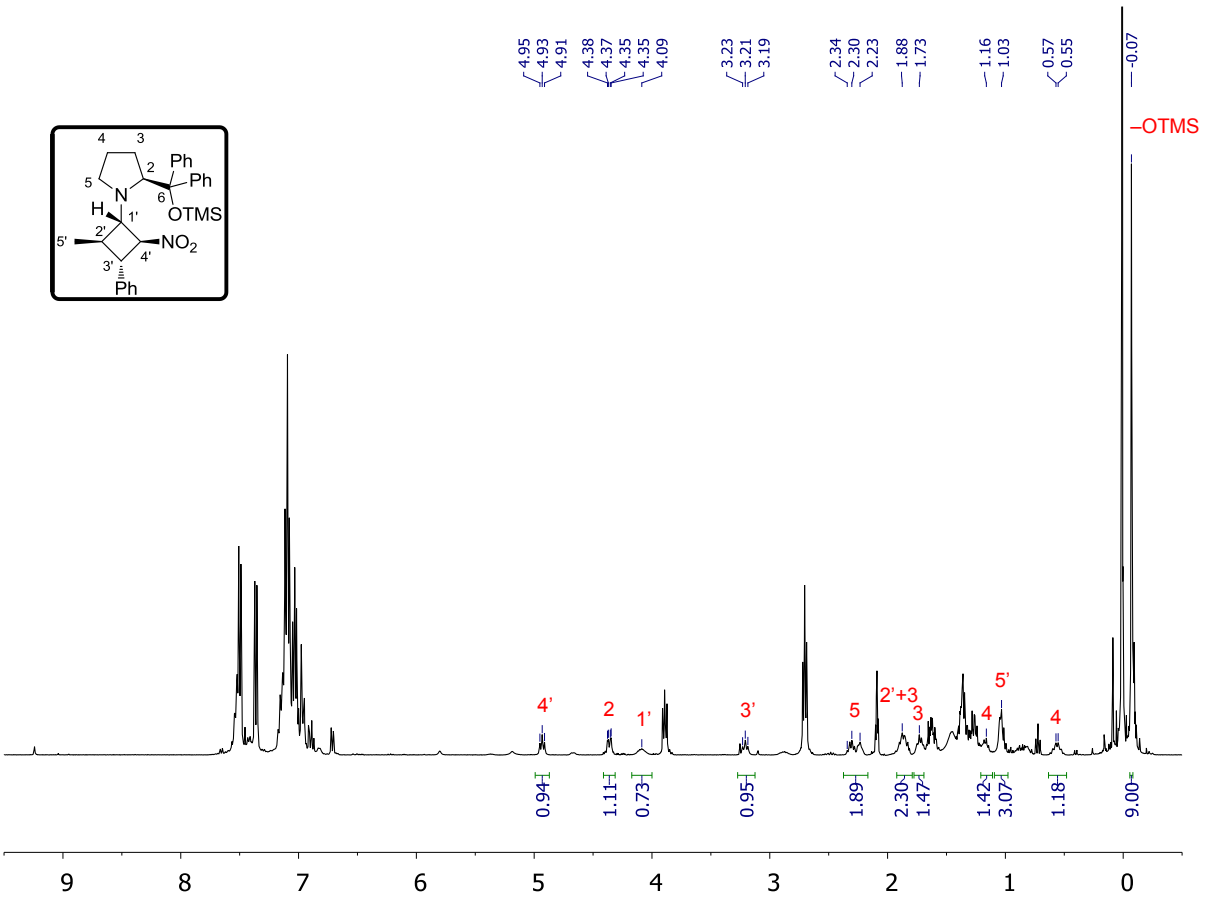


Figure 10. ^{1}H-NMR of propanal cyclobutane (5)

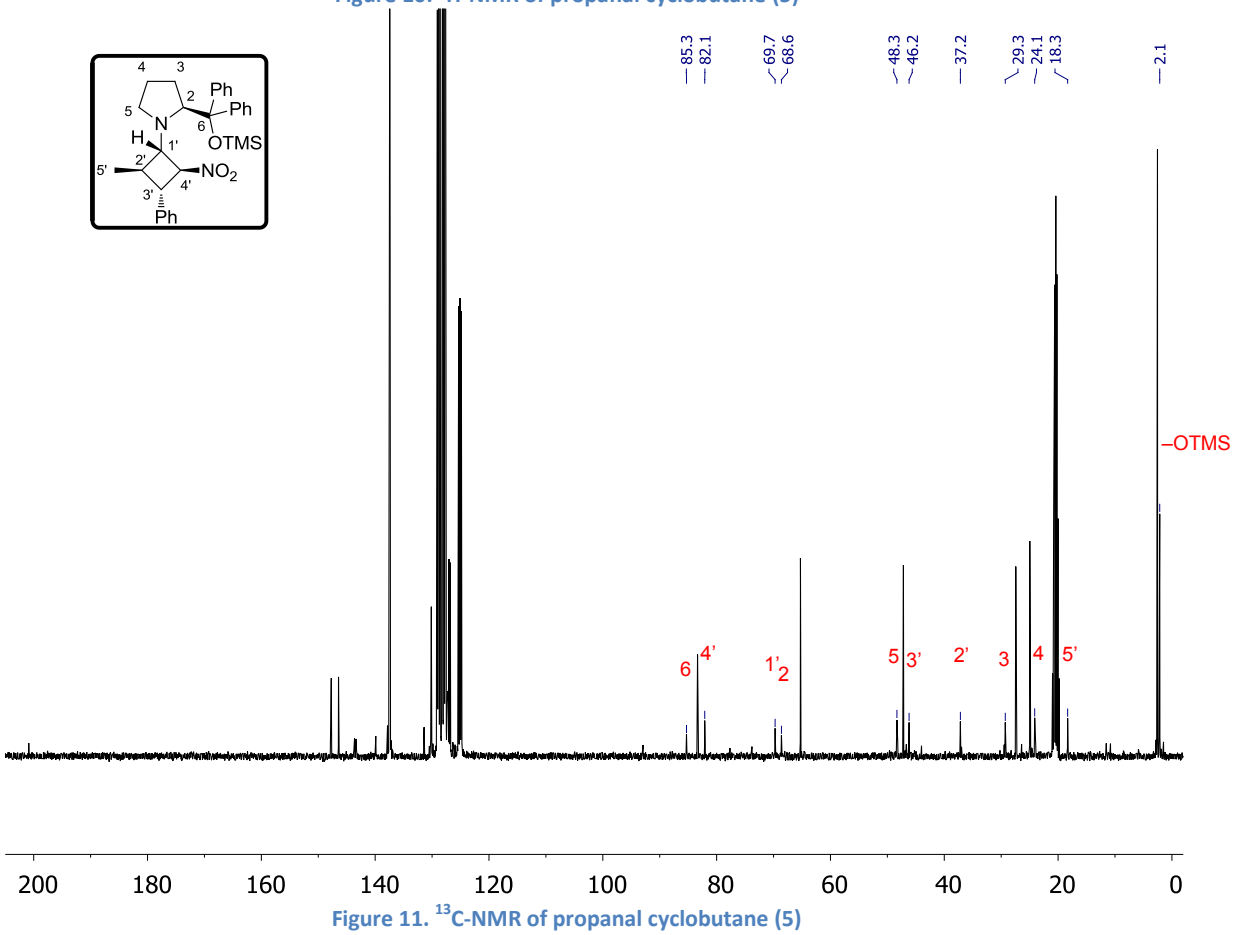


Figure 11. ^{13}C-NMR of propanal cyclobutane (5)

The relative stereochemistry of the cyclobutane was assigned by a NOESY spectrum. nOe contacts between H1'–H3', H1'–H5', H3'–H5' and H2'–H4' were observed. This confirms the relative *trans* orientation of all the substituents in the cyclobutane ring.

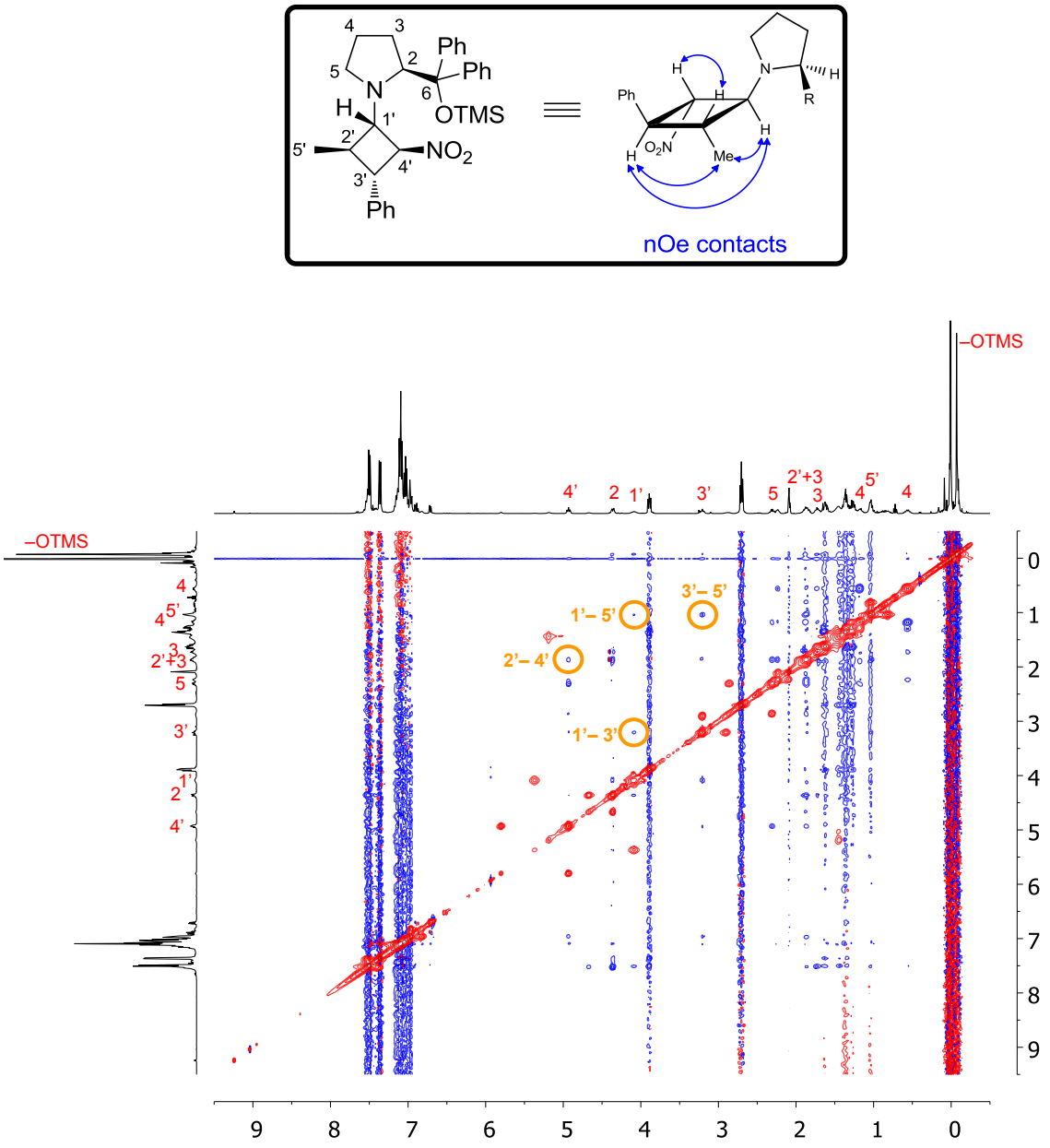
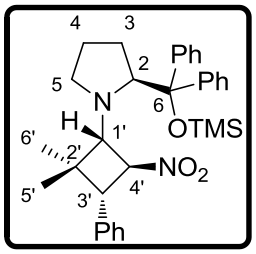


Figure 12. NOESY of propanal cyclobutane (5)

4.2. Isobutyraldehyde cyclobutane identification in the reaction media (13)

100 µL (0.06 mmol) of a 0.6 M solution of (*S*)-(–)-α,α-diphenyl-2-pyrrolidinemethanol trimethylsilyl ether in toluene-d8 to a 0.4 mL (0.60 mmol of *β*-nitrostyrene and 0.72 mmol of isobutyraldehyde) of a solution of *β*-nitrostyrene (1.5 M) and isobutyraldehyde (1.8 M) in toluene-d8.



(*S*)-1-((1*S*,3*R*,4*S*)-2,2-dimethyl-4-nitro-3-phenylcyclobutyl)-2-(diphenyl((trimethylsilyl)oxy)methyl)pyrrolidine (13): ^{1}H-NMR (400 MHz, toluene-d8) δ –0.05 (s, 9H; OTMS), 0.67 (s, 3 H; C(5')H_3 or C(6')H_3), 0.63–0.76 (m, 1 H; C(4)H), 1.48–1.57 (m, 1 H; C(4)H), 1.93–2.04 (m, 1 H; C(3)H), 2.17–2.26 (m, 1 H; C(3)H), 2.38–2.50 (m, 1 H, C(5)H), 2.83–2.93 (m, 1 H, C(5)H), 3.51 (d, 1H, *J* = 8.9; C(3')H), 4.58 (d, 1 H, *J* = 8.9; C(1')H), 4.58 (dd, 1 H, *J* = 8.9, *J* = 3.4, C(2)H), 5.60 (t, 1 H, *J* = 8.9).

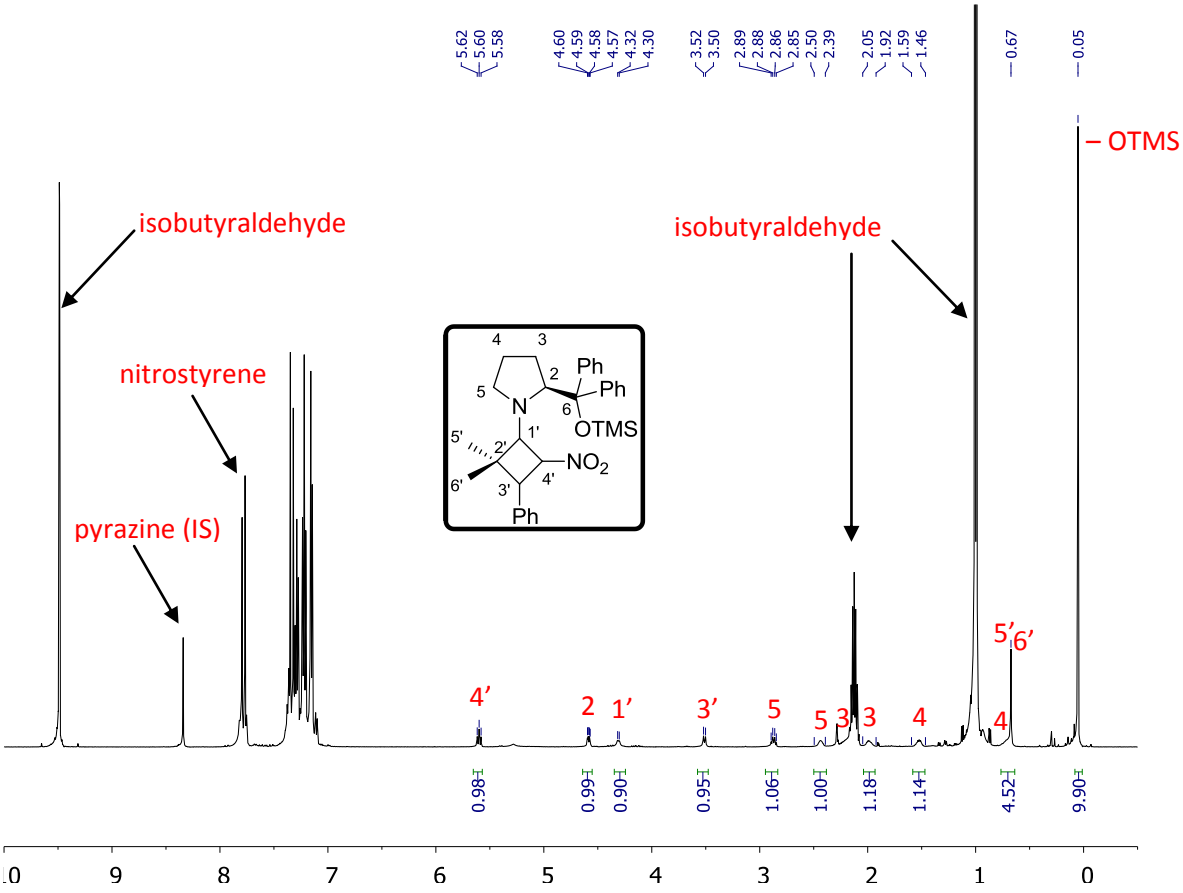


Figure 13. ^{1}H-NMR of the crude reaction that contains isobutyraldehyde cyclobutane

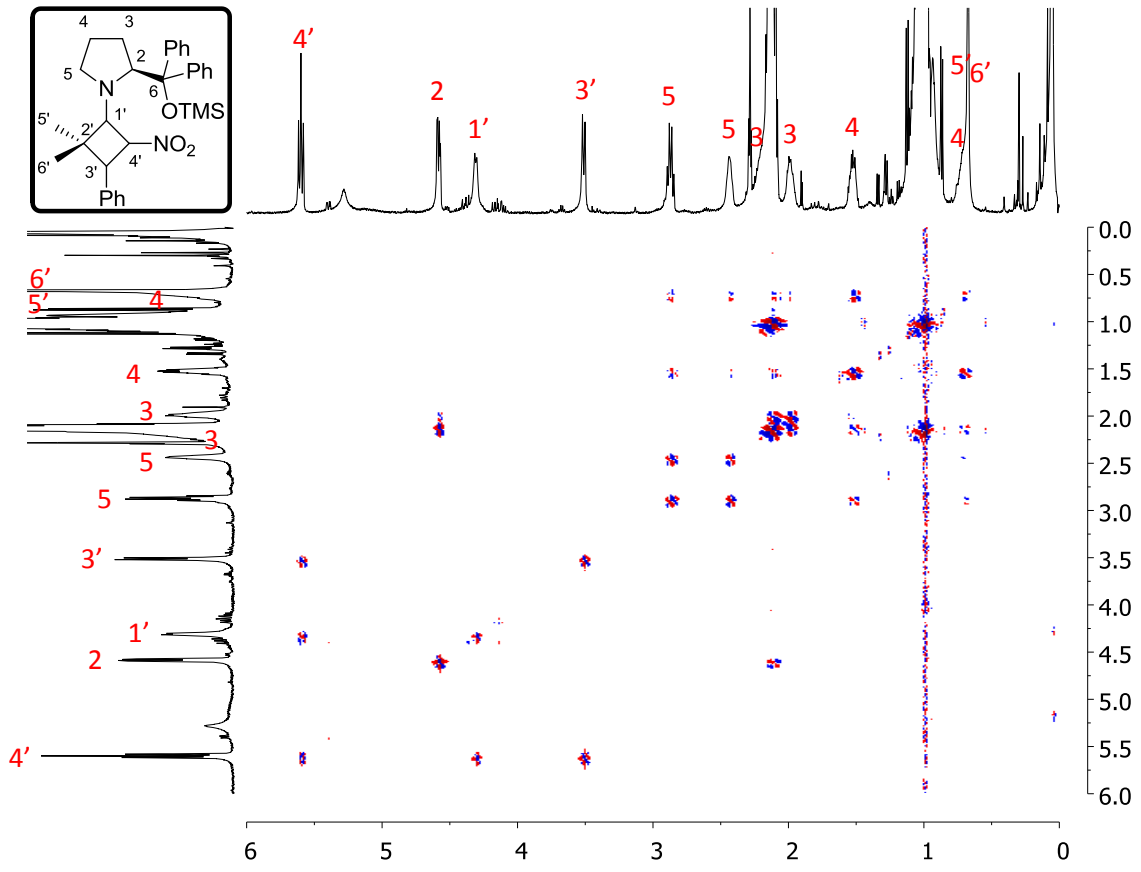
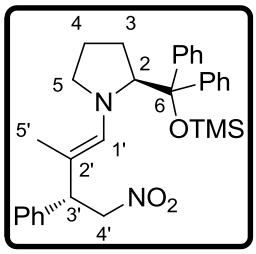


Figure 14. COSY of the crude reaction that contains isobutyraldehyde cyclobutane

4.3. Product enamine (6)

31.5 mg (0.094 mmol) of (*S*)-(–)-α,α-diphenyl-2-pyrrolidinemethanol trimethylsilyl ether was added to an NMR tube that contained 46.8 mg (0.226 mmol) of the enantiopure product of the reaction in 0.6 mL of toluene-d8 in the presence of 4 Å molecular sieves.



(2*S*)-(diphenyl((trimethylsilyl)oxy)methyl)-1-((*E*)-2'-methyl-4'-nitro-3'-phenylbut-1'-en-1'-yl)pyrrolidine: **^{1}H-NMR** (400 MHz, toluene-d8) δ –0.13 (s, 9H; OTMS), 0.84–0.87 (m, 1 H; C(4)H), 1.16–1.25 (m, 1 H; C(4)H), 1.32 (s, 3 H; C(5')H_3), 1.62–1.86 (m, 2 H; C(3)H_2), 2.60–2.72 (m, 2 H; C(5)H_2), 3.84–3.90 (m, 1 H; C(3')H), 4.07 (dd, 1 H, J = 8.4, J = 5.2; C(2)H), 4.18–4.29 (m, 2H; C(4')H_2), 5.96 (s, 1 H; C(1')H); **^{13}C-NMR** (100.6 MHz, toluene-d8) δ 140.7 (C1'), 110.4 (C2'), 84.2 (C4'), 73.0 (C2), 55.4 (C5), 50.7 (C3'), 28.2 (C3), 24.7 (C4), 12.8 (C5'), 2.1 (OTMS).

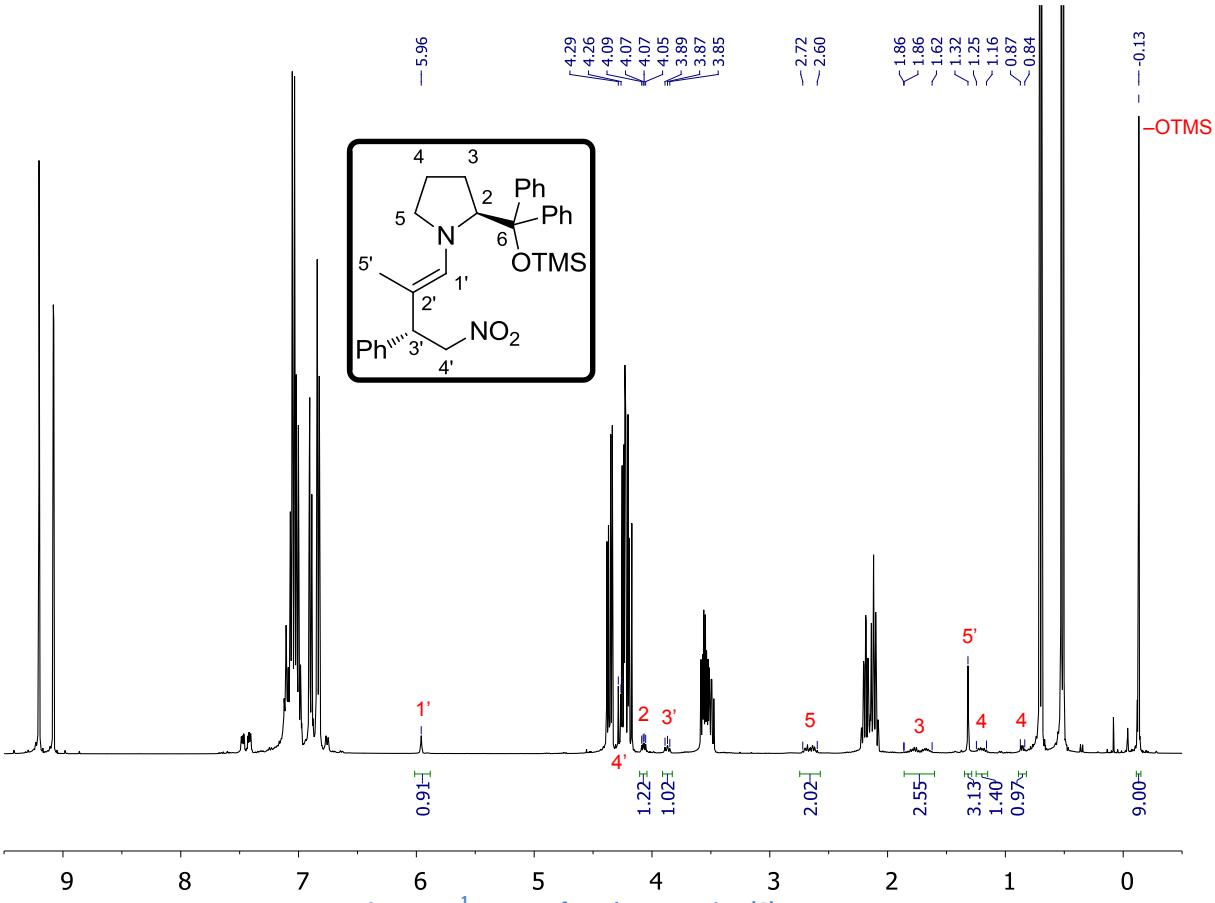


Figure 15. ^{1}H-NMR of product enamine (6)

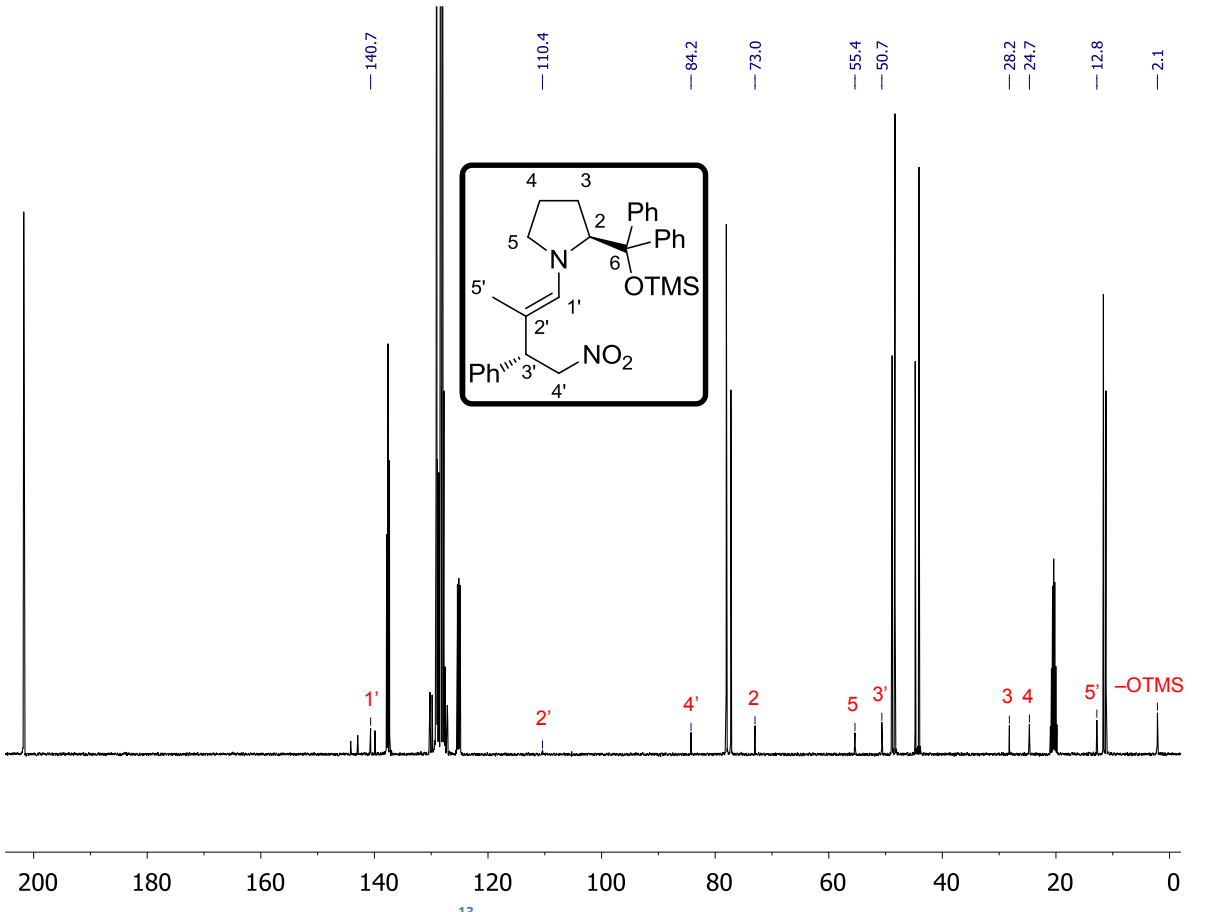


Figure 16. ^{13}C-NMR of product enamine (6)

4.4. Isobutyraldehyde enamine identification

300 µL (0.075 mmol) of a 0.25 M solution of isobutyraldehyde was added to 300 µL (0.075 mmol) of a 0.25 M solution of (*S*)-(–)-α,α-diphenyl-2-pyrrolidinemethanol trimethylsilyl ether.

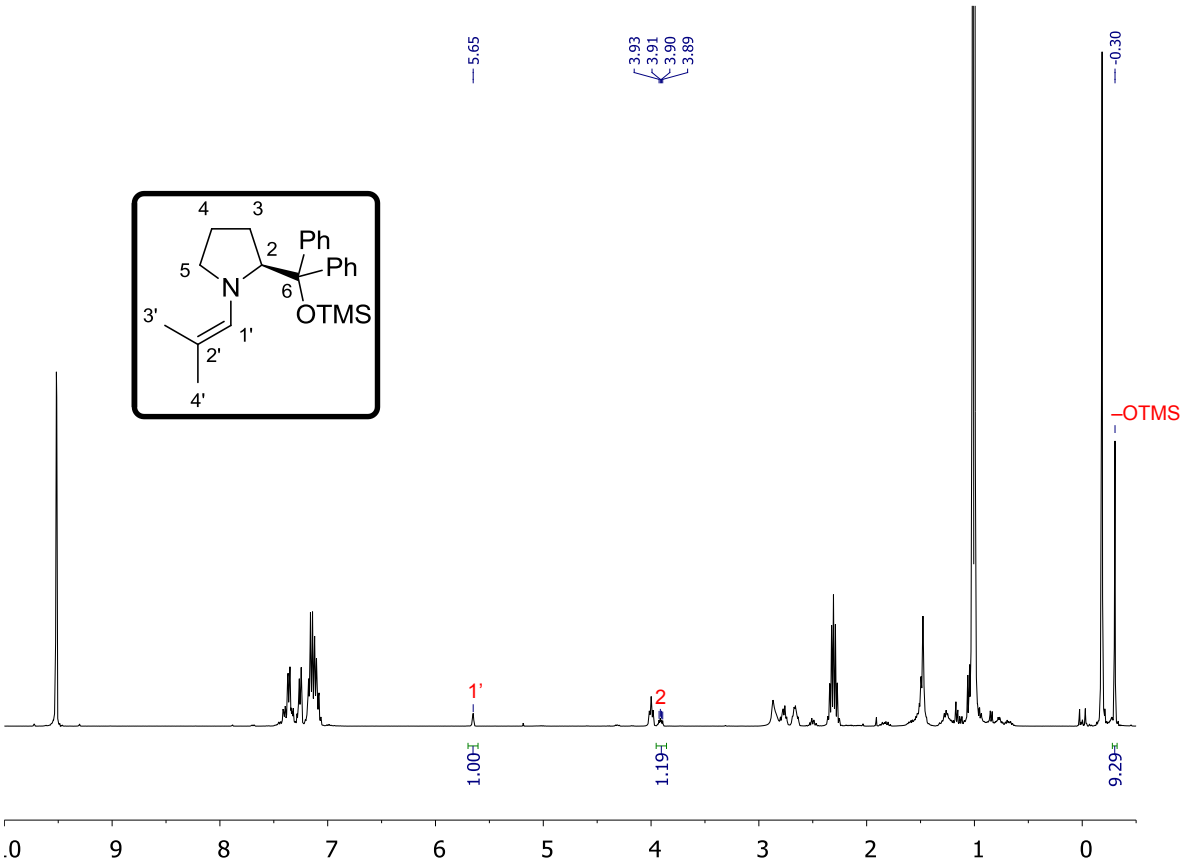


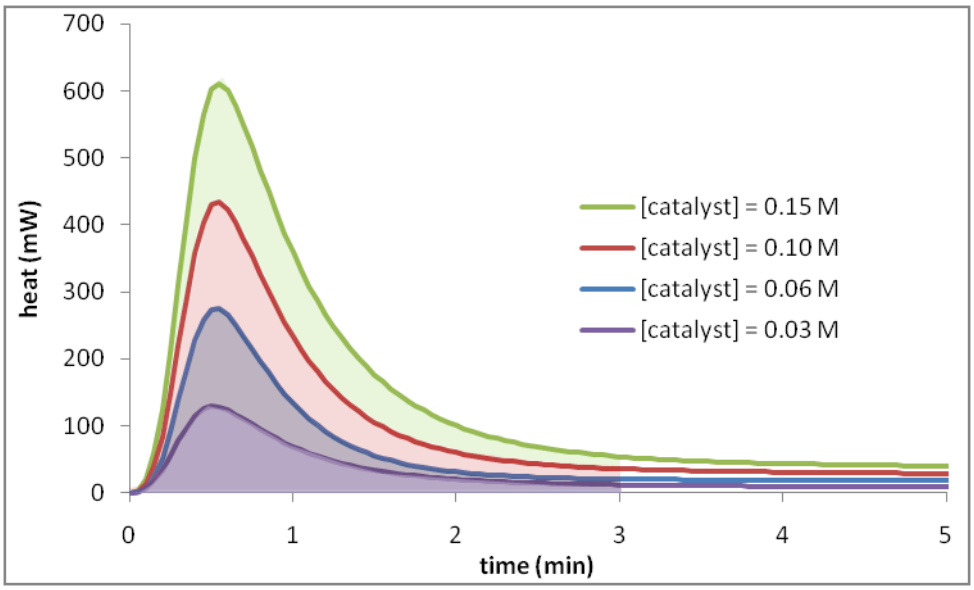
Figure 17. ^{1}H-NMR of isobutyraldehyde enamine with the characteristic signals used to quantify this intermediate

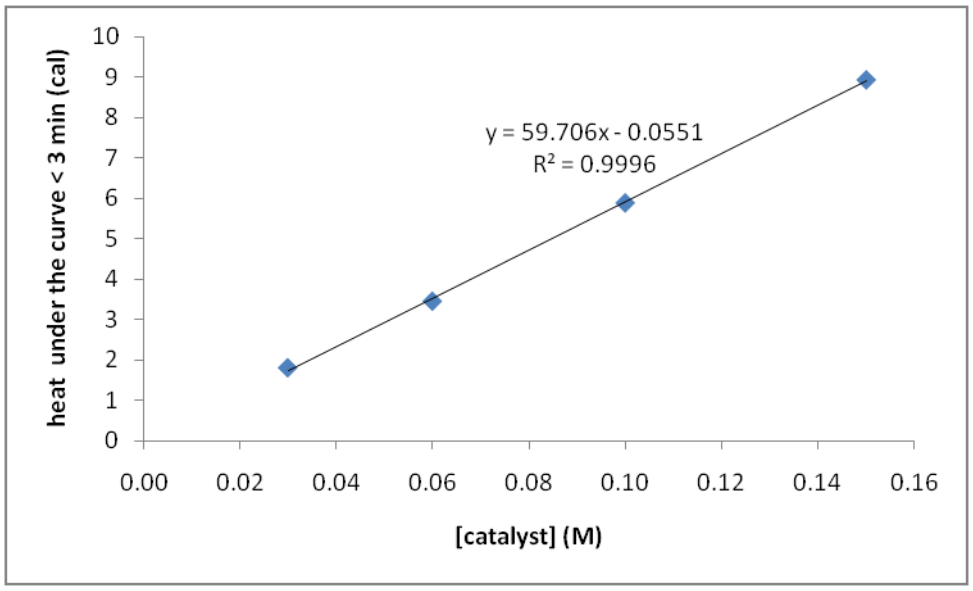
5. Experimental results

5.1. Relation between the initial spike and the [catalyst]

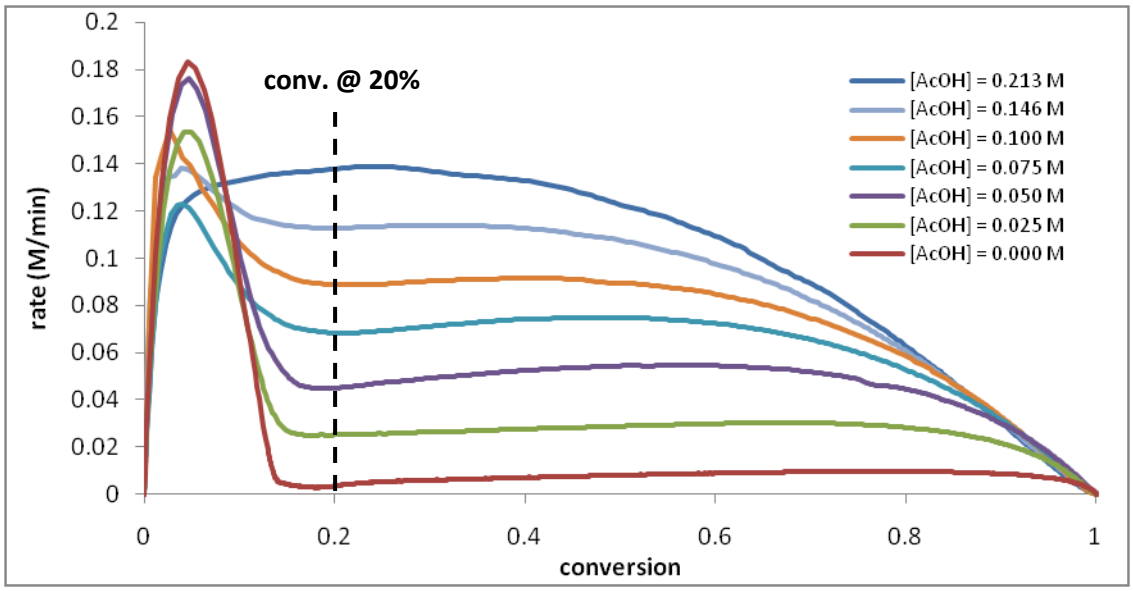
To show the direct relation between the heat of the initial spike and the [catalyst] we carried out the reaction with different concentrations of catalyst and the area under the curve until minute 3 was integrated.

[nitrostyrene]	[propanal]	[catalyst]	area (< 3 min)
1.0 M	1.2 M	0.03 M	1.804 cal
1.0 M	1.2 M	0.06 M	3.452 cal
1.0 M	1.2 M	0.10 M	5.888 cal
1.0 M	1.2 M	0.15 M	8.936 cal

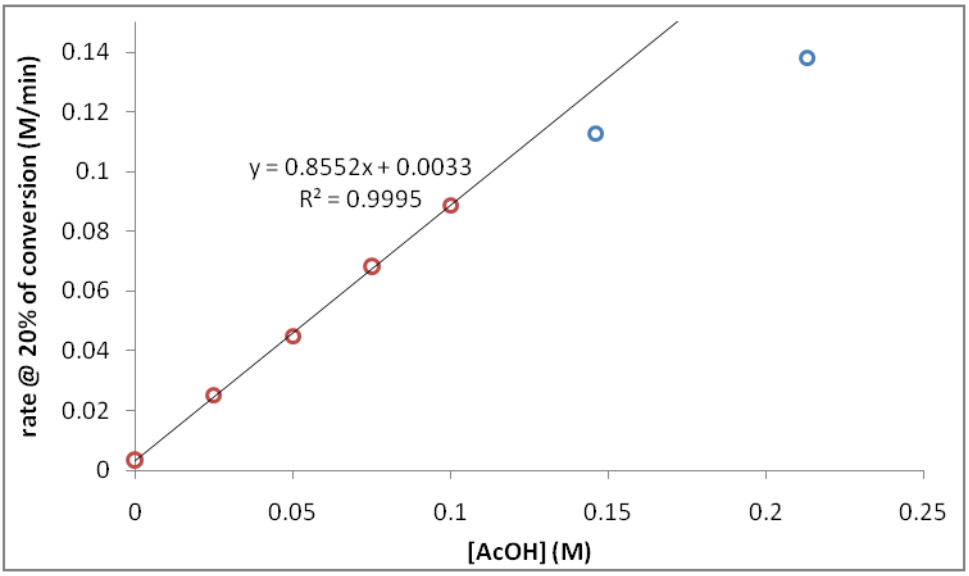




5.2. Effect of acid in the rate of the reaction



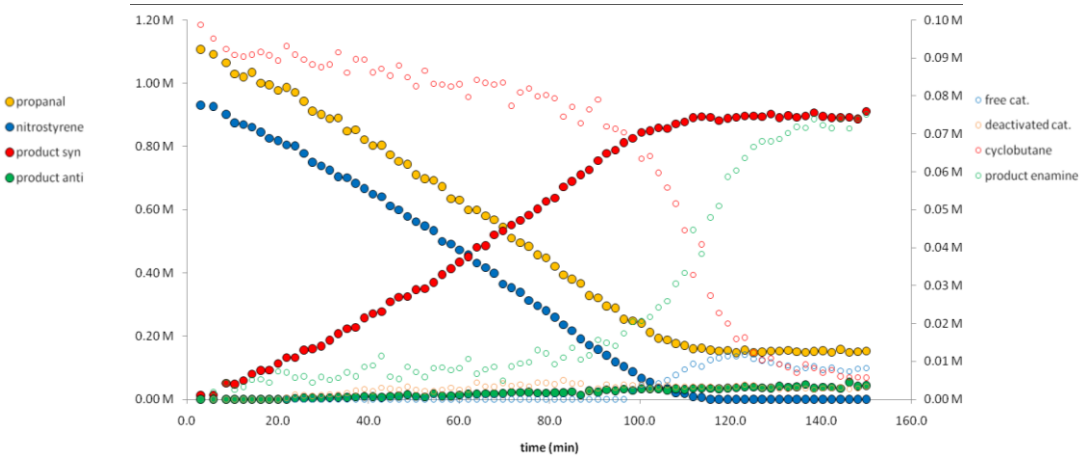
[AcOH]	rate @ 20% of conv.
0.000 M	0.0034 M/min
0.025 M	0.0251 M/min
0.050 M	0.0449 M/min
0.075 M	0.0683 M/min
0.100 M	0.0888 M/min
0.146 M	0.1127 M/min
0.213 M	0.1380 M/min



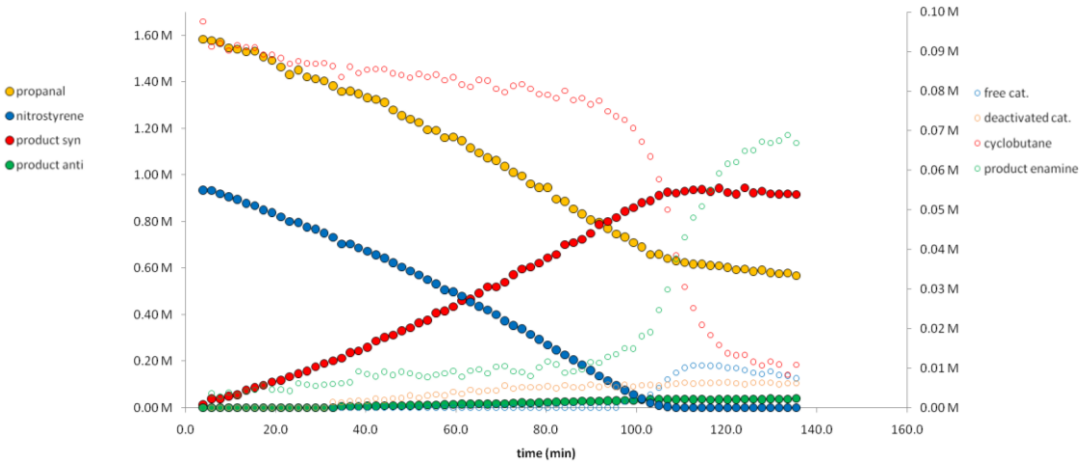
5.3. Species distribution during the reaction

Reaction	A	B	C
$[nitrostyrene]_o$	1.0 M	1.0 M	1.5 M
$[propanal]_o$	1.2 M	1.7 M	1.7 M
$[catalyst]_o$	0.1 M	0.1 M	0.1 M

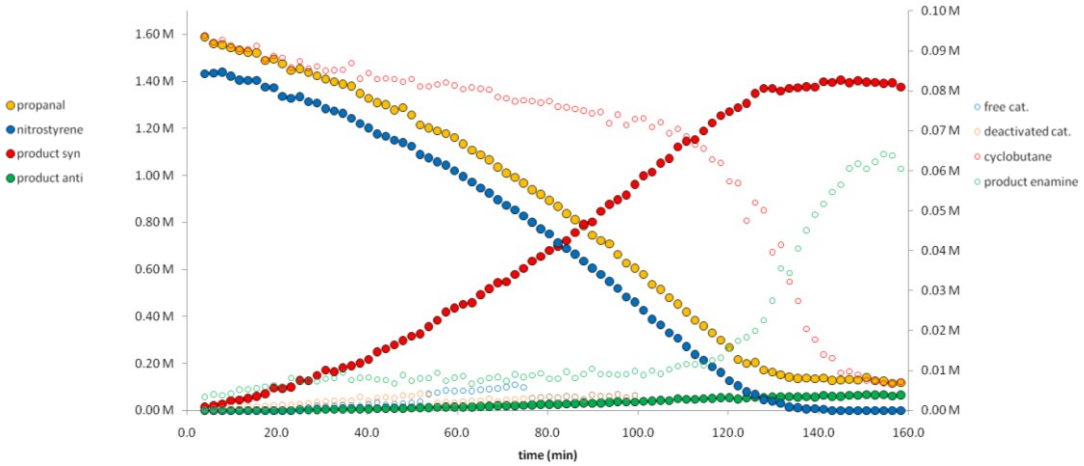
Reaction A



Reaction B



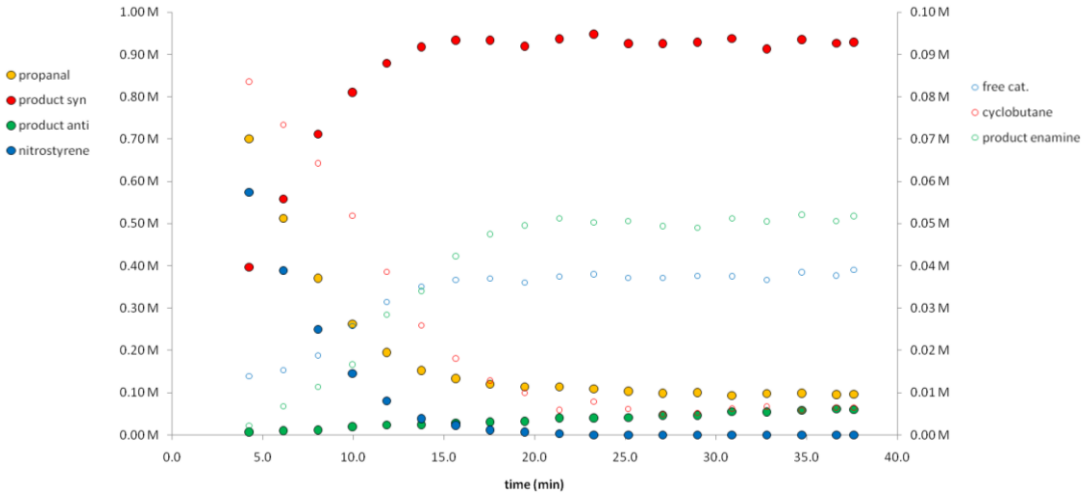
Reaction C



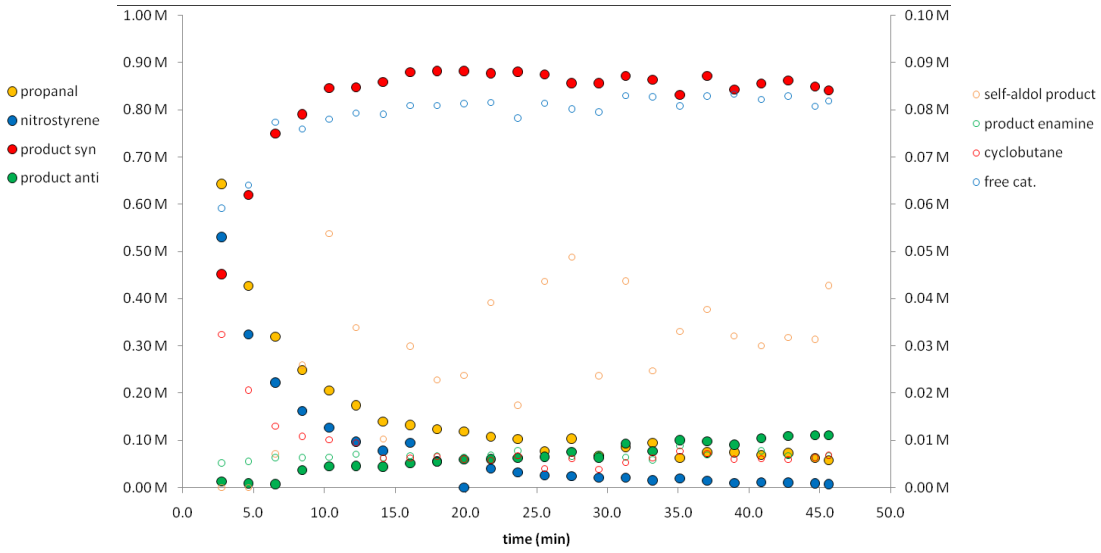
5.4. Effect of acid in the species distribution during the reaction

conditions	0.1 M of AcOH	0.5 M of AcOH
$[nitrostyrene]_o$	1.0 M	1.0 M
$[propanal]_o$	1.2 M	1.2 M
$[acetic\ acid]_o$	0.1 M	0.5 M
$[catalyst]_o$	0.1 M	0.1 M

0.1 M of AcOH



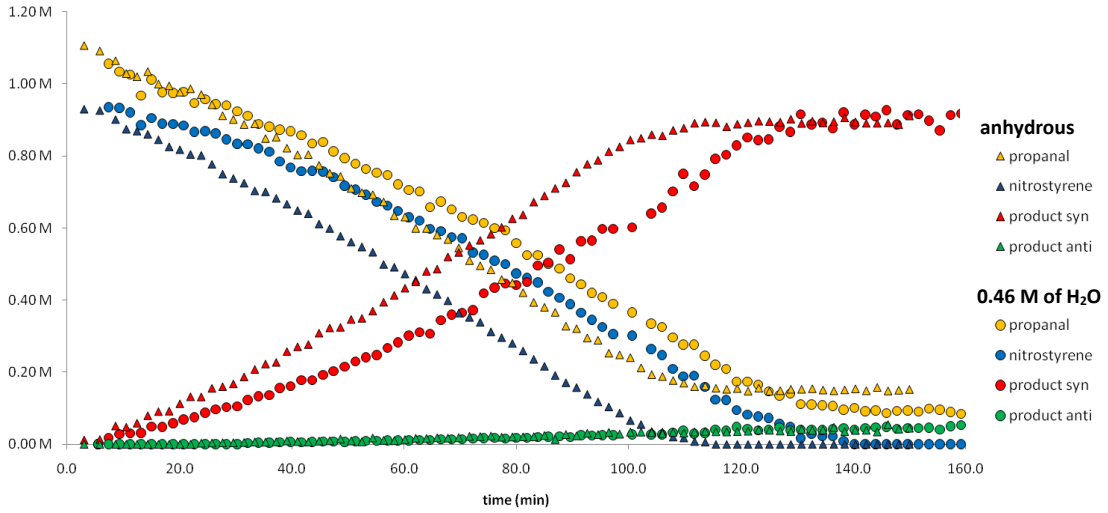
0.5 M of AcOH



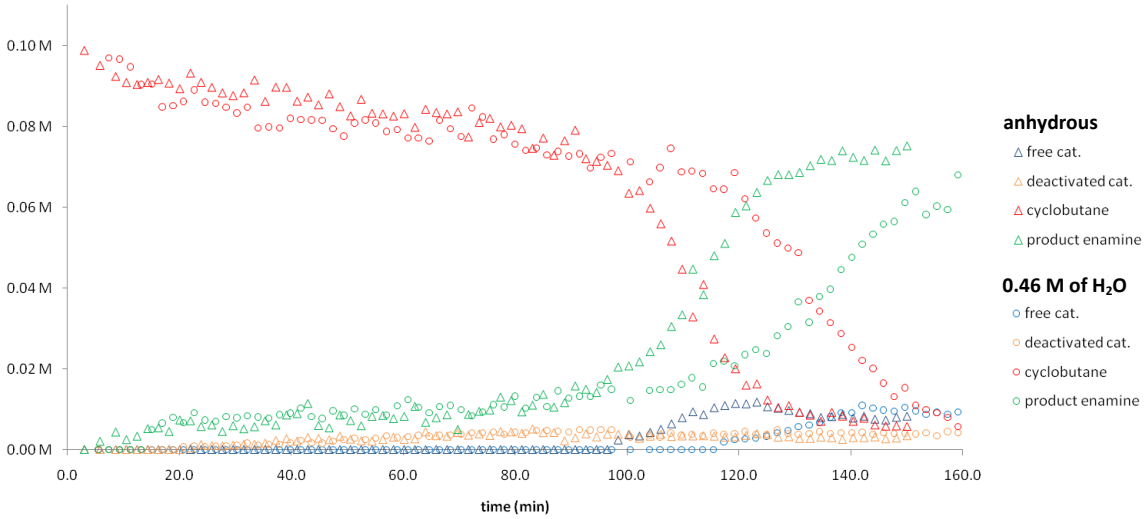
5.5. Comparison of the kinetics with water added

conditions	anhydrous	0.46 M of H_2O
$[nitrostyrene]_o$	1.00 M	1.00 M
$[propanal]_o$	1.20 M	1.20 M
$[H2O]_o$	0.00 M	0.46 M
$[catalyst]_o$	0.10 M	0.10 M

- **Reagents**



- **Catalytic species**



5.6. Effect of additives in the rate of the reaction

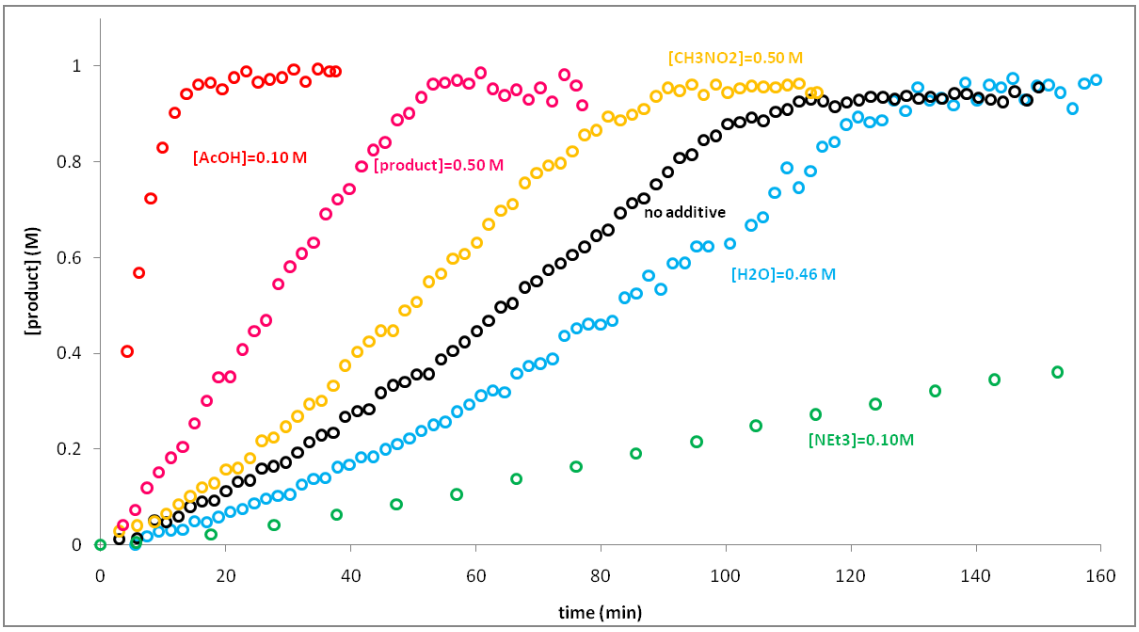


Figure 18. Different additives drastically affect the rate of total product (*syn* + *anti*) formation

5.7. Crossover experiments to prove the reversibility of the cyclobutane formation

We did two different crossover experiments, one changing the nitroolefin and the other one changing the aldehyde.

In the first one, we added 100 µL (0.06 mmol) of a 0.6 M solution of 4-methoxy-β-nitrostyrene in toluene-d8 to a mixture of 100 µL (0.06 mmol) of a 0.6 M solution of propanal in toluene-d8 and 0.4 mL (0.06 mmol) of a solution of a 0.15 M of (*S*)-(–)-α,α-diphenyl-2-pyrrolidinemethanol trimethylsilyl ether in toluene-d8 placed in a NMR tube in the presence of 4 Å molecular sieves. After the ^{1}H-NMR spectrum of this mixture was registered, we added 100 µL (0.06 mmol) of a 0.6 M solution of β-nitrostyrene and we registered ^{1}H-NMR spectrum every 2 min.

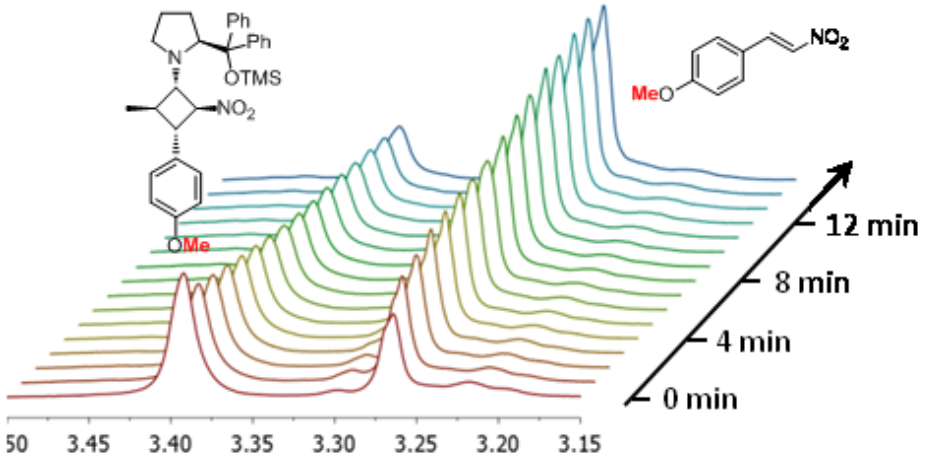


Figure 19. ^{1}H-NMR showing the liberation of 4-methoxy-β-nitrostyrene after the addition of β-nitrostyrene

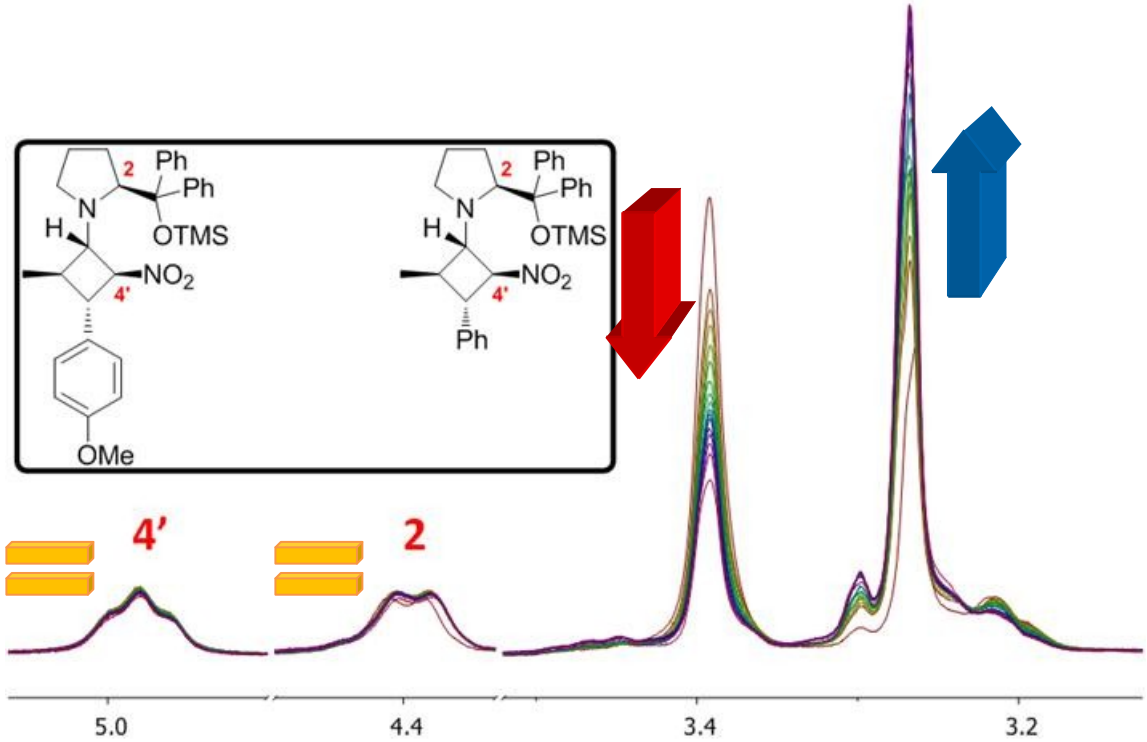
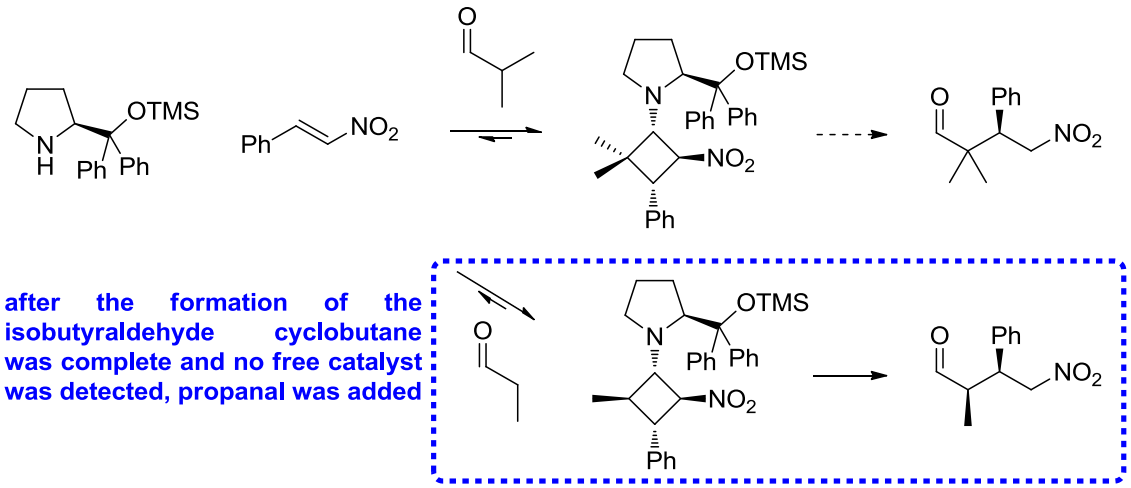


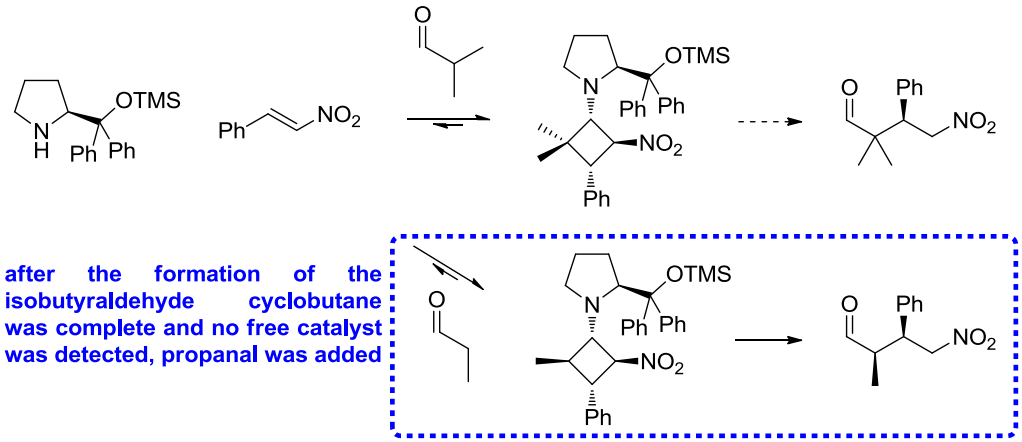
Figure 20, ^{1}H-NMR spectra showing the change in the concentration of 4-methoxy-β-nitrostyrene cyclobutane and free 4-methoxy-β-nitrostyrene, whereas common signals remain unchanged

The second crossover experiment was done changing the aldehyde. First, we prepared the corresponding cyclobutane with isobutyraldehyde in the standard reaction conditions. When all the catalyst was captured as the isobutyraldehyde cyclobutane and no free catalyst was observed, propanal (much more reactive) was added in order to displace the isobutyraldehyde cyclobutane and react with nitrostyrene.

Procedure:

We added 100 µL (0.06 mmol) of a 0.6 M solution of catalyst in toluene-d8 to a 400 µL of a solution of β-nitrostyrene (1.5 M) and isobutyraldehyde (1.8 M) in toluene-d8 and we started to collect ^{1}H-NMR spectra. When the formation of the cyclobutane with isobutyraldehyde was complete and no free catalyst was observed, 100 µL (0.72 mmol) of a 6.0 M solution of propanal were added and we collected ^{1}H-NMR spectra over the reaction using the method described in section 3 of the Supporting Information.





- **Reagents**

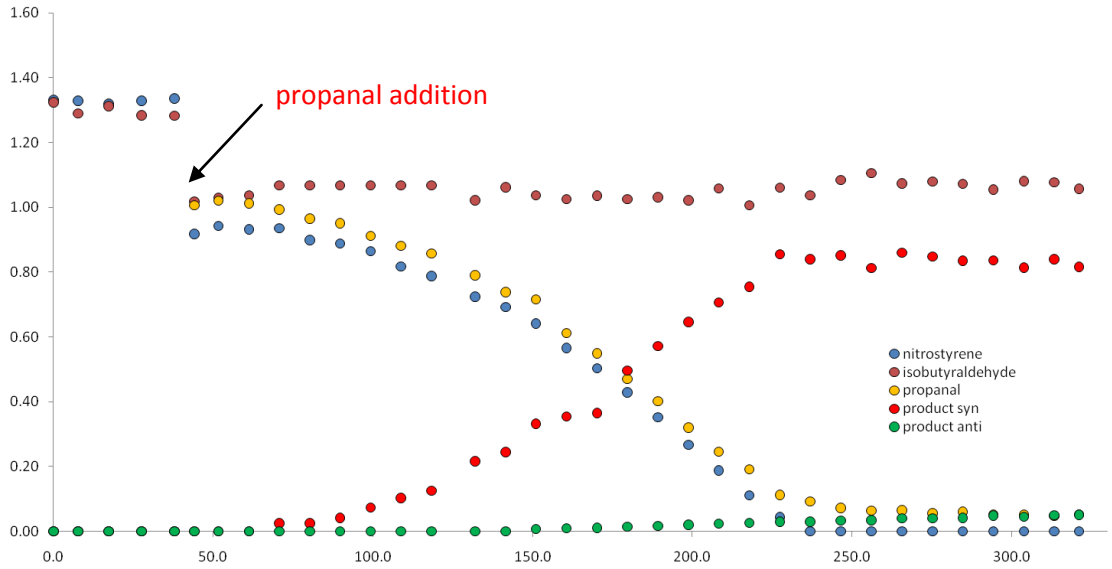


Figure 21. The reaction with propanal works even after the preformation of isobutyraldehyde cyclobutane

- **Catalytic species**

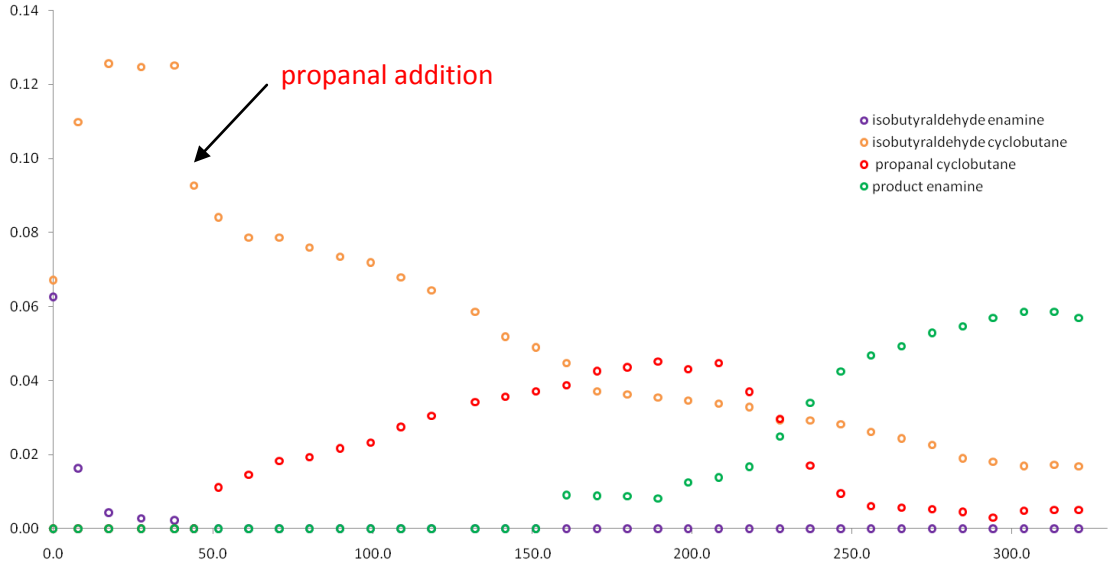
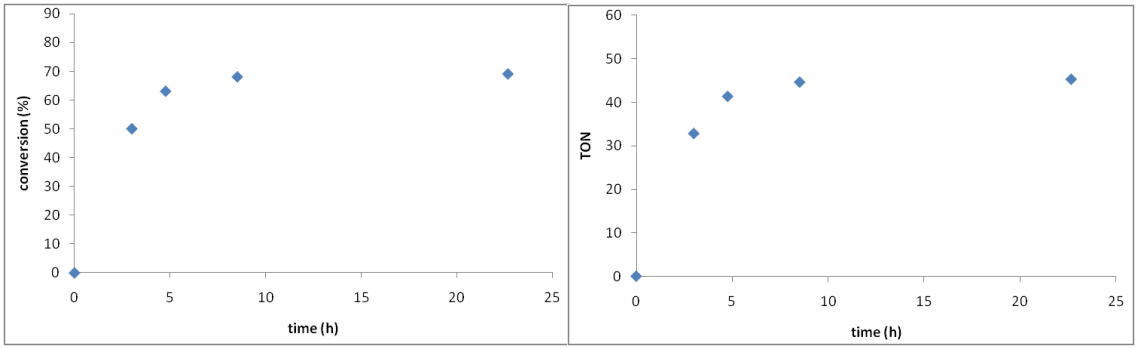


Figure 22. The propanal cyclobutane formed displaces the isobutyraldehyde cyclobutane, even during the course of the reaction where propanal cyclobutane is being consumed

5.8. Reactions without solvent

- **with a large excess of aldehyde and low loading catalyst**

nitrostyrene	1.97 mmol
propanal	6.97 mmol
catalyst	0.03 mmol

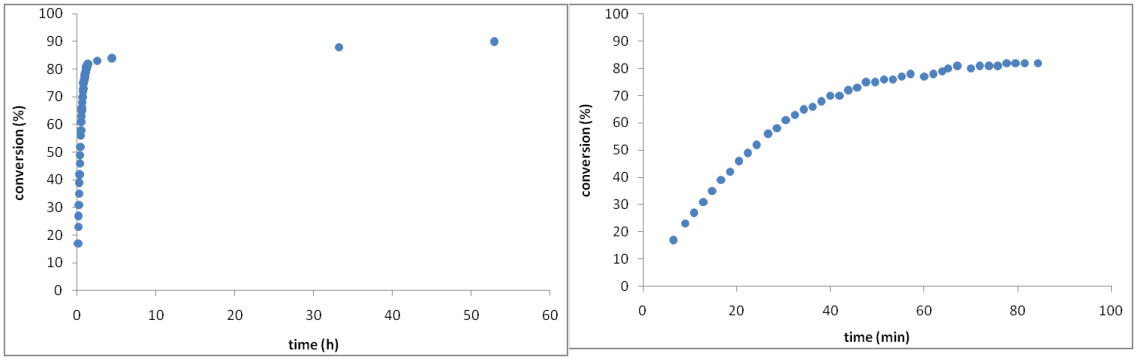


The reactions stops at 69% conversion (TON=45.3).

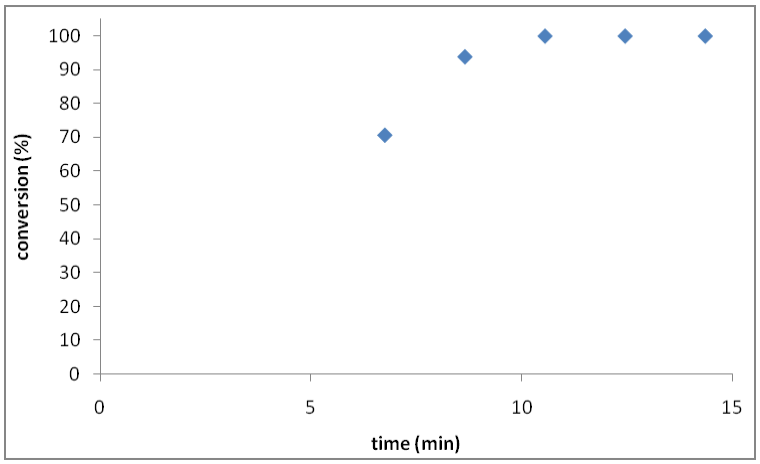
- **without a large excess of aldehyde**

reaction	**without acid**	**with acid**
nitrostyrene	1.60 mmol	1.60 mmol
propanal	2.29 mmol	2.29 mmol
catalyst	0.04 mmol	0.04 mmol
AcOH	0.00 mmol	0.04 mmol

without acid



with acid



In both cases the diastereoselectivity and enantioselectivity are the same than in the standard reaction.

To check this data we carried out a reaction with 1.00 g of nitrostyrene (6.57 mmol), 665 mg of propanal (11.45 mmol), 12 mg of acetic acid (0.20 mmol) and 67 mg of (*S*)-(–)-α,α-diphenyl-2-pyrrolidinemethanol trimethylsilyl ether (0.20 mmol, 3 mol%). The reaction was quenched after 15 min with cold 1 M HCl solution and extracted with CH_2Cl_2. The crude was purified by SiO_2 chromatographic column to obtain 1.33 g of product (98 % yield).

5.9. Variability in diastereoselectivities in literature

As we show in the article, the precise control of the final point of the reaction is crucial to obtain the Michael adduct with good diastereoselectivity because it is eroded after the end of the reaction especially in the presence of acid.

The arguments in the article provide good explanations for different effects reported previously in the literature than remained still without a satisfactory explanation. In this regard, the higher catalyst loading or the use of acid reduce reaction times (making more difficult to measure exactly the end of the reaction) and accelerate the erosion of the diastereomeric ratio after the reaction is finished. Obviously, under identical conditions longer reaction times result in further loss of diastereoselectivity.

- Zhu, S.; Wang, Y.; Ma, D., Enantioselective organocatalytic conjugate addition of aldehydes to α,β-unsaturated thiol esters. *Adv. Synth. Catal.* **2009,** *351* (16), 2563-2566.

In entries 6 and 7 of table 1, they compare the diastereoselectivity using AcOH and PhCOOH with almost identical reaction conditions. When they use the stronger acid (PhCOOH) the product diastereomeric ratio decrease from 7:1 to 2:1.

In entries 6 and 8 of table 1, they compare the effect of the AcOH loading. Under identical condition reactions, the use of 10 mol% instead of 50 mol% of AcOH means an increase from 7:1 to 11:1 in the product diastereomeric ratio.

- Zhu, S.; Yu, S.; Ma, D., Highly efficient catalytic system for enantioselective Michael addition of aldehydes to nitroalkenes in water. *Angew. Chem., Int. Ed.* **2008,** *47* (3), 545-548.

In entries 4 and 6 of table 1, the authors compare two identical Michael reactions using different acid loading. When they reduce the quantities of acid from 100 mol% to 50 mol% they found a increase in the product diastereomeric ratio from 53:47 to 64:36.

In entries 5 and 6 of table 1, they compare the diastereoselectivity of the reaction product after 2.0 h using 5 mol% of catalyst and after 1.5 h using 10 mol% of catalyst. Even with 0.5 h more of reaction time, the reduction of catalyst loading increases the product diastereomeric ratio from 64:36 to 97:3.

- Wang, J.; Ma, A.; Ma, D., Organocatalytic Michael Addition of Aldehydes to γ-Keto-α,β-unsaturated Esters. An Efficient Entry to Versatile Chiral Building Blocks. *Org. Lett.* **2008,** *10* (23), 5425-5428.

In entries 1 and 3 of table 1, the authors compare the use of 10 mol% of catalyst and 50 mol% of benzoic acid with the use of 5 mol% of catalyst and 10 mol% of benzoic acid. Both the reduction in the catalyst loading and the use of less acid help to achieve a 4:1 instead of a 1.3:1 diastereomeric ratio.

In entries 3 and 4 of table 1, they change the benzoic acid for acetic acid (milder acid) and this increases the final diastereomeric ratio from 4:1 to 10:1.

- Hayashi, Y.; Gotoh, H.; Hayashi, T.; Shoji, M., Diphenylprolinol silyl ethers as efficient organocatalysts for the asymmetric Michael reaction of aldehydes and nitroalkenes. *Angew. Chem., Int. Ed.* **2005,** *44* (27), 4212-4215.

In entries 4 and 6 of table 1, the authors compare the use of 10 mol% of catalyst for 1 h and the use of 5 mol% for 38 h. In this case, even with a longer reaction time, the use of a smaller amount of catalyst allows them to increase the product diastereomeric ratio from 85:15 to 96:4.