Università degli Studi di Salerno
Dipartimento di Chimica e Biologia
Dottorato di Ricerca in Chimica (XII Ciclo)

Transport properties of drug precursor molecules in nanoporous polymers

funded by FP7 UE project
CUSTOM
"Drug and precursor sensing by complementing low cost multiple techniques"

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CUSTOM project

This PhD thesis is framed in the European project CUSTOM, *“Drug and precursor sensing by complementing low cost multiple techniques”* (EU 7th FP), a consortium set up by different European companies and research centres, whose coordinator is SELEX-FINMECCANICA. The project is part of the European strategies to fight the illegal drug trafficking.

Recently **drug traffickers used to smuggle drug precursor molecules,** that more easily escape checks respect to the finished drugs.

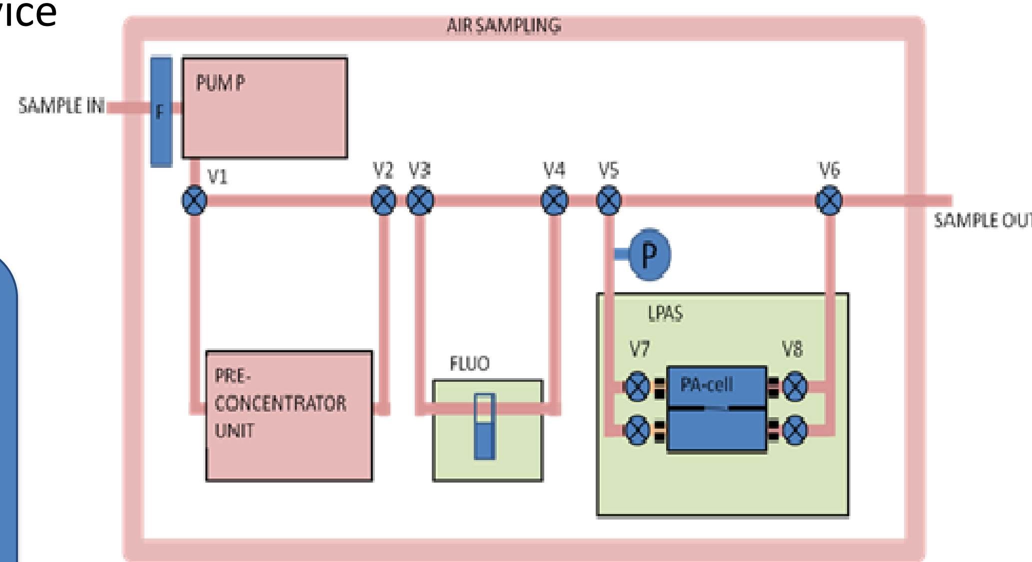
CUSTOM project aims to develop a portable device capable, in a short time, to detect drug precursor molecules present in the air in **traces**

CUSTOM Demonstrator Device

Fundamental modules of the CUSTOM device

✓Pump & **preconcentrator**

✓Detectors (LPAS and FLUO)



The low concentration (traces) of drug precursors requires a preconcentrator to concentrate as much as possible the analytes, to improve sensitivity and selectivity of sensors.

UNISA role within CUSTOM project:

✓prepare and characterize the concentrating material in morphologies optimizing performances

✓test the capacity and kinetics of drug precursor sorption

✓test the selectivity of the sorption

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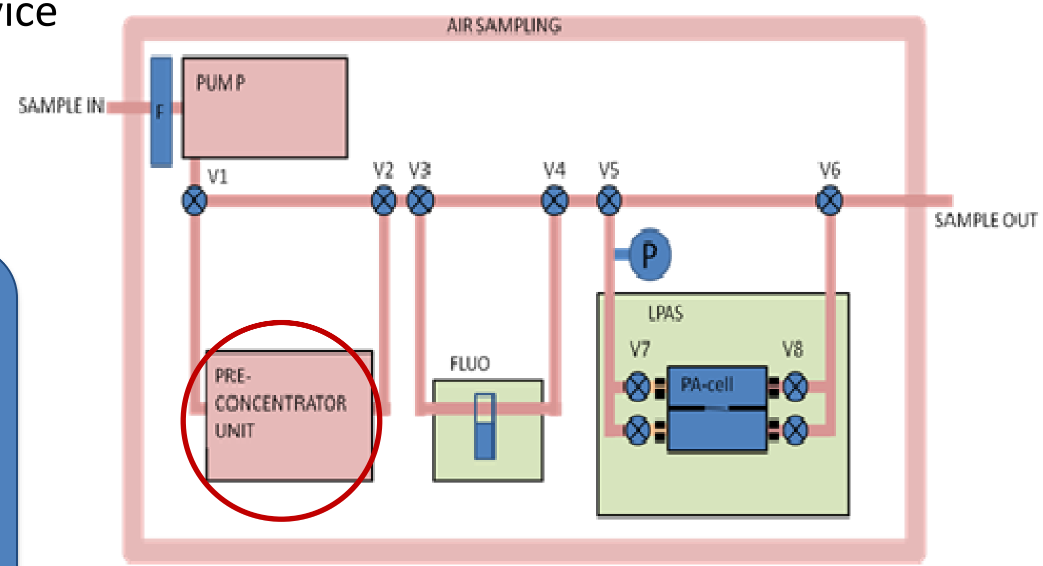

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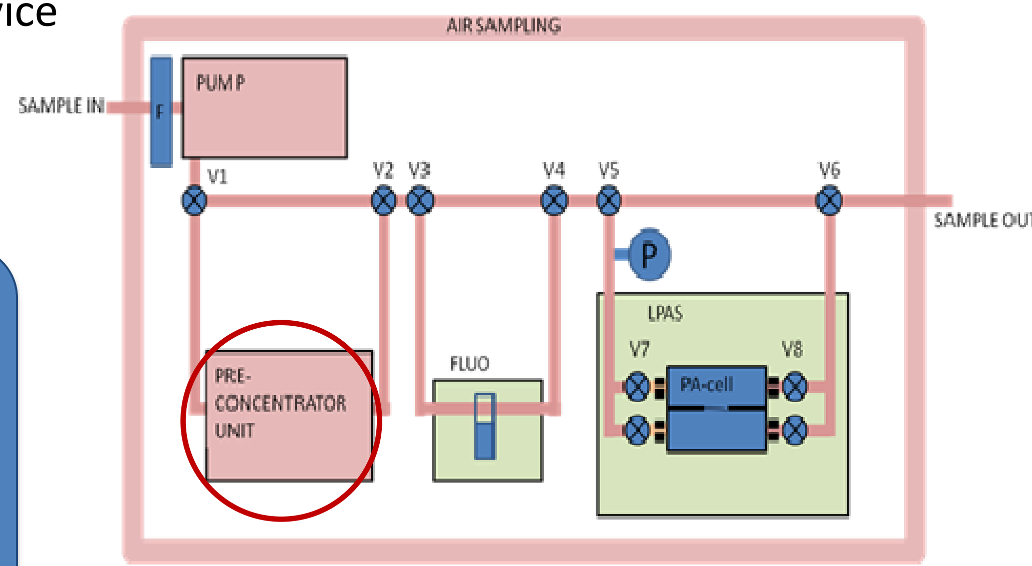

UNISA role within CUSTOM project:

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✓test the selectivity of the sorption

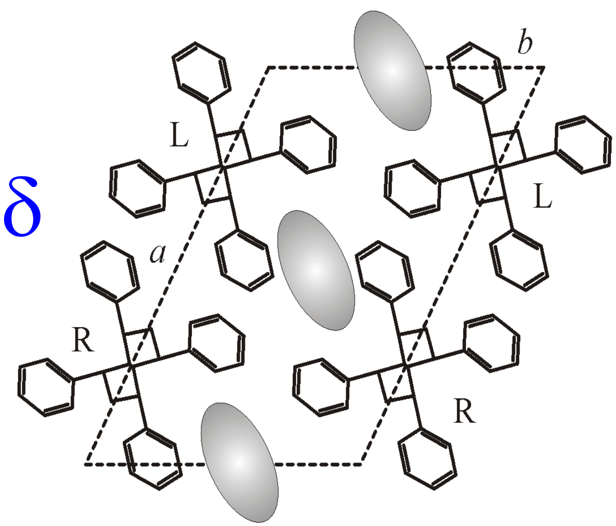
Concentrating material: **syndiotactic polystyrene (sPS)**

Concentrating material: syndiotactic polystyrene

sPS is a semi-crystalline hydrophobic thermoplastic material with excellent mechanical properties, chemical and thermal resistant.

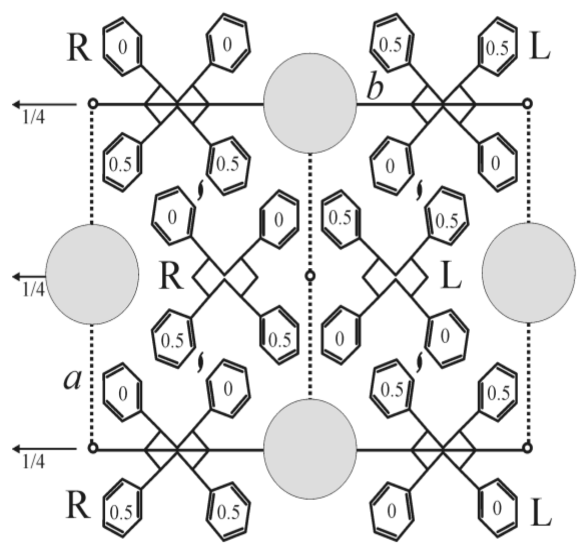
sPS δ and ε forms ensure high sorption capacity of guests at low activity, due to the presence of nanoporous cavities and channels in the crystalline phase.

δ



isolated cavities

ε



channels

$\rho_\delta \approx \rho_\varepsilon \approx$ **0.98 g/cm^3**

ρ_{am} **=1.05 g/cm^3**

δ and ε
absorb reversibly
guest molecules also
at very low activity

sPS prepared in highly porous morphologies: **aerogels**

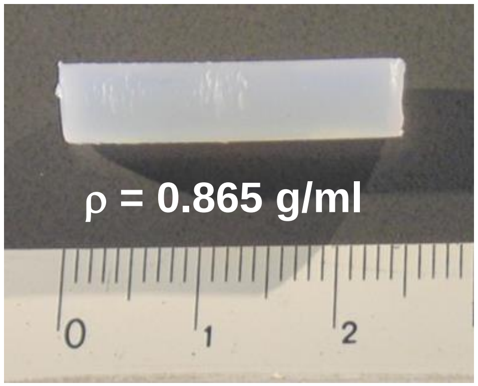
Venditto V., De Girolamo Del Mauro A., Mensitieri G., Milano G., Musto P., Rizzo P., Guerra G. *Chem. Mater.* **2006,** 18, 2205.
Petraccone, V.; Ballesteros, O. R. D.;Tarallo, O.; Rizzo, P. *Chem. Mater*., **2008**, 20, 3663.

Concentrating material: syndiotactic polystyrene

The high surface area of the aerogels ensures fast sorption kinetics.

sPS gel

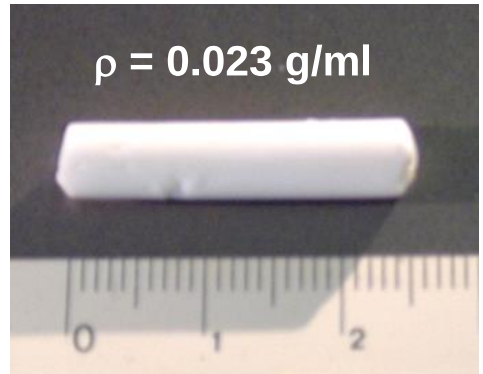
sPS/toluene 2/98 g/g



CO_2 extraction

sPS aerogel

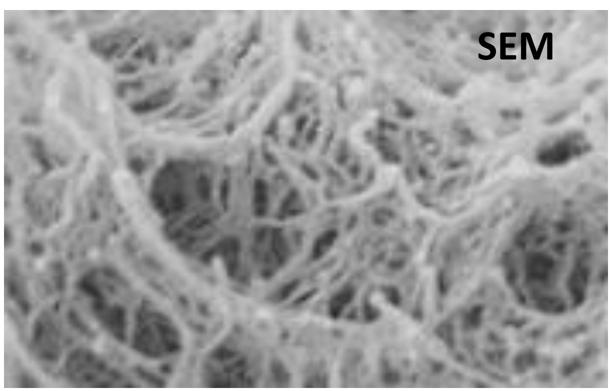
porosity ≈ 98%

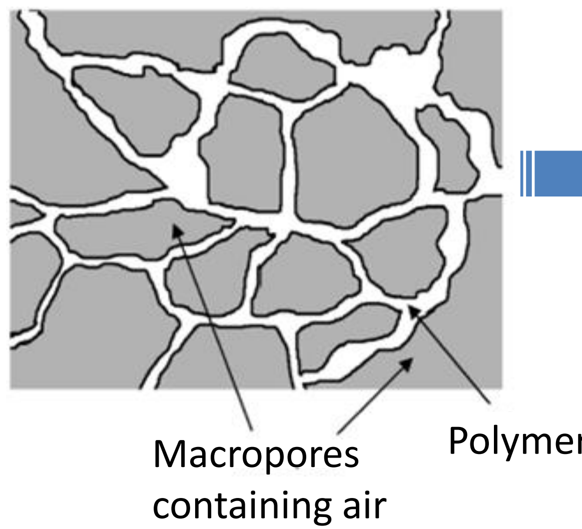


surface area 260 m^2/g

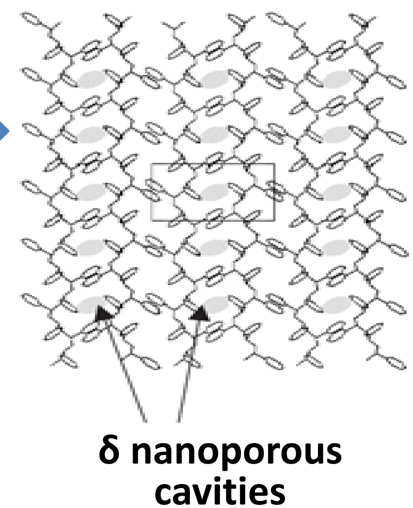
Physical gel:

junctions between chains consist of crystalline regions





sPS *δ* form aerogel crystalline structure



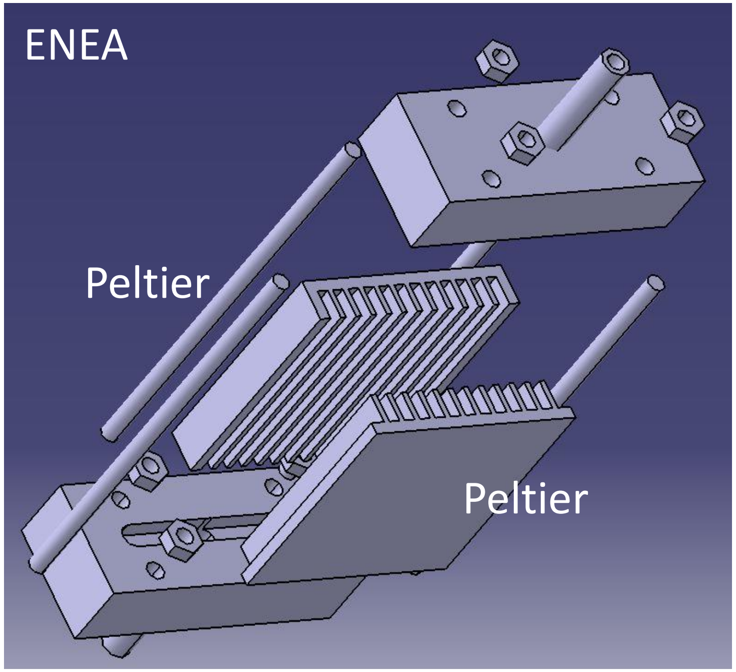
Daniel, C.; Giudice, S.; Guerra, G. *Chem. Mater.* ***2009***, 21, 1028.

Daniel, C.; Alfano, D.; Venditto, V.; Cardea, S.; Reverchon, E.; Larobina, D.; Mensitieri, G.; Guerra, G. *Adv. Mater*. **2005**, 17, 1515.

Concentrating material: syndiotactic polystyrene

Aerogel in beads shape guarantee low hydraulic impedance and good thermal conductivity, as tested by ENEA CUSTOM partner on the basis of thermal and fluid-dynamics analysis of sPS aerogels having different porosity and shape.

Mechanical part of preconcentrator unit



Beads of δ sPS aerogel

Beads characteristics:

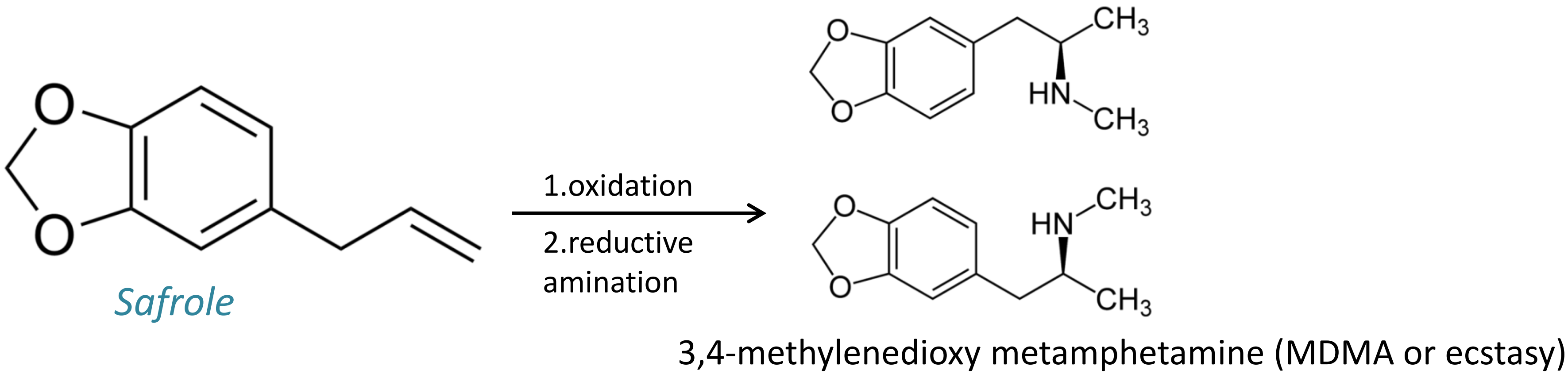
size range: 500-1000 μm
aerogel porosity: 90%
amount : 300 mg

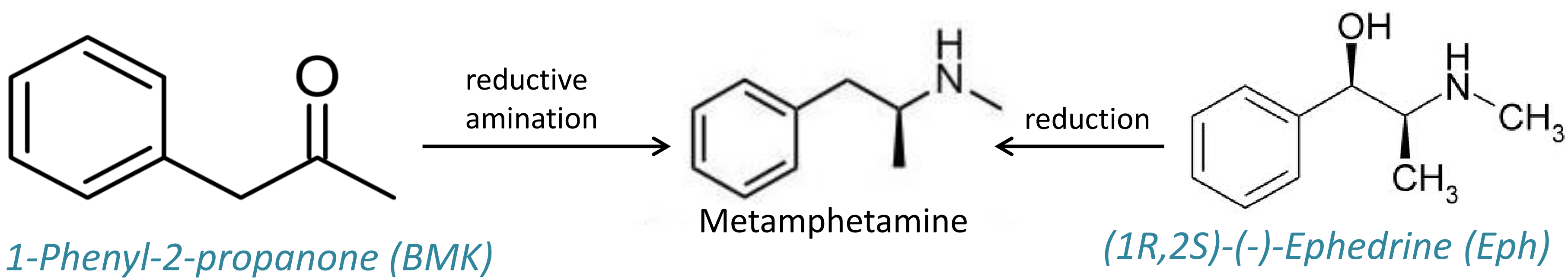
Beads ensure tortuosity respect to linear pathways, allowing the air flow containing precursors to be stationed long enough to absorb them.

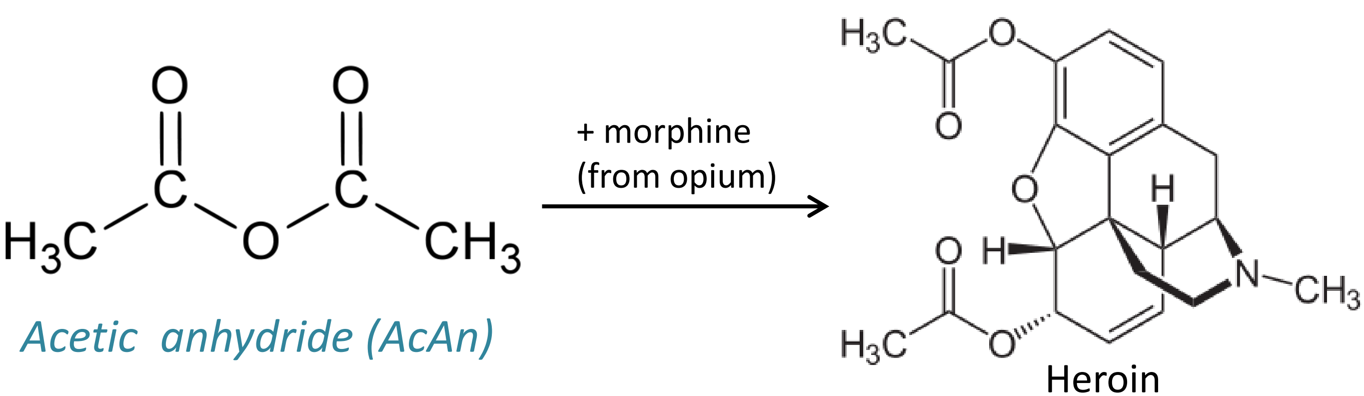
This geometry provides the same T in the preconcentrator.

Cooling/heating cycles maximize absorbed amount and kinetics.

Target drug precursors







Burgess, J. L. *Clandestine Drug Laboratories*, Section III, 746-765.
Pellegrino, S. *Biochimica clinica*, **2006**, *30 (2)*, 115.
Martyny, J., Arbuckle, S., Mccammonjr, C., Esswein, E., Erb, N., Vandyke, M. *Journal of Chemical Health and Safety*, **2007**, *14*(4), 40.

sPS aerogel beads preparation procedure

- **preparation of gel beads**

  sPS / chloroform 10%wt solution is added drop wise into a polymer non-solvent (i.e. diethyl ether) in which the sPS coagulates forming gel beads

Best solvent/non-solvent couple and concentration:

quite regular shape and small dimensions

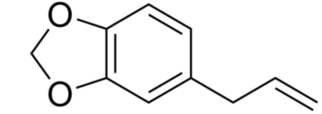
- supercritical CO_2 extraction

  chloroform is removed from gel beads and aerogel beads are achieved

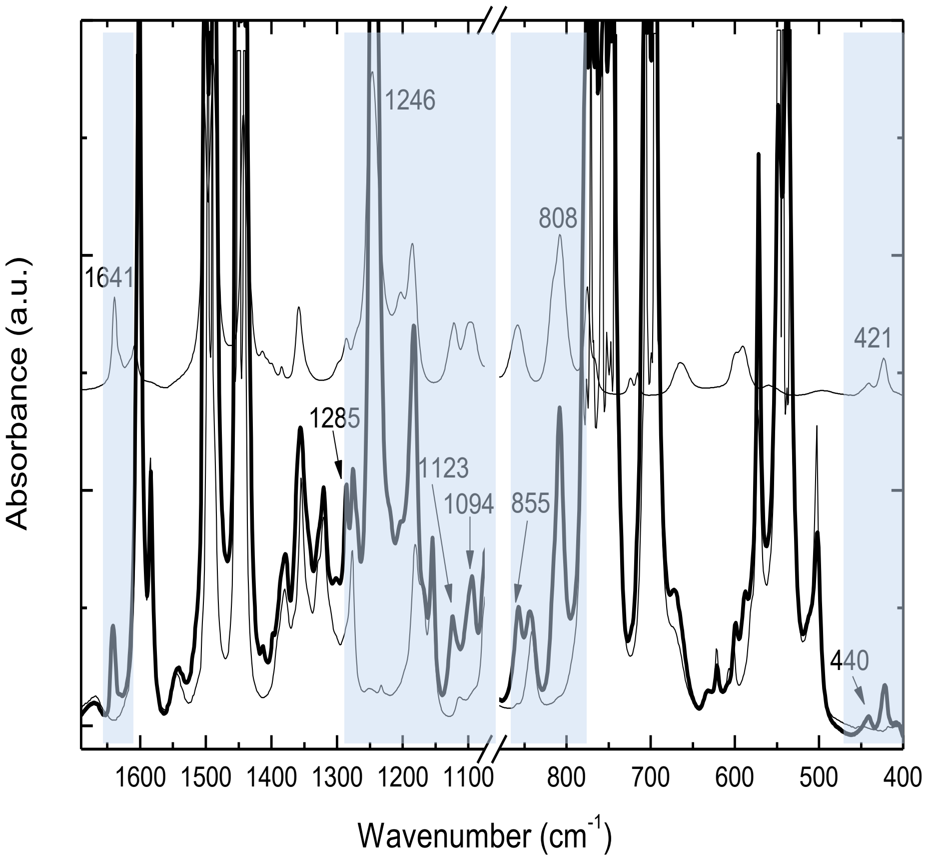
Extraction conditions:

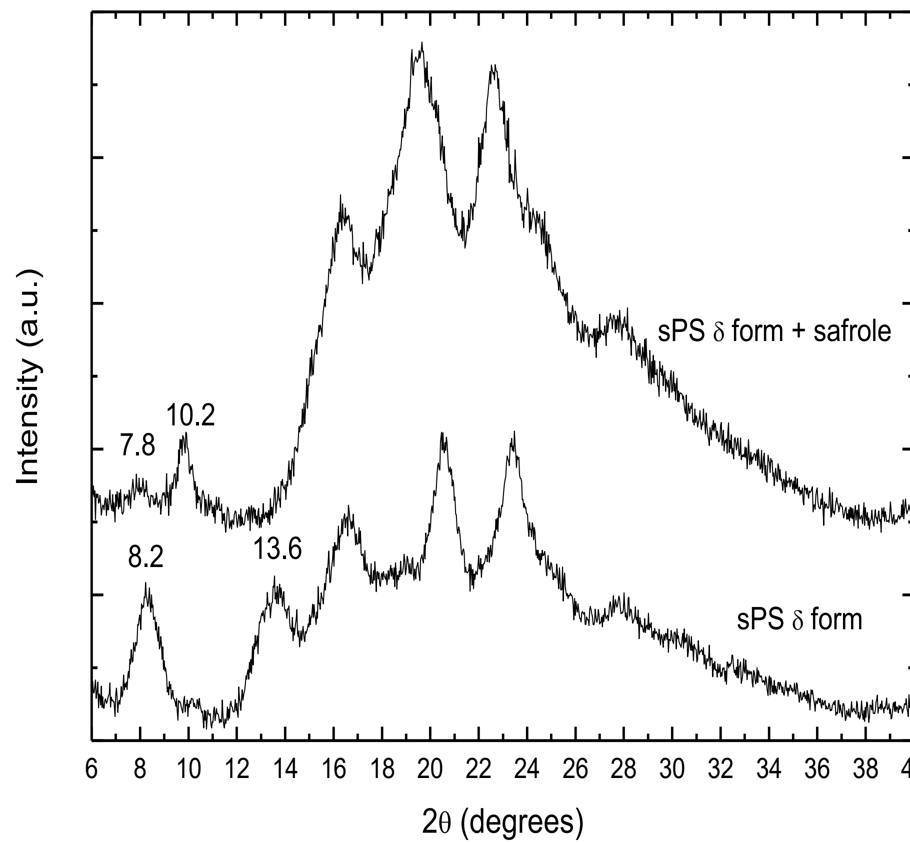
T=40°C, P=200 bar, t=180 min

Safrole sorption tests



δ sPS aerogel exposed to Safrole vapours for 30 min at T = 40°C





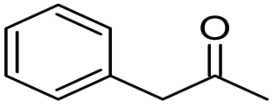
Thick line: Safrole vapours absorbed in δ sPS aerogel
Thin lines: δ sPS aerogel (bottom)-Safrole (top)

Typical pattern of a δ sPS co-crystalline structure

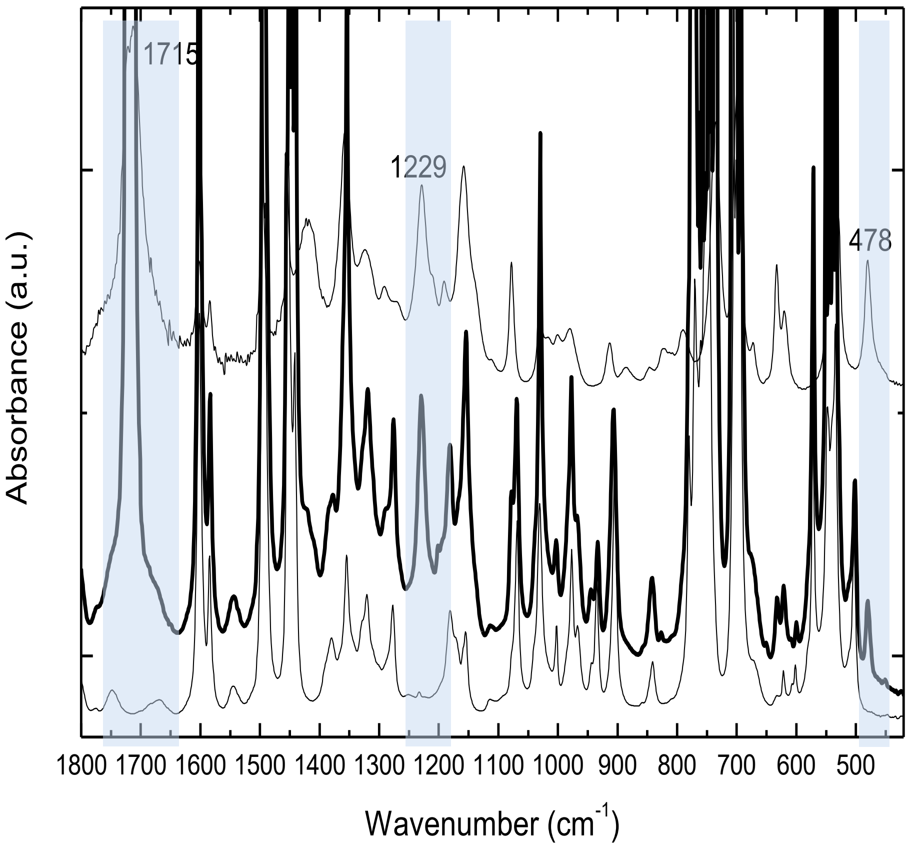
Typical infrared absorption bands of Safrole @ 1641, 1285, 1246, 1123, 1094, 855, 808, 440, 421 cm^{-1}

De Rosa, C.; Guerra, G.; Petraccone, V.; Pirozzi, B. *Macromolecules* **1997**, 30, 4147

BMK sorption tests

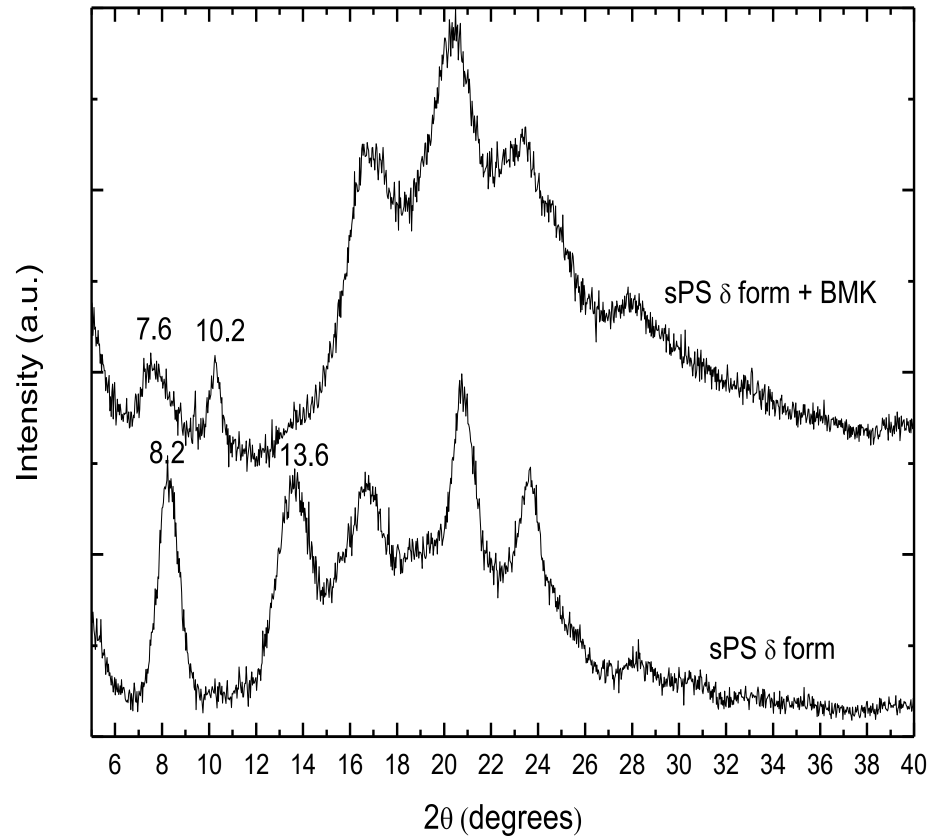


δ sPS aerogel exposed to BMK vapours for 2 hours at T = 40°C



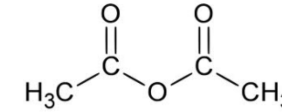
Thick line: BMK vapours absorbed in δ sPS aerogel
Thin lines: δ sPS aerogel (bottom)-BMK (top)

Typical infrared absorption bands of BMK @ 1715, 1229, 478 cm^{-1}

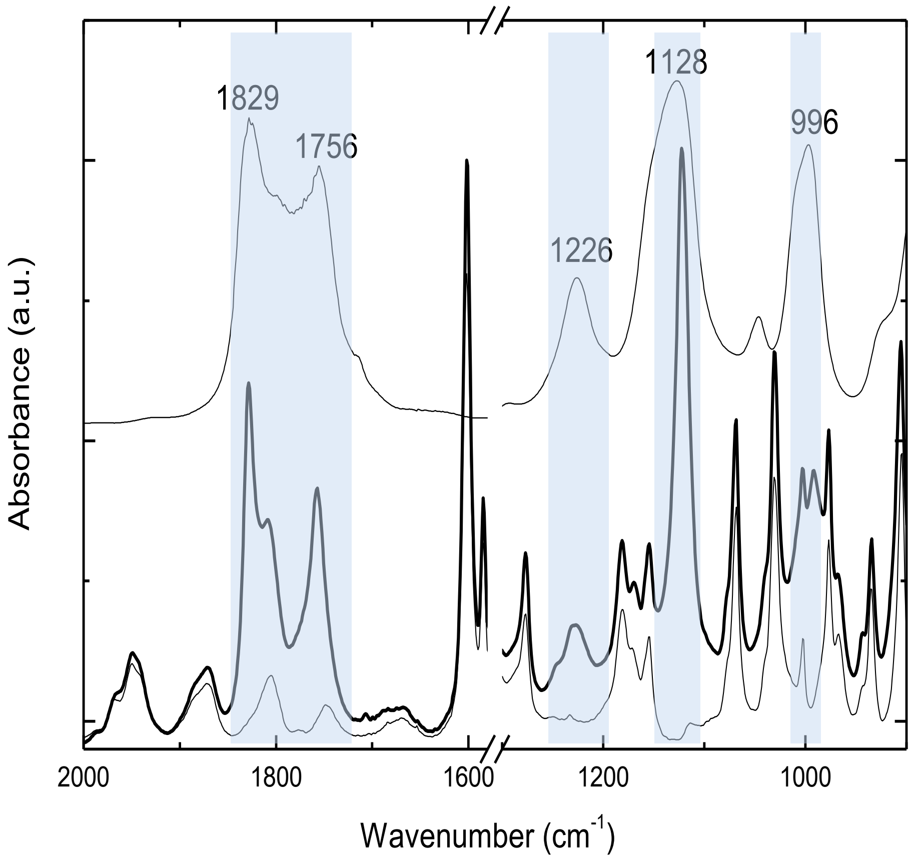


Typical pattern of a δ sPS co-crystalline structure

AcAn sorption tests

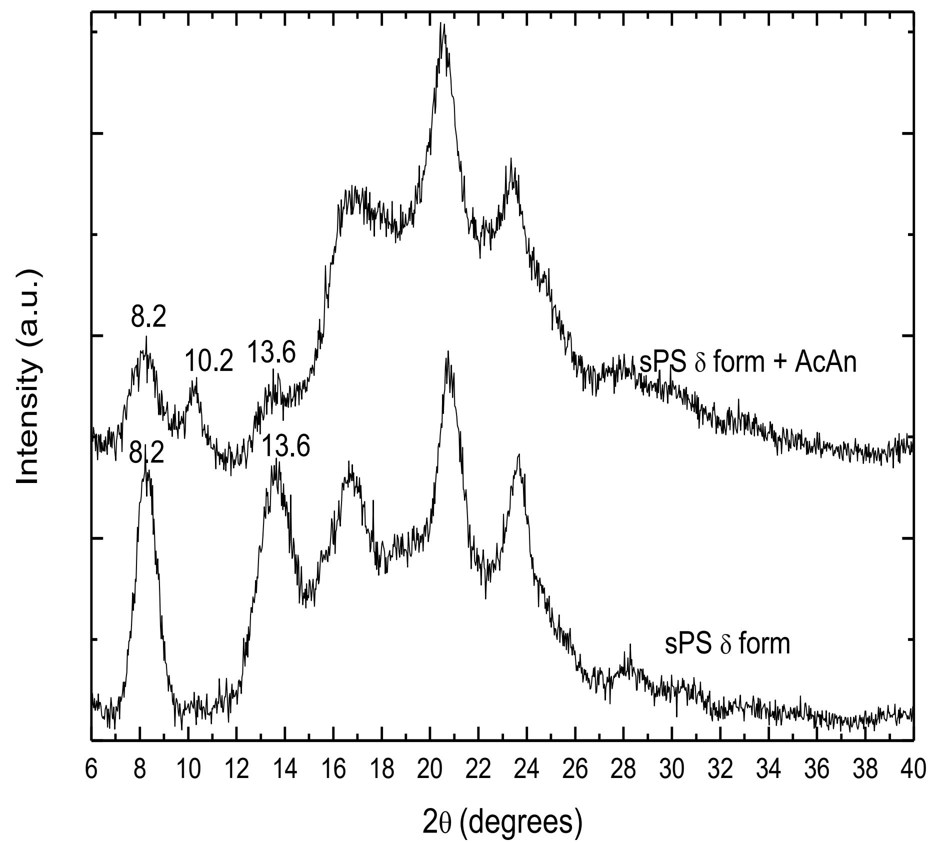


δ sPS aerogel exposed to AcAn vapours for few minutes at RT



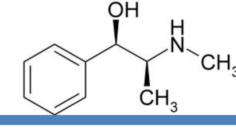
Thick line: AcAn vapours absorbed in δ sPS aerogel
Thin lines: δ sPS aerogel (bottom)-AcAn (top)

Typical infrared absorption bands of AcAn @ 1829, 1756, 1226, 1128, 996 cm^{-1}



Typical pattern of a δ sPS co-crystalline structure

Eph sorption tests



sPS aerogel samples have been:

- ✓ exposed to EPH vapours at T=40°C
- ✓ merged in different EPH aqueous solutions

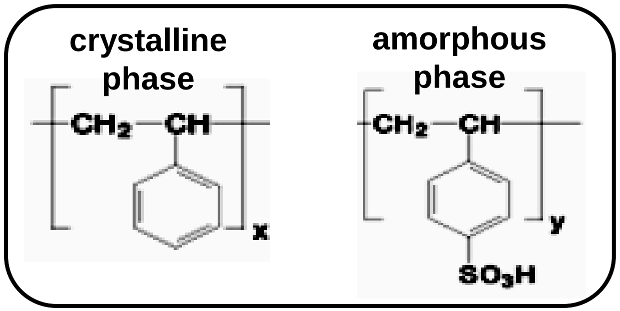
→ δ sPS does not absorb Eph

Poor affinity between Ephedrine and sPS:

- ✓ Ephedrine has strong polarity
- ✓ sPS is a nonpolar polymer

→ Eph is not soluble in δ sPS

Also sulfonated sPS * were tested

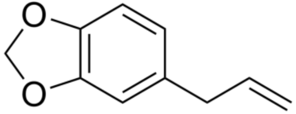


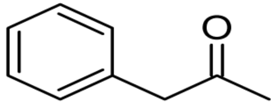
δ sPS with amorphous phase selectively sulfonated is a partially polar polymer potentially able to absorb polar molecules as Eph

Eph was not absorbed by sulfonated δ sPS

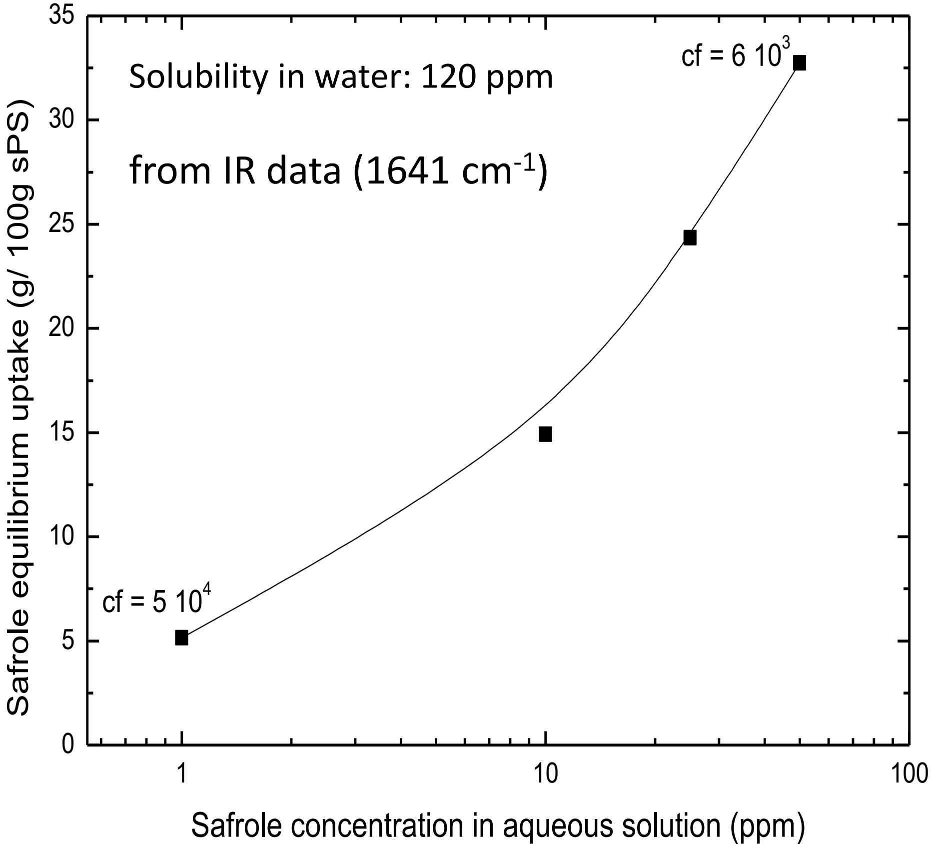
* Borriello, A.; Agoretti, P.; Ambrosio, L.; Fasano, G.; Pellegrino, M.; Venditto, V.;Guerra;, G. *Chem. Mater.*, **2009**, *21*, 3191.
Venditto V, Guerra G. et al. *Italian Pat. Appl. SA2009/A000002* (04.02.2009)

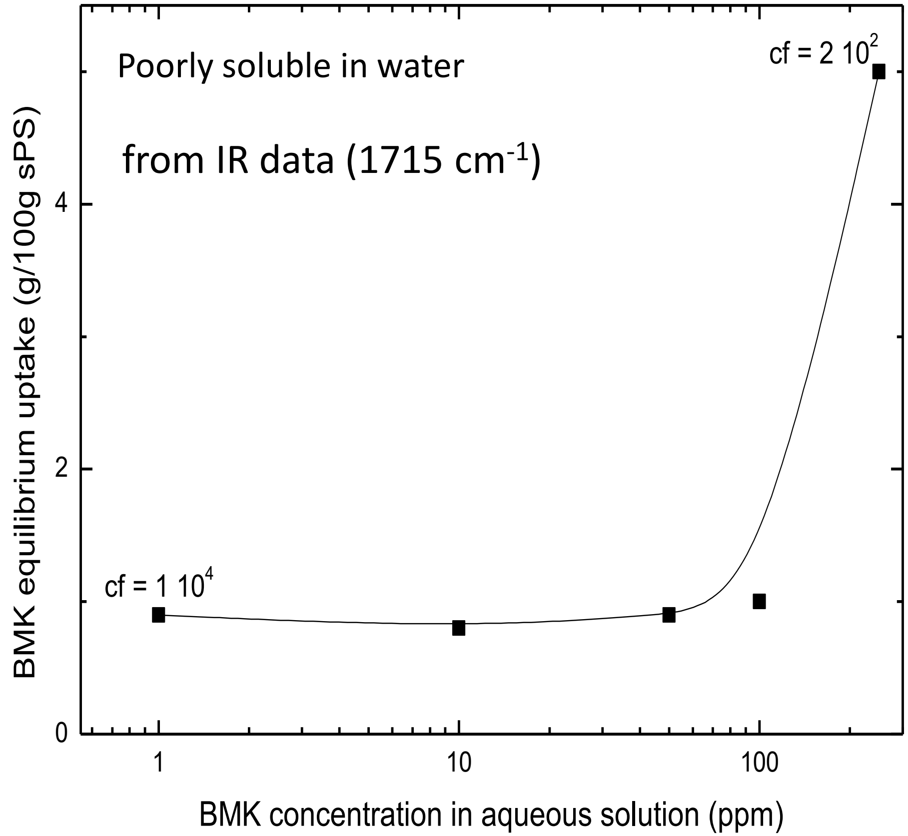
Safrole and BMK sorption tests





δ sPS aerogel immersed in diluted aqueous solutions at different precursors concentrations.



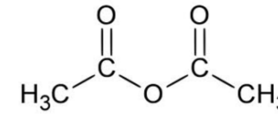


Concentration factor (cf) of Safrole into δ sPS aerogel immersed in 1 ppm aqueous solution is 5 10^4

Concentration factor (cf) of BMK into δ sPS aerogel immersed in 1 ppm aqueous solution is 1 10^4

$$cf = \frac{\text{concentration of analyte in the polymer}}{\text{concentration of analyte in the aqueous solution}}$$

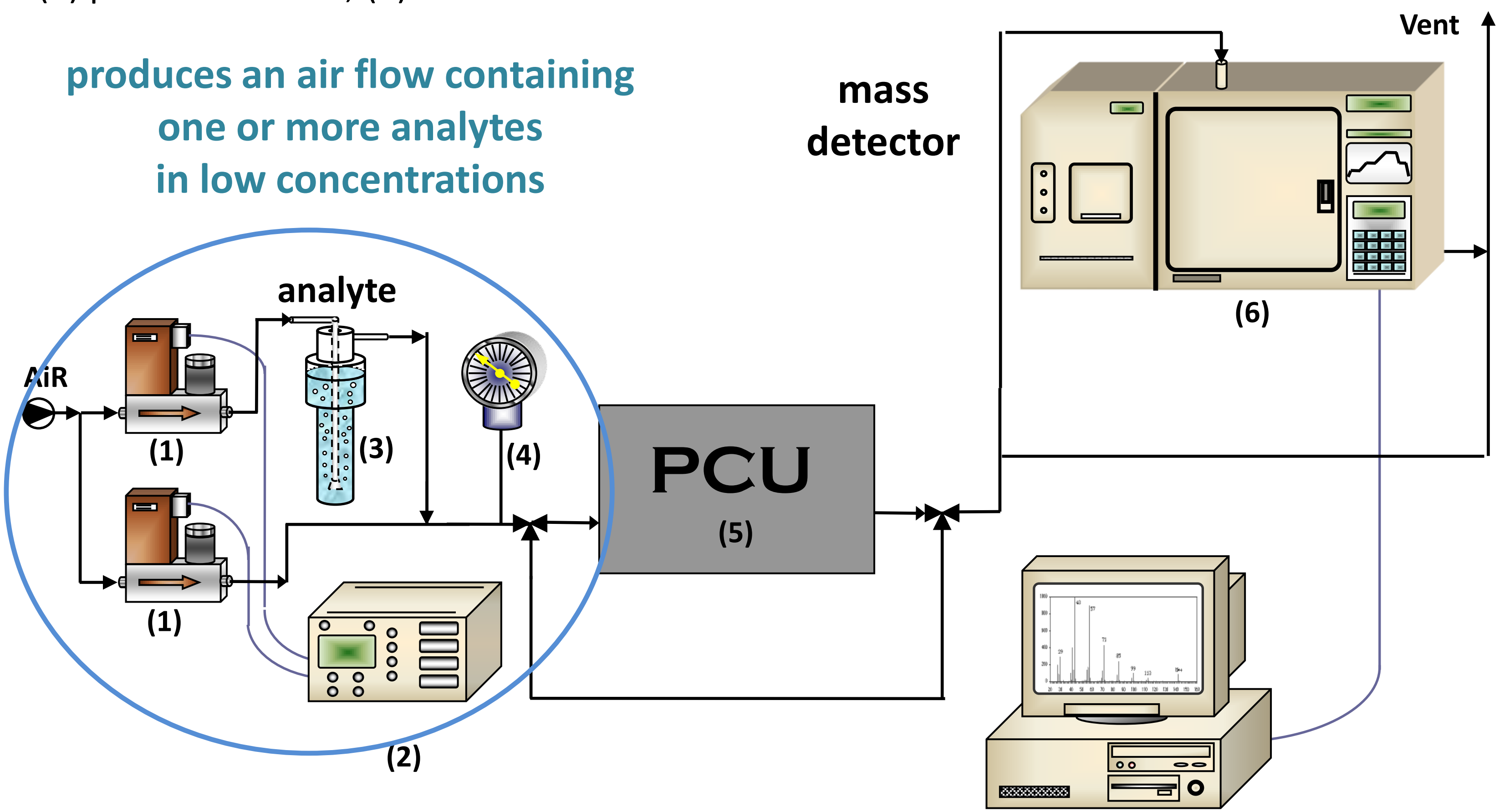
AcAn sorption tests



Experiments in gas phase

(1) mass flow controllers (MFC); (2) MFC control unit;
(3) analyte saturator; (4) manometer;
(5) preconcentrator; (6) mass detector

produces an air flow containing one or more analytes in low concentrations



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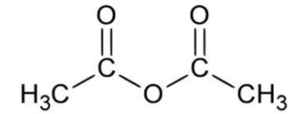
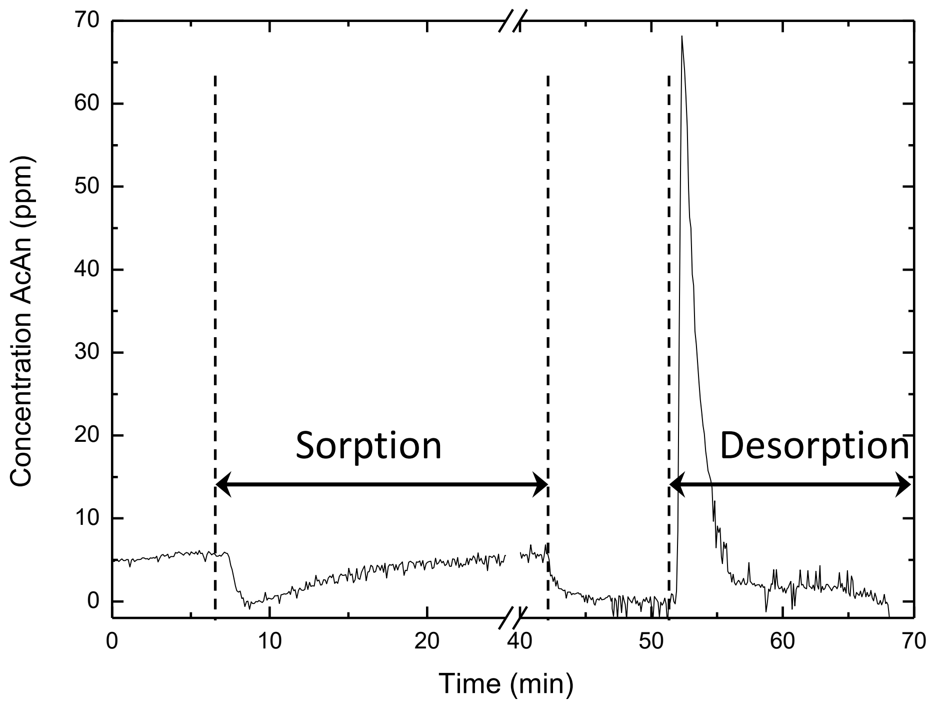




PCU temperature | Air flow rate

➤ sorption 15°C | air flow-in 128 NL/h

➤ desorption 50°C | air flow-out 60NL/h

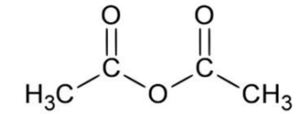
δ sPS aerogel amount 350 mg

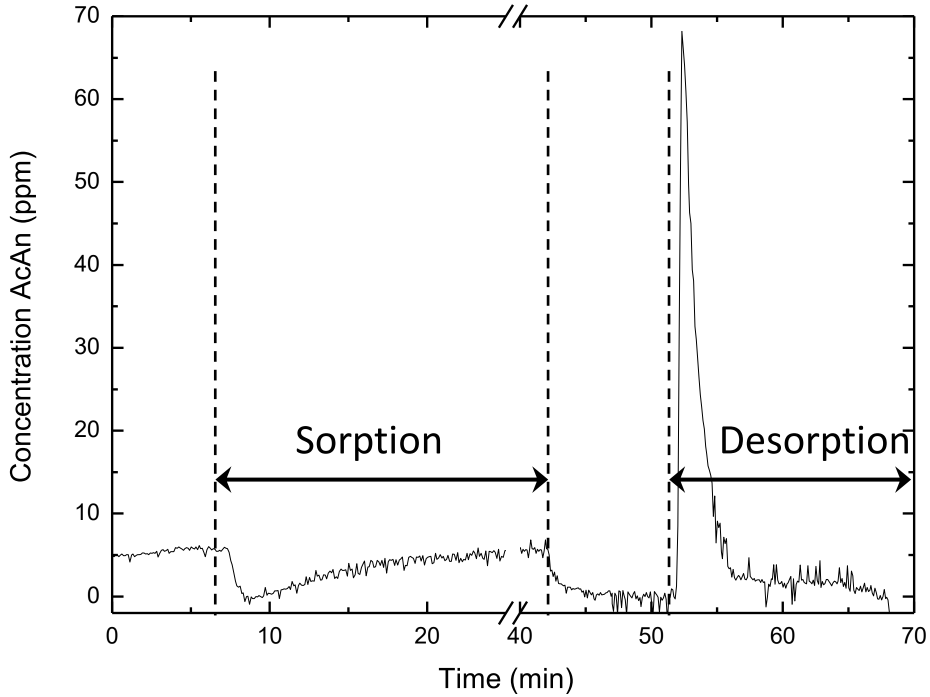
concentration factor in the air ≈ 13

$$cf = \frac{concentration\ of\ analyte\ in\ the\ outlet\ air\ flow}{concentration\ of\ analyte\ in\ the\ inlet\ air\ flow}$$

equilibrium AcAn uptake into
δ sPS aerogel
0.32 mg

AcAn sorption tests





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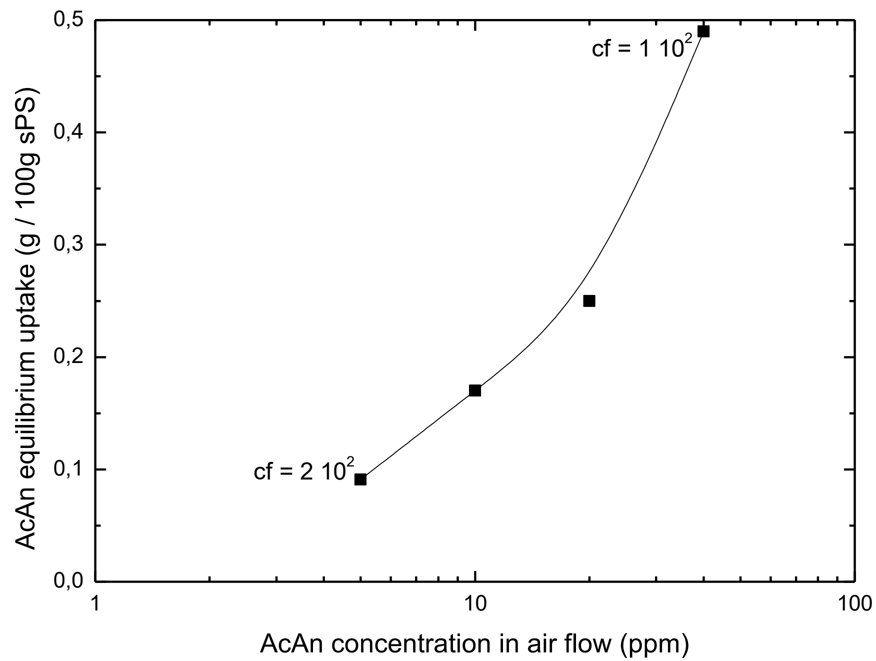
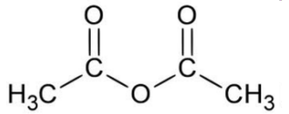
equilibrium AcAn uptake into
δ sPS aerogel
0.32 mg

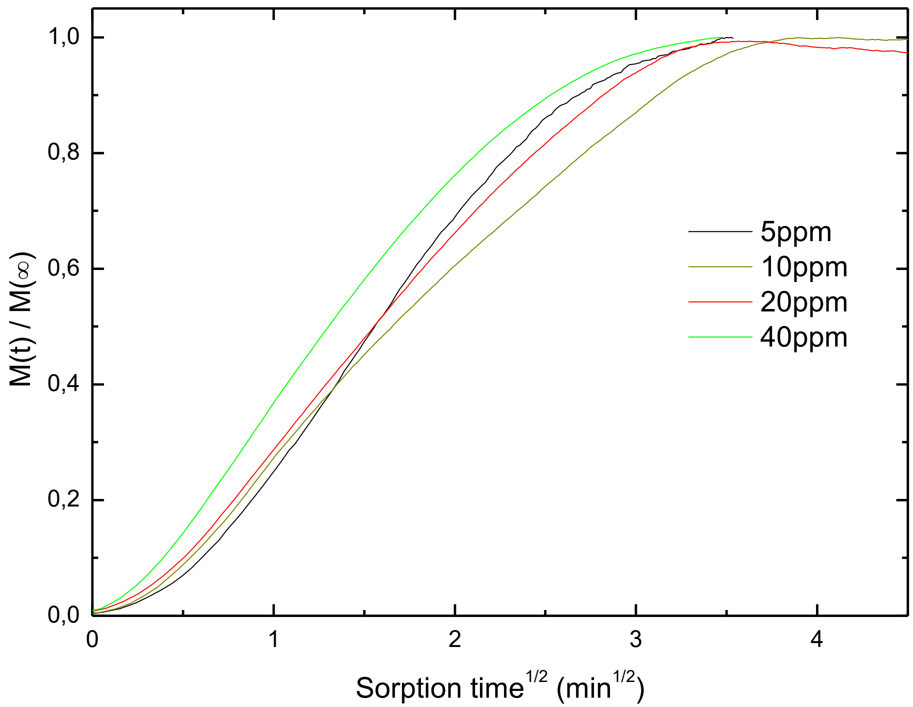
Concentration factor (cf) of AcAn into δ sPS aerogel exposed to 5 ppm AcAn vapours is 2 10^2

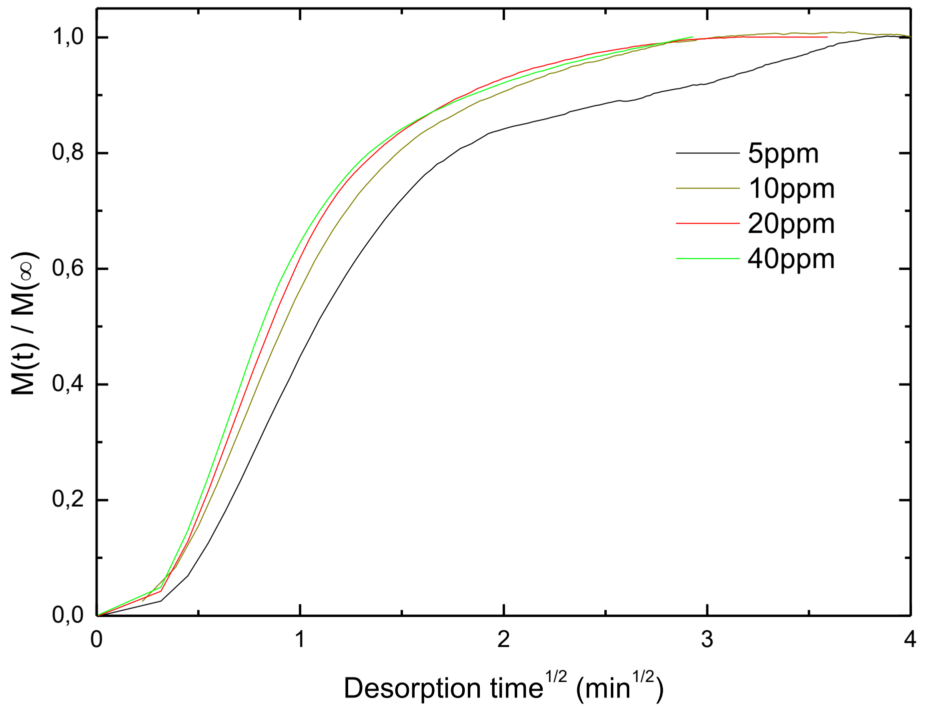


AcAn sorption/desorption kinetics



AcAn sorption and desorption kinetic curves

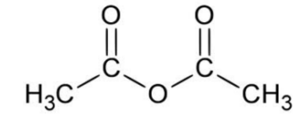




complete sorption happens in 16 min

complete desorption occurs in 5 min

AcAn sorption/desorption kinetics



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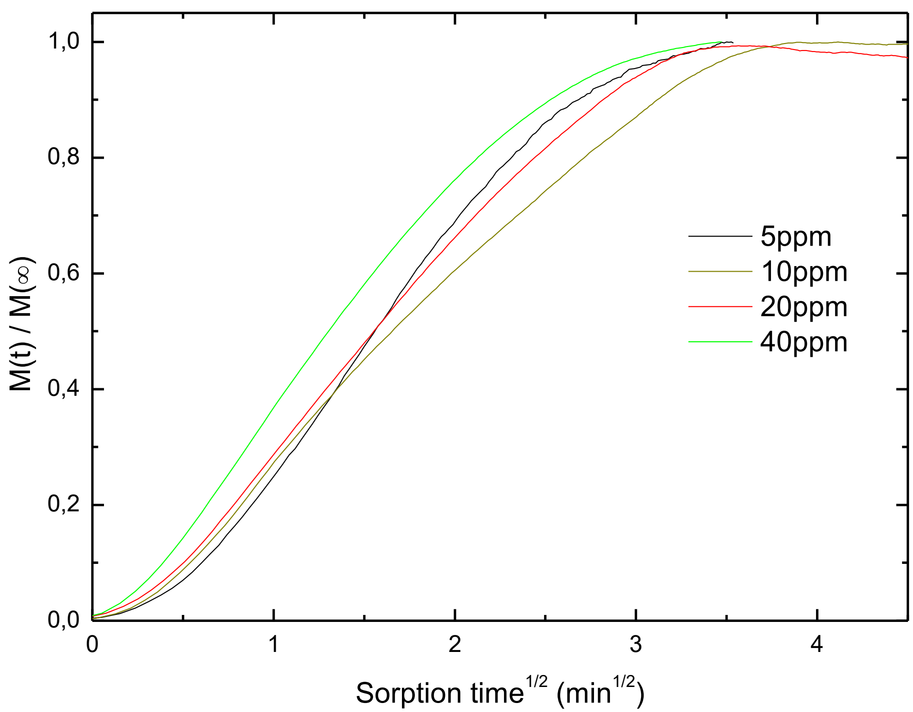

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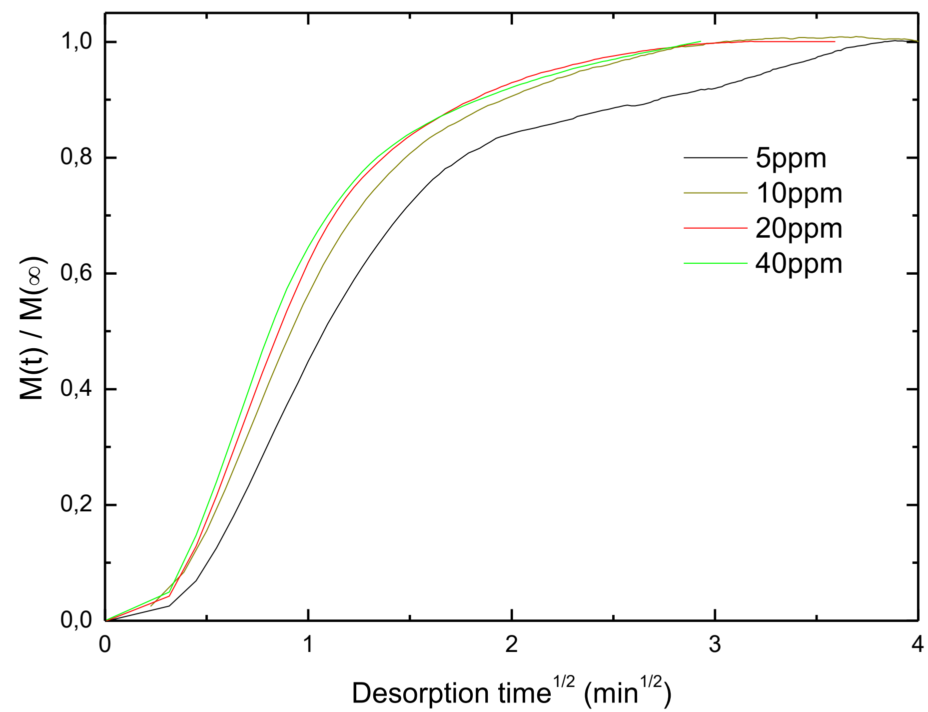
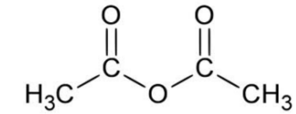


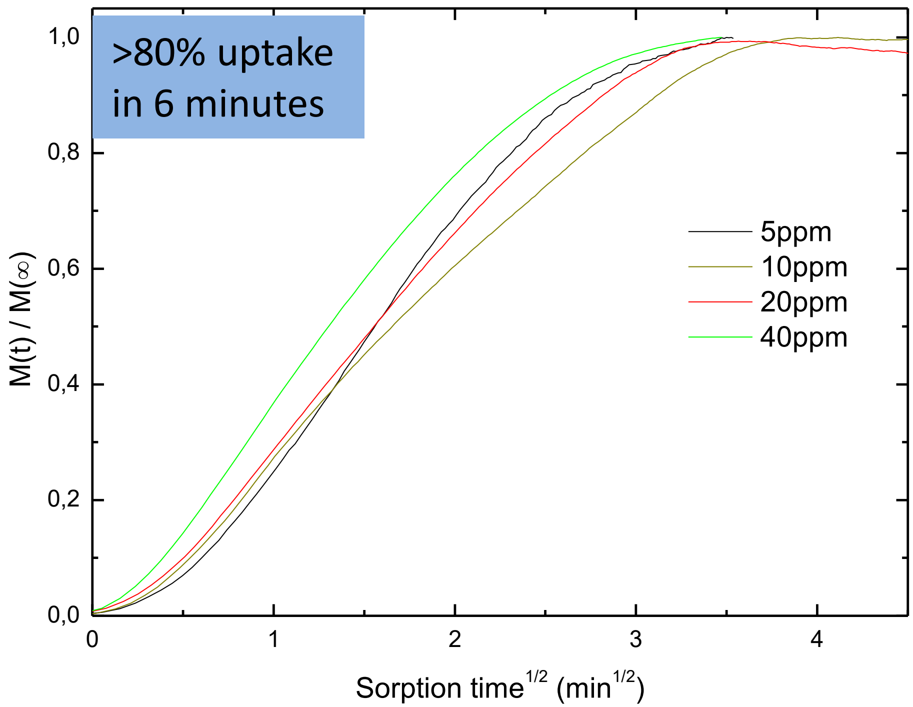
complete desorption occurs in 5 min

The sorption and desorption kinetics are only dependent on temperature and air flow rate, but not on the AcAn concentration in the inlet air

AcAn sorption/desorption kinetics



AcAn sorption and desorption kinetic curves



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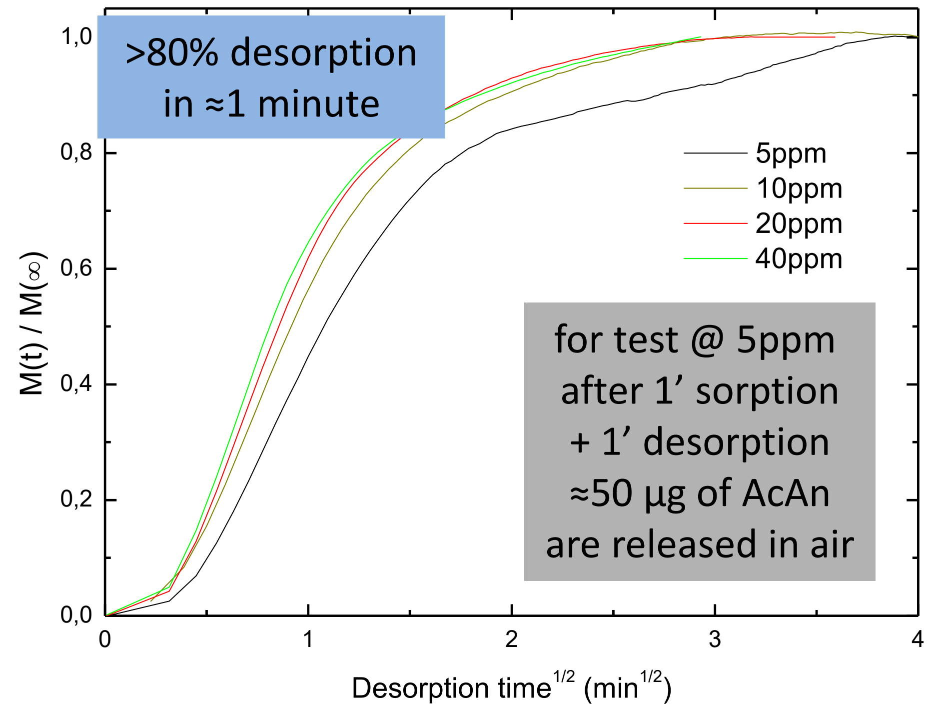
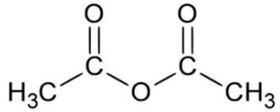


complete desorption occurs in 5 min

The sorption and desorption kinetics are only dependent on temperature and air flow rate, but not on the AcAn concentration in the inlet air

AcAn diffusivity



From the slopes of the sorption and desorption kinetic curves, considered in the range 0.5÷2 min$^{1/2}$, the diffusivity of AcAn in the δ sPS aerogel beads was calculated:

$$\frac{M_{(t)}}{M_{(\infty)}} = 4\sqrt{\frac{D}{\pi R^2}}\sqrt{t}$$

M(t) = mass of AcAn at any given time

M(∞) = amount of AcAn absorbed at the equilibrium condition

D = diffusivity

t = time

R = average sPS beads radius (~750 μm)

Air flow-in AcAn concentration (ppm)	D [cm^2/s] (sorption)	D [cm^2/s] (desorption)
5	3.3 10^{-6}	0.8 10^{-5}
10	3.0 10^{-6}	1.0 10^{-5}
20	2.8 10^{-6}	1.3 10^{-5}
40	3.8 10^{-6}	1.5 10^{-5}

Crank, J. *THE MATHEMATICS OF DIFFUSION*; Clarendon Press, Oxford, 1975.

Interfering agents

Sensors in the CUSTOM device:

- LED-IF *(Light Emitting diode – Induced Fluorescence)* infrared optochip is highly selective with respect to the various drug specimens for a low probability of false alarm.
- LPAS *(Laser Photo-acoustic Spectroscopy)* technique has high sensitivity with respect to other techniques based on infrared spectroscopy for a high probability of detection.

Possibility of false positive response due to interfering molecules commonly present in polluted air.

The selectivity of the polymer towards certain types of molecules allows to narrow the range of the interferents

Interfering agents

Air component molecule	Maximum concentration [ppm]
H_2O	60000
CO_2	1000
CH_4	10
CO	9
N_2O	1
NO_2	0,1
NO	0,1
O_3	0,1
SO_2	0,03

Interferent (gas)	Upper limit [ppm]
Butane	0,033
Ethylene	0,010
Propylene	0,010
1,3-butadiene	0,005

Interferent (liquid)	Upper limit [ppm]
Toluene	2,382
m, p-xylene	0,649
Ethylene glycol	0,491
Formaldehyde	0,400
Ethanol	0,146
Acetic acid	0,092
Naphthalene	0,071
Chloroform	0,038
Benzene	0,034
Ammonia	0,022
Methanol	0,016
o-xylene	0,016
Styrene	0,014
Acrylonitrile	0,011
Acrolein	0,011

Interfering agents

Air component molecule	Maximum concentration [ppm]
H_2O	60000
CO_2	1000
CH_4	10
CO	
N_2O	
NO_2	0,1
NO	0,1
O_3	0,1
SO_2	0,03

are not stably absorbed in δ sPS*

Interferent (gas)	Upper limit [ppm]
Butane	0,033
Ethyl	
Prop	
1,3-butadiene	0,005

are not stably absorbed in δ sPS*

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***Annunziata, L.; Albunia, A.R.; Venditto, V.; Mensitieri, G.; Guerra, G. *Macromolecules* 2006, *39*, 9166.**
Albunia, A.R.; Venditto, V; Guerra, G. *Journal of Polymer Science Part B: Polymer Physics* 2012, 50, 1474.

Interfering agents

Air component molecule	Maximum concentration [ppm]
H_2O	60000
CO_2	1000
CH_4	10
CO	
N_2O	
NO_2	0,1
NO	0,1
O_3	0,1
SO_2	0,03

are not stably absorbed in δ sPS*

Interferent (gas)	Upper limit [ppm]
Butane	0,033
Ethyl	
Prop	
1,3-butadiene	0,005

are not stably absorbed in δ sPS*

are not absorbed at all in δ sPS

Interferent (liquid)	Upper limit [ppm]
Toluene	2,382
m, p-xylene	0,649
Ethylene glycol	**0,491**
Formaldehyde	0,400
Ethanol	0,146
Acetic acid	0,092
Naphthalene	0,071
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Albunia, A.R.; Venditto, V; Guerra, G. *Journal of Polymer Science Part B: Polymer Physics* 2012, 50, 1474.**

Interfering agents

Interferent (liquid)	Upper limit [ppm]
Formaldehyde	0,400
Ethanol	0,146
Acetic acid	0,092
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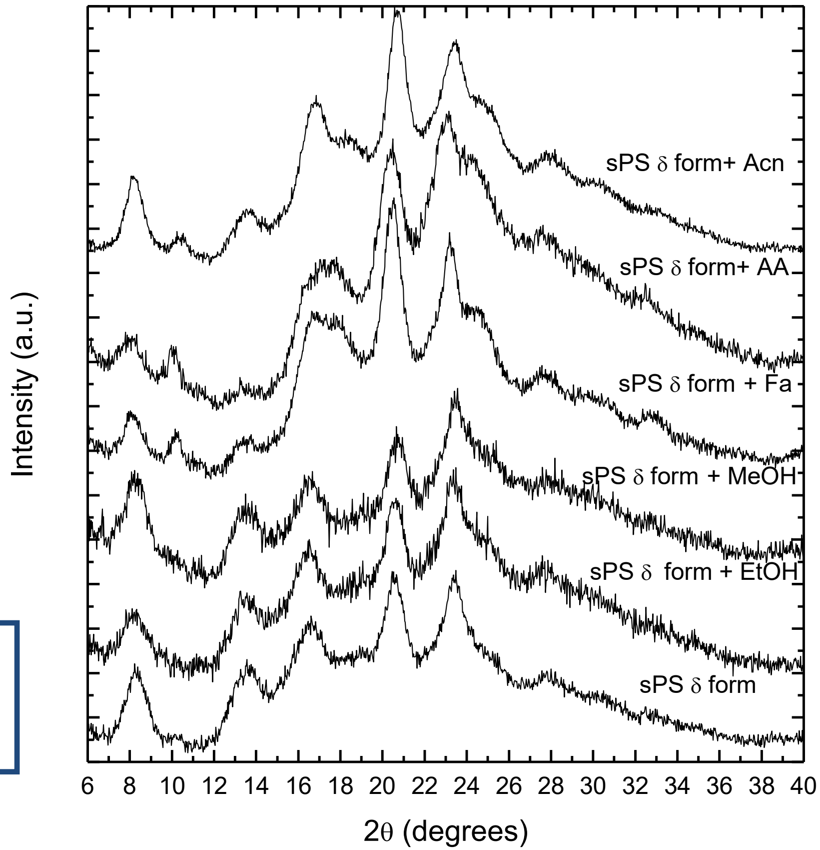


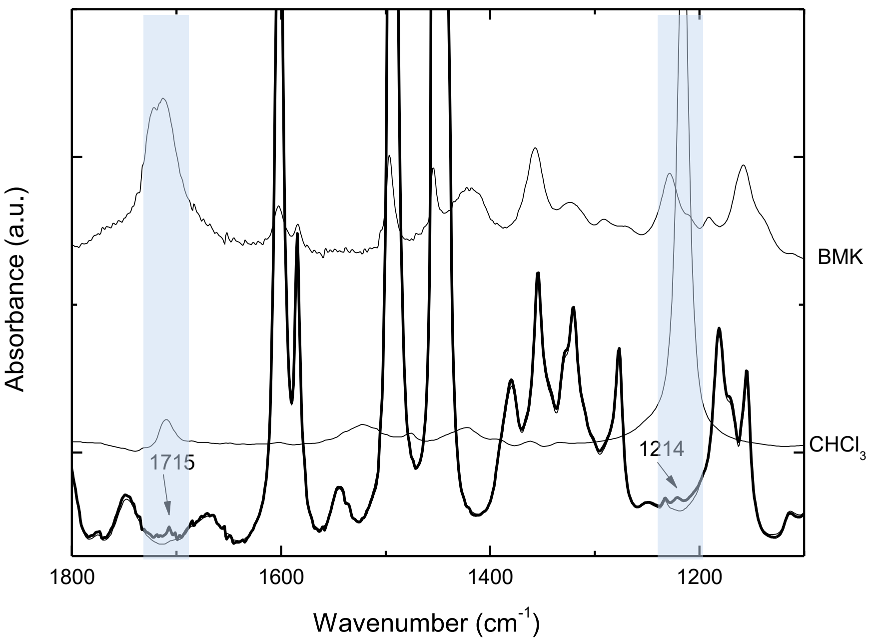
Formaldehyde, acetic acid and acrylonitrile are absorbed in δ sPS crystalline phase

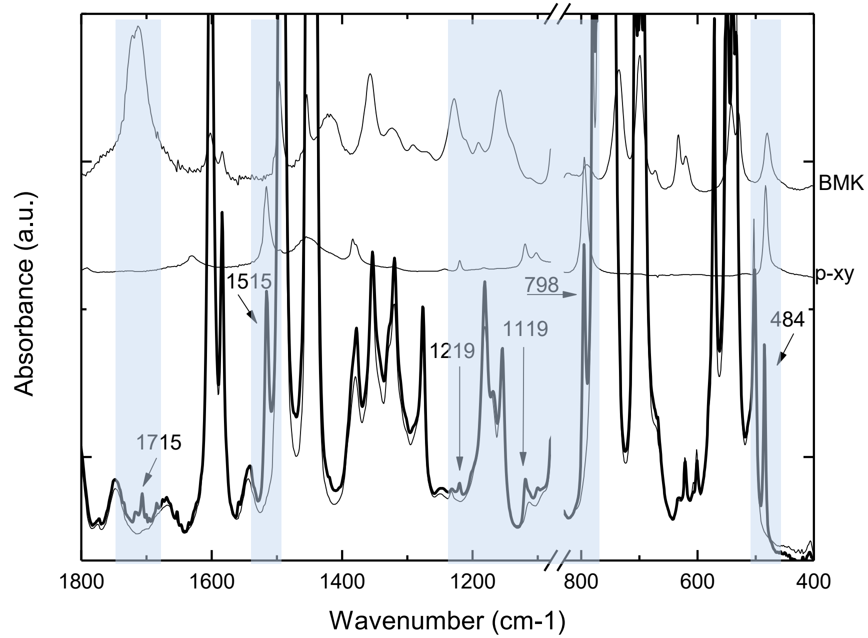
MeOH and EtOH are not absorbed in δ sPS crystalline phase

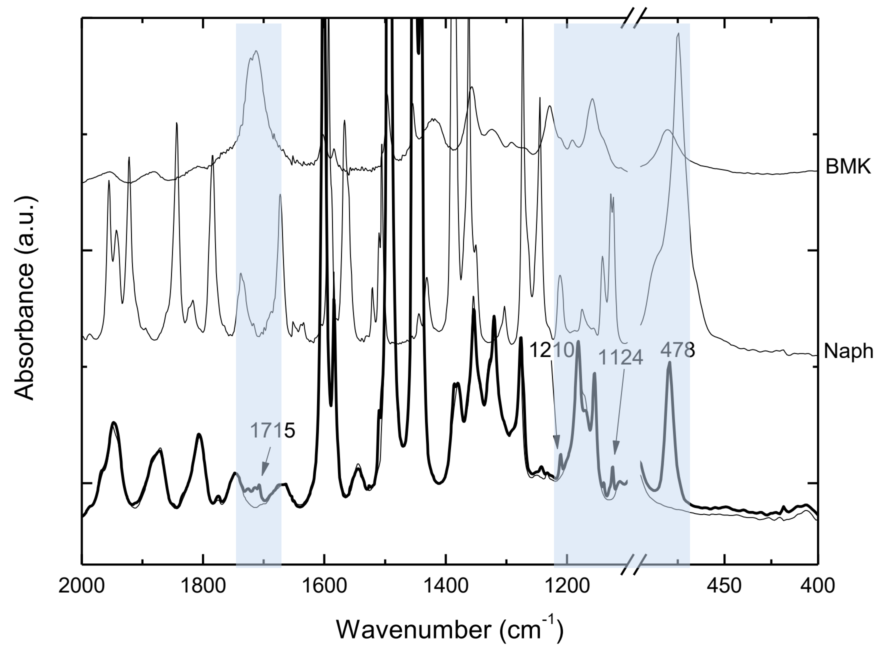
Interfering agents

Aqueous solutions BMK/interferent : 10/1

Tested interferents:
chloroform, *p*-xylene, naphthalene







cf of BMK is not affected by the presence of the interfering agents

Conclusions

Development of a procedure to achieve δ sPS aerogel , the absorbing material suitable for CUSTOM project aims, in beads shape.

δ sPS aerogel is a suitable material to concentrate 3 drug precursors, because it ensures high concentration factors (1 10^4 for BMK, 5 10^4 for Safrole, 2 10^2 for AcAn; higher than those obtainable with other absorbing materials, i.e. activated carbon) and presents fast sorption and desorption kinetics.

Validation of the operation mode of the preconcentrator realized by ENEA for the CUSTOM project: in laboratory tests it effectively concentrates at least 1 of the target precursors.

Selectivity of the absorbing material (δ sPS) allows to narrow the field of possible interfering agents; however, in the preconcentrator it effectively absorbs precursors even in presence of interferents, i.e. in environmental conditions very similar to those that presumably occur in real use conditions (e.g. in customs).


Thanks!

Data on equilibrium uptake

Conditions for BMK vapours sorption:

T = 40°C
Exposure time = 2 h

Conditions for Safrole vapours sorption:

T = 40°C
Exposure time = 30 min

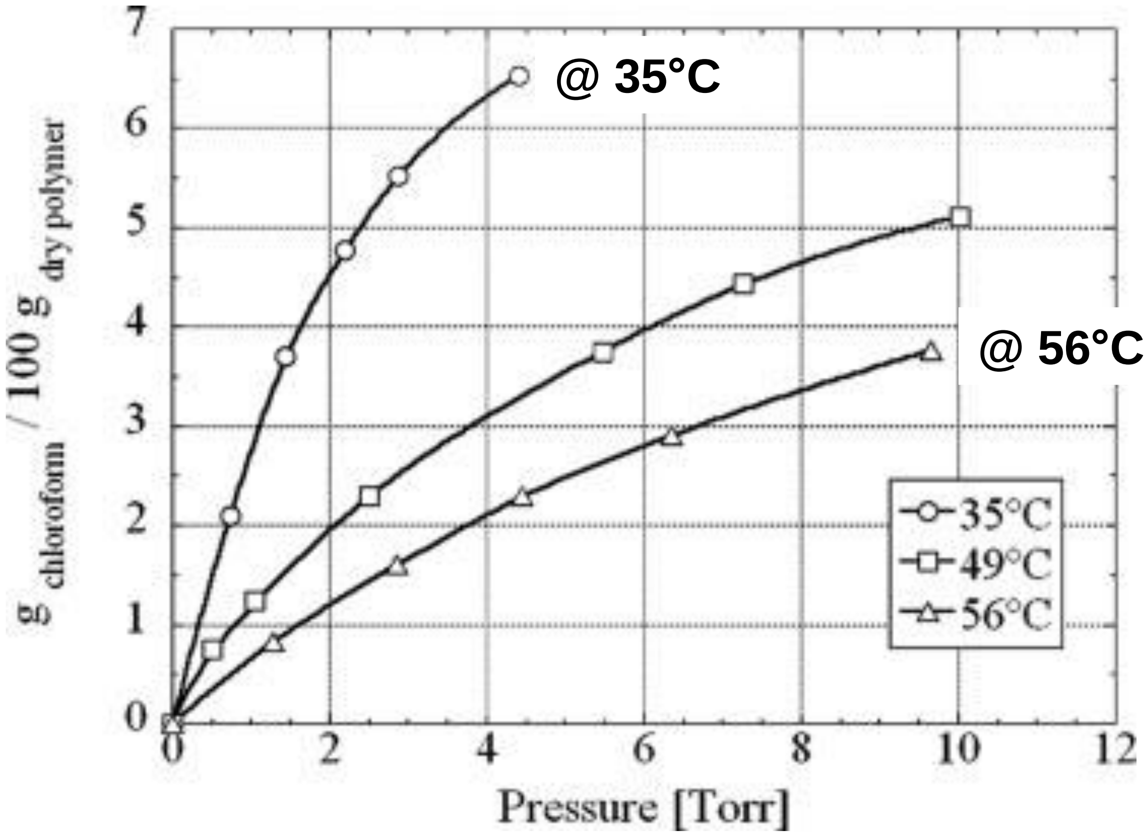
Conditions for AcAn vapours sorption:

T = 23°C
Exposure time = 2 min

Drug Precursor	**%wt sorption in δ sPS (from vapours)**	**Filled cavities of crystal lattice of δ sPS**
BMK	30%	90%
Safrole	20%	50%
AcAn	4%	17%

Influence of temperature on VOCs sorption

Chloroform sorption isotherms in s-PS δ-form films



sorption process has

exothermic nature

due to the adsorption into the

crystalline nanocavities of sPS δ

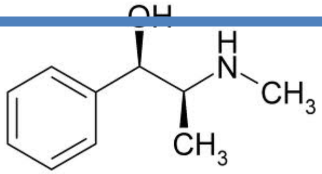
form

sorption is maximized @ low temperature

desorption is maximized @ high temperature

Mensitieri, Larobina, Guerra, Venditto, Fermeglia, Pricl, *J.Polym.Scie.B,* 2008, *46*, 8-15

Stability/degradation of Ephedrine

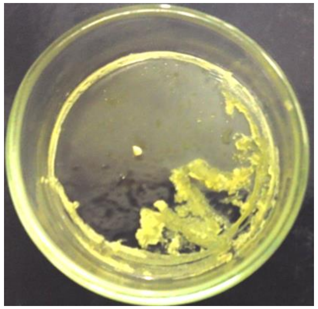


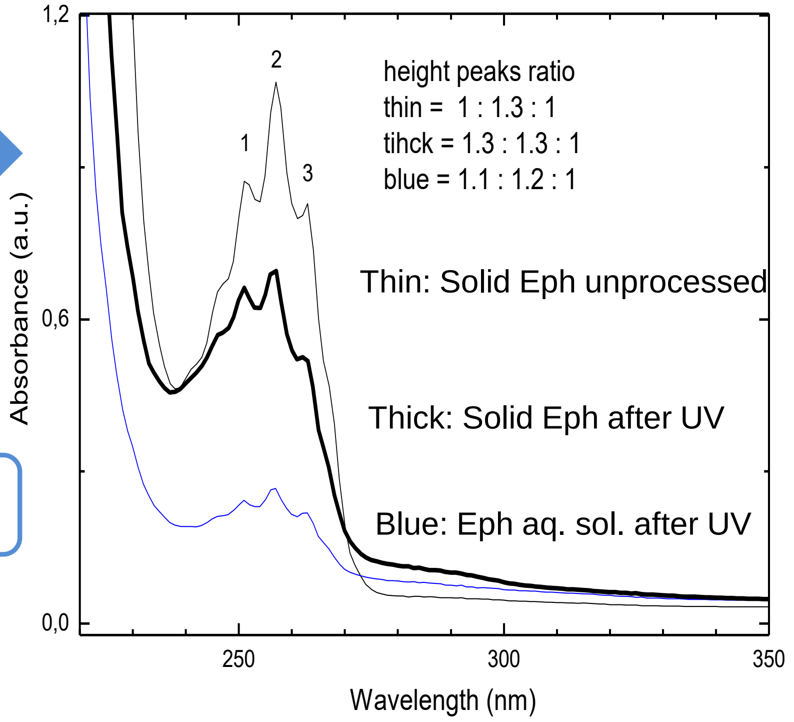
Ephedrine:

✓water and alcohol solutions are stable even at solvent boiling temperature

✓decomposes on exposure to UV light developing a smell of benzaldehyde

2 h under UV light
λ = 254 nm,
100 J/cm²

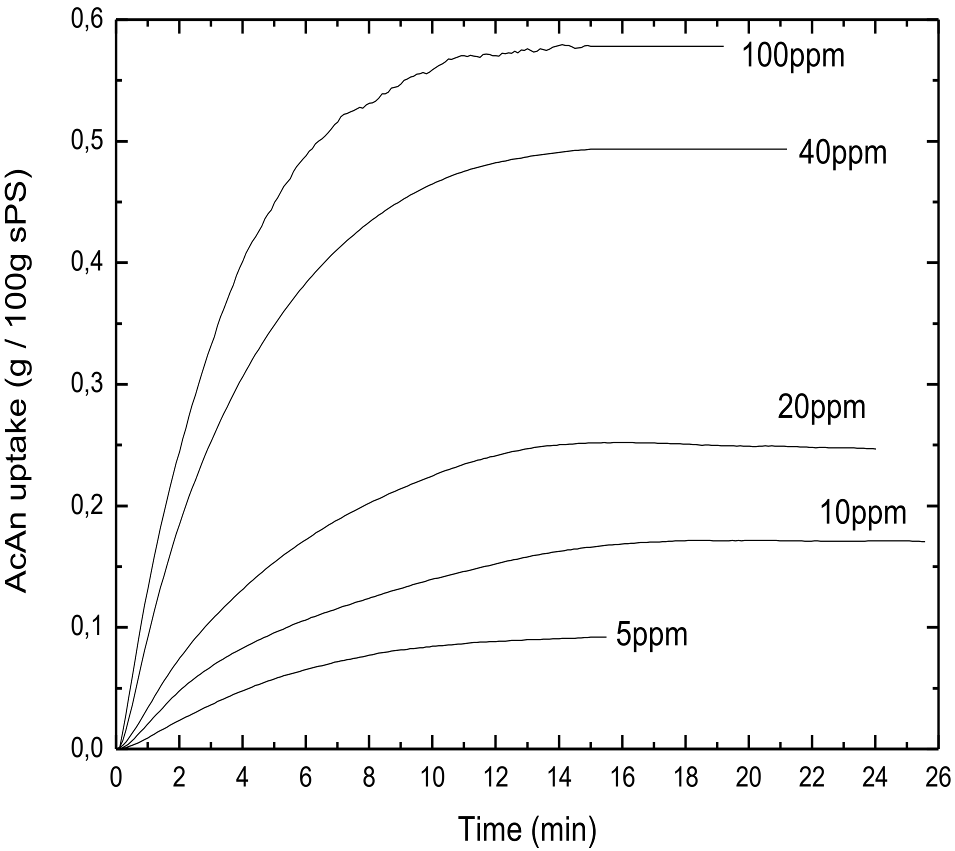




Ephedrine decomposes on exposure to UV light

Chou, T.Q., *J. Biol. Chem.*, **1926**, 109.
Manske & Holmes, *The Alkaloids*, Vol III, 344-347, Academic Press, **1953**.
Moore, E.E.; Moore, M.B., *Industrial and Engineering Chemistry*, **1931**, Vol. 23, No. 1, 21.

AcAn equilibrium uptake



AcAn initial concentration (ppm)	Total amount of AcAn absorbed (mg)
5	0.32
10	0.60
20	0.88
40	1.73
100	2.16

$$n_{AnAc} = \frac{I_{(t)}}{10^6} \cdot Q_{air} \cdot \frac{1}{22{,}414}$$

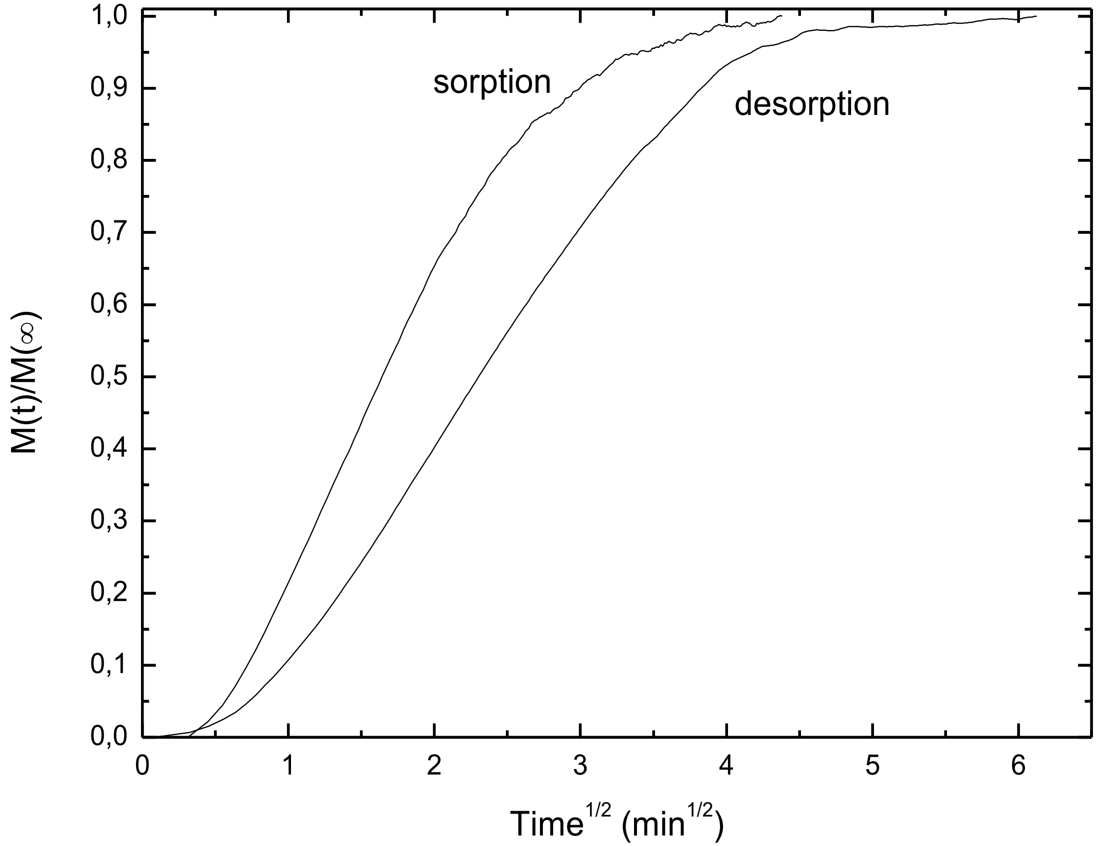
$$\left(mol = \frac{ppm \cdot min}{ppm} \cdot \frac{NL}{min} \cdot \frac{mol}{NL}\right)$$

Sorption and desorption at 100 ppm of AcAn

Sorption and desorption of AcAn at 100 ppm air flow-in

T sorption/desorption = 15°C
Air flow-in = 128 NL/h
Air flow-out = 60 NL/h

Diffusivity:
Sorption = 3.5 10^6 (cm^2/s)
Desorption = 1.9 10^6 (cm^2/s)



The test at 100ppm of AcAn has been performed at 15°C, both in sorption and in desorption phase, to verify the correct estimation of diffusivity coefficient, D. The value of

D in this case is of the same magnitude order than other cases studied.

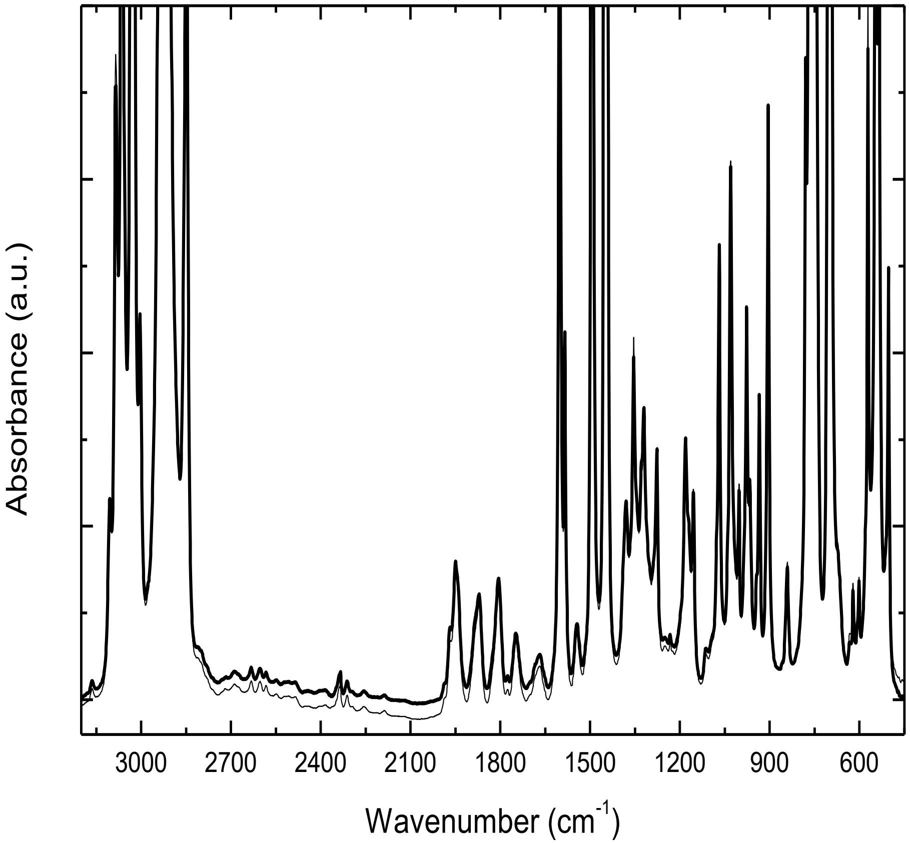
Comparison between AcAn and DCE diffusivity

Air flow-in AcAn concentration (ppm)	D [cm^2/s] (sorption)	D [cm^2/s] (desorption)
5	$3.3\ 10^{-6}$	$0.8\ 10^{-5}$
10	$3.0\ 10^{-6}$	$1.0\ 10^{-5}$
20	$2.8\ 10^{-6}$	$1.3\ 10^{-5}$
40	$3.8\ 10^{-6}$	$1.5\ 10^{-5}$

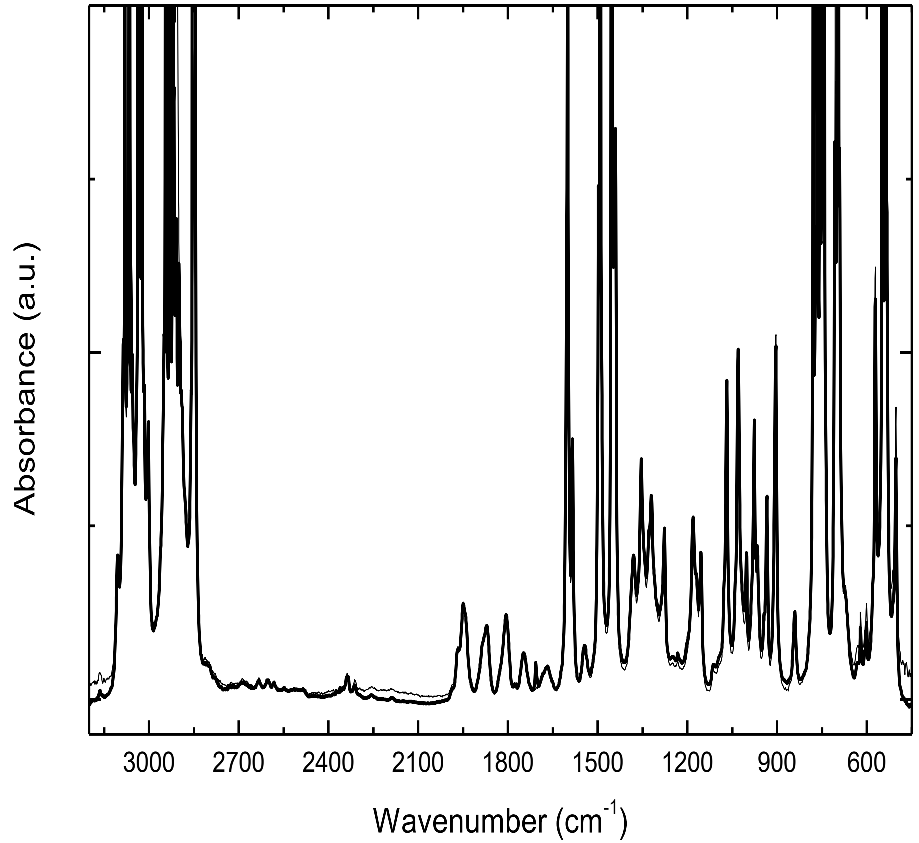
DCE aqueous solution concentration (ppm)	D [cm^2/s] (sorption)	D [cm^2/s] (desorption)
10	$2.3\ 10^{-8}$	-
100	$1.7\ 10^{-7}$	$1.6\ 10^{-7}$

Daniel, C.; Sannino, D.; Guerra, G. *Chem. Mater.*, **2008**, *20*, 577.

FTIR spectra of interferents

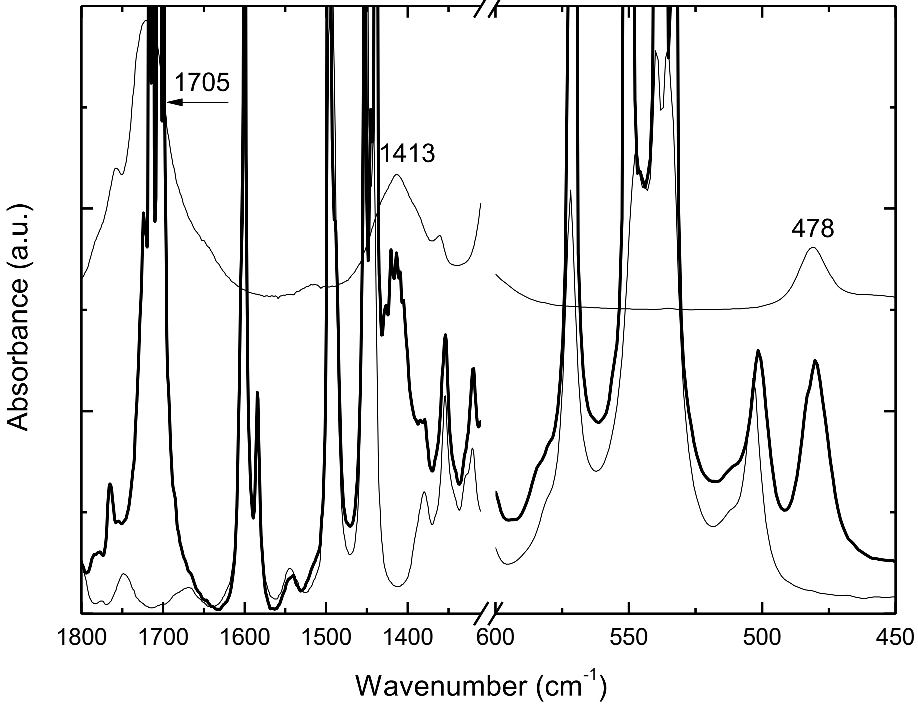


δ sPS aerogel + Ethylene glycol vapours

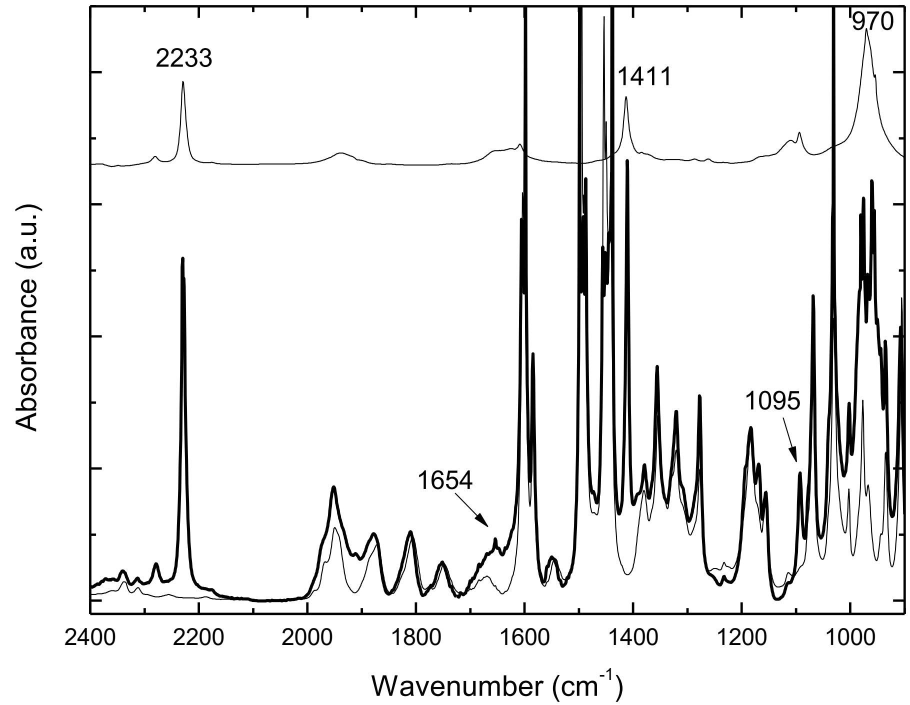


δ sPS aerogel + Ammonia vapours

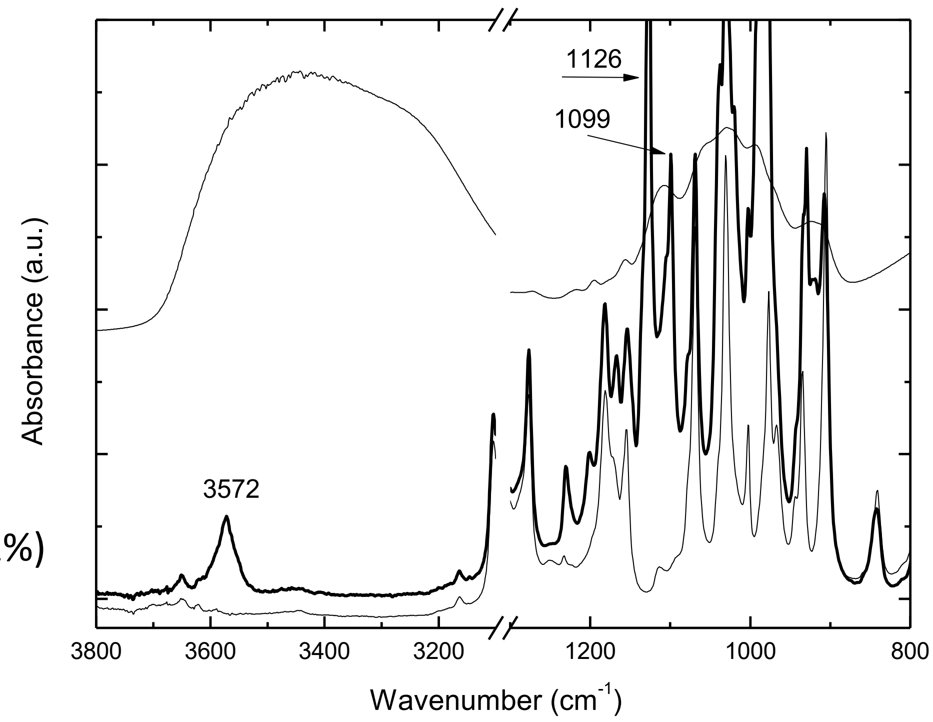
No absorbance



δ sPS aerogel +
Acetic acid vapours (5%)

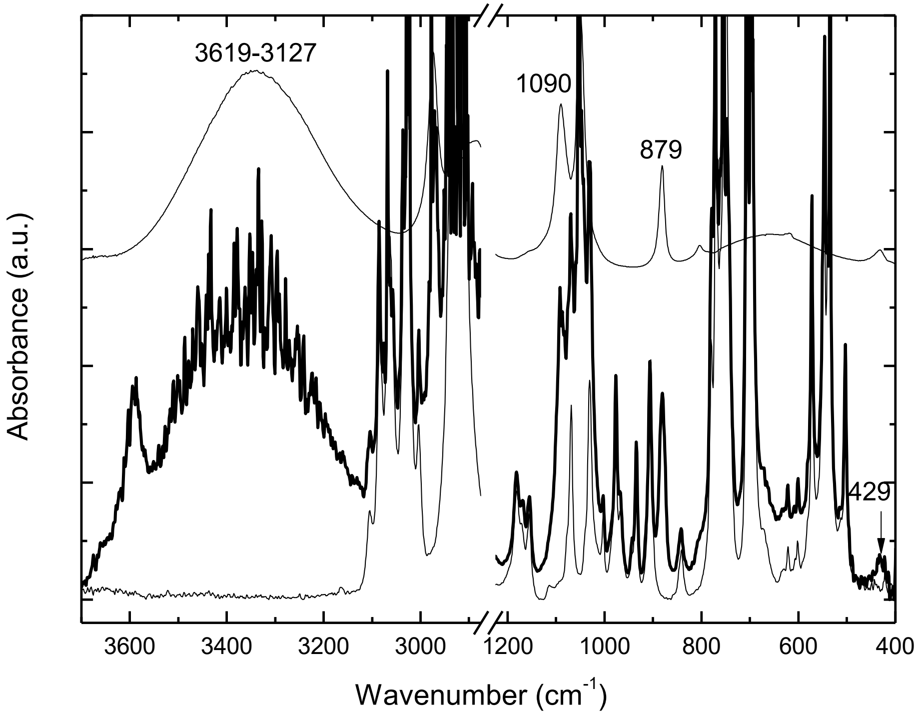


δ sPS aerogel +
Acrylonitrile vapours (25%)

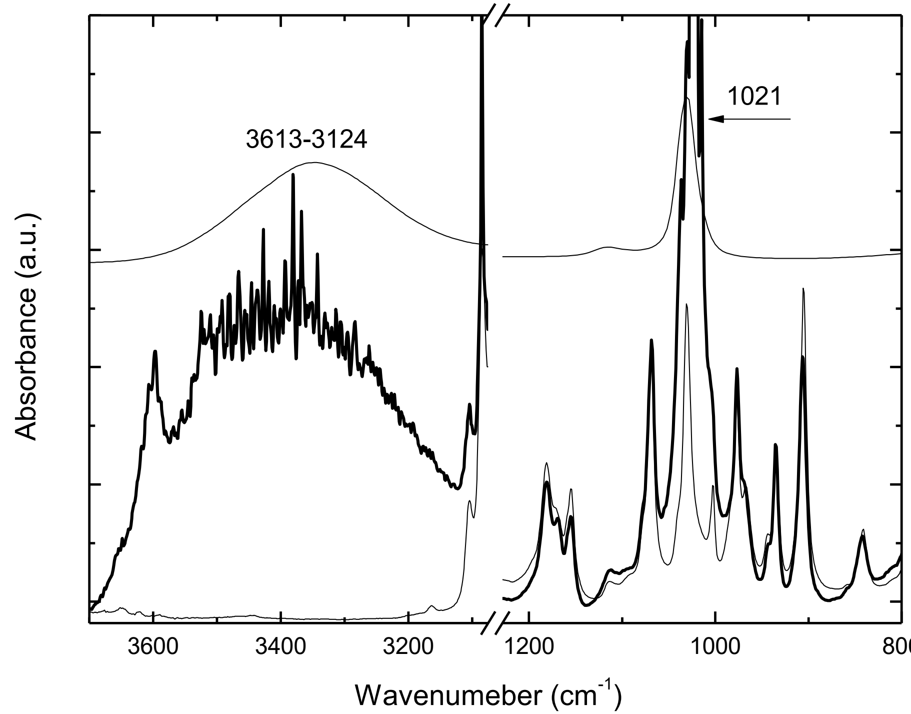


δ sPS aerogel +
Formaldehyde vapours (11%)

Absorbance in the crystalline phase too



δ sPS aerogel + Ethanol vapours (22%)

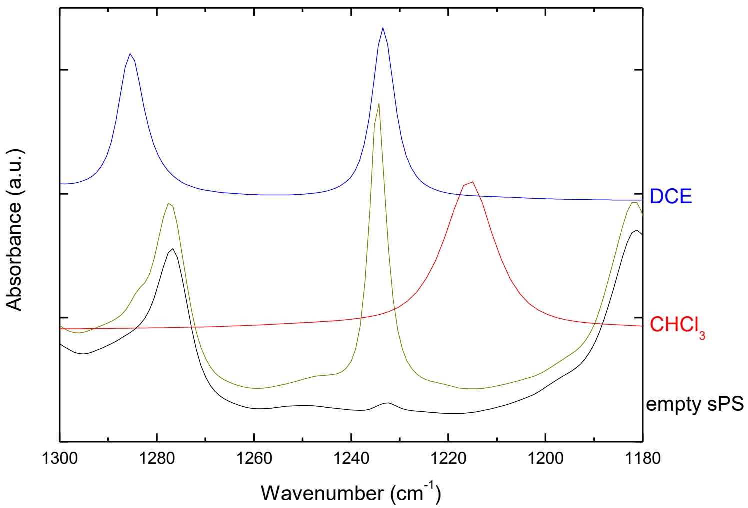


δ sPS aerogel + Methanol vapours (32%)

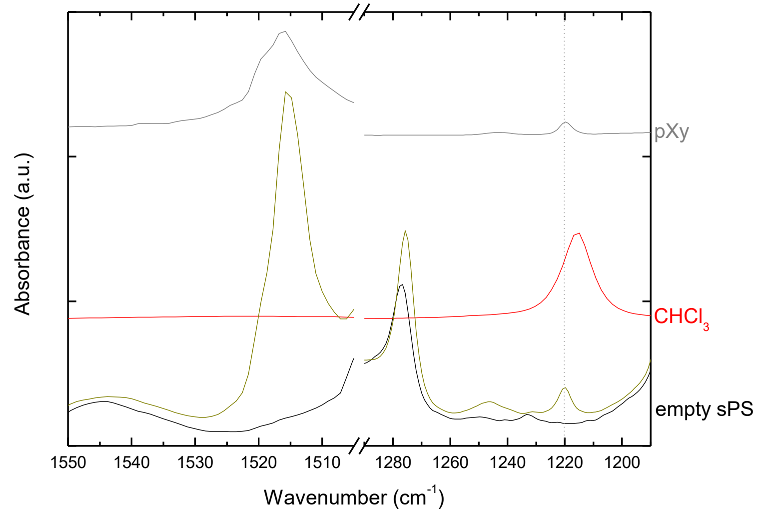
Absorbance in the amorphous phase only

Interfering agents

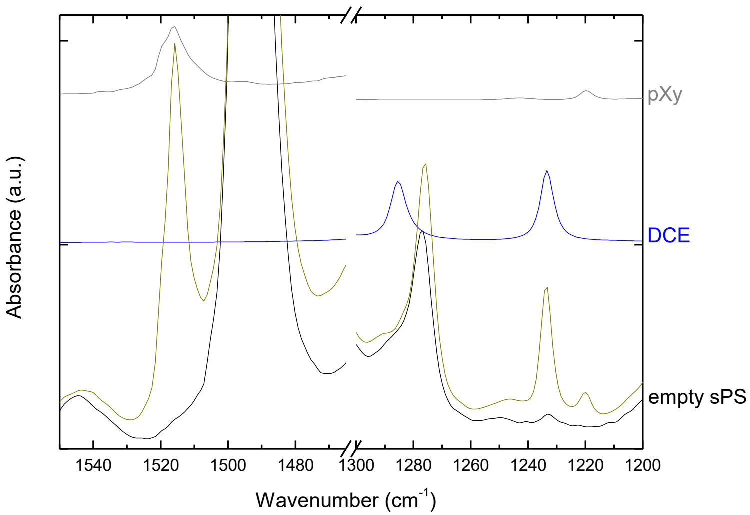
Interferents mixtures 1/1



cf: $CHCl_3$ not absorbed, DCE $2{\cdot}10^4$



cf: $CHCl_3$ not absorbed, *p*-xylene $3{\cdot}10^4$



cf: DCE $1{\cdot}10^4$, *p*-xylene $2{\cdot}10^4$

sPS is selective towards DCE and pXy when in mixture with $CHCl_3$.

cf of DCE and pXy in the polymer remains essentially unchanged if the polymer is exposed to a 1:1 mixture of these two VOCs.