A New Stationary Phase for Confirming Organic Volatile Impurity Testing in Pharmaceutical Products

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RESTEK

GC Analysis of OVI by USP <467>

- ## Method I: G27 30m x 0.53mm x 5.0 df
  - Direct Aqueous
- ## Method IV: G43 30m x 0.53mm x 3.0 df
  - Static Headspace
- ## Method V: G43 30m x 0.53mm x 3.0 df
  - Direct Aqueous
- ## Method VI: choice of 9 columns, depending on monograph
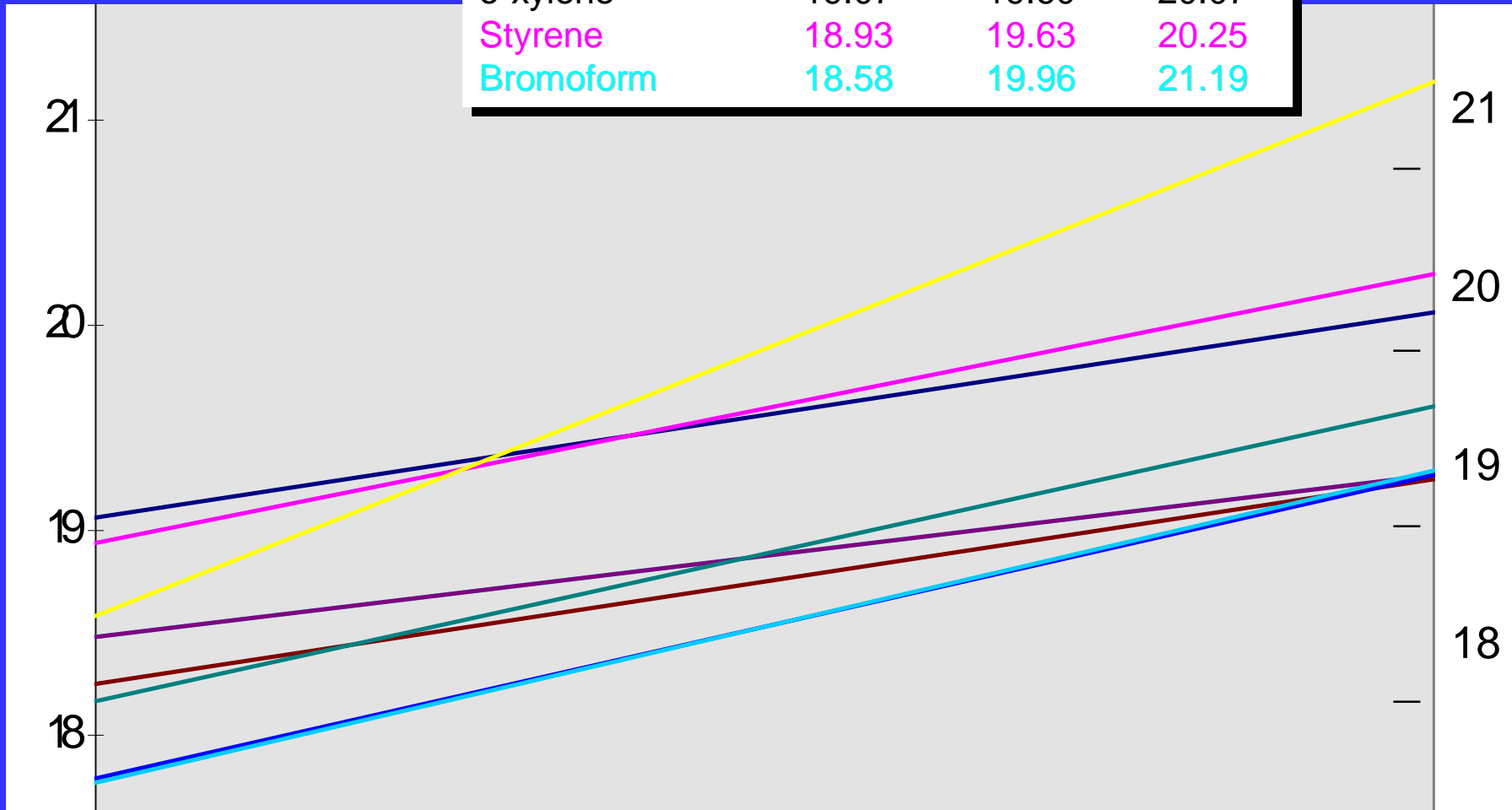
Confirmation Column Criteria

- Change in selectivity
- Low bleed
- Critical resolution
- FID or MS detection

- Column Design

Modeling

	Rtx-1	Rtx-502	Rtx-35
Chlorobenzene	17.79	18.57	19.27
1112te ethane	17.78	18.58	19.29
E benzene	18.26	18.78	19.25
m/p-xylene	18.48	18.90	19.27
o-ClF benzene	18.16	18.93	19.61
o-xylene	19.07	19.60	20.07
Styrene	18.93	19.63	20.25
Bromoform	18.58	19.96	21.19

Predicted vs. Actual Retention Times

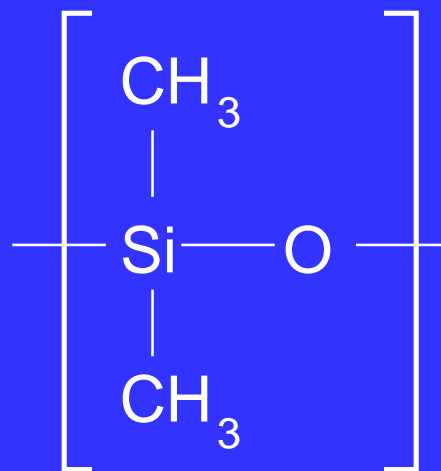|	pred	actual	differ
Chlorobenzene	18.57	18.74	-0.17
1112tet ethane	18.58	18.75	-0.17
E benzene	18.78	18.84	-0.06
m/p-xylene	18.90	18.98	-0.08
1CL2F benzene	18.93	19.13	-0.20
0-xylene	19.60	19.68	-0.08
stryrene	19.63	19.72	-0.09
bromoform	19.96	20.25	-0.29
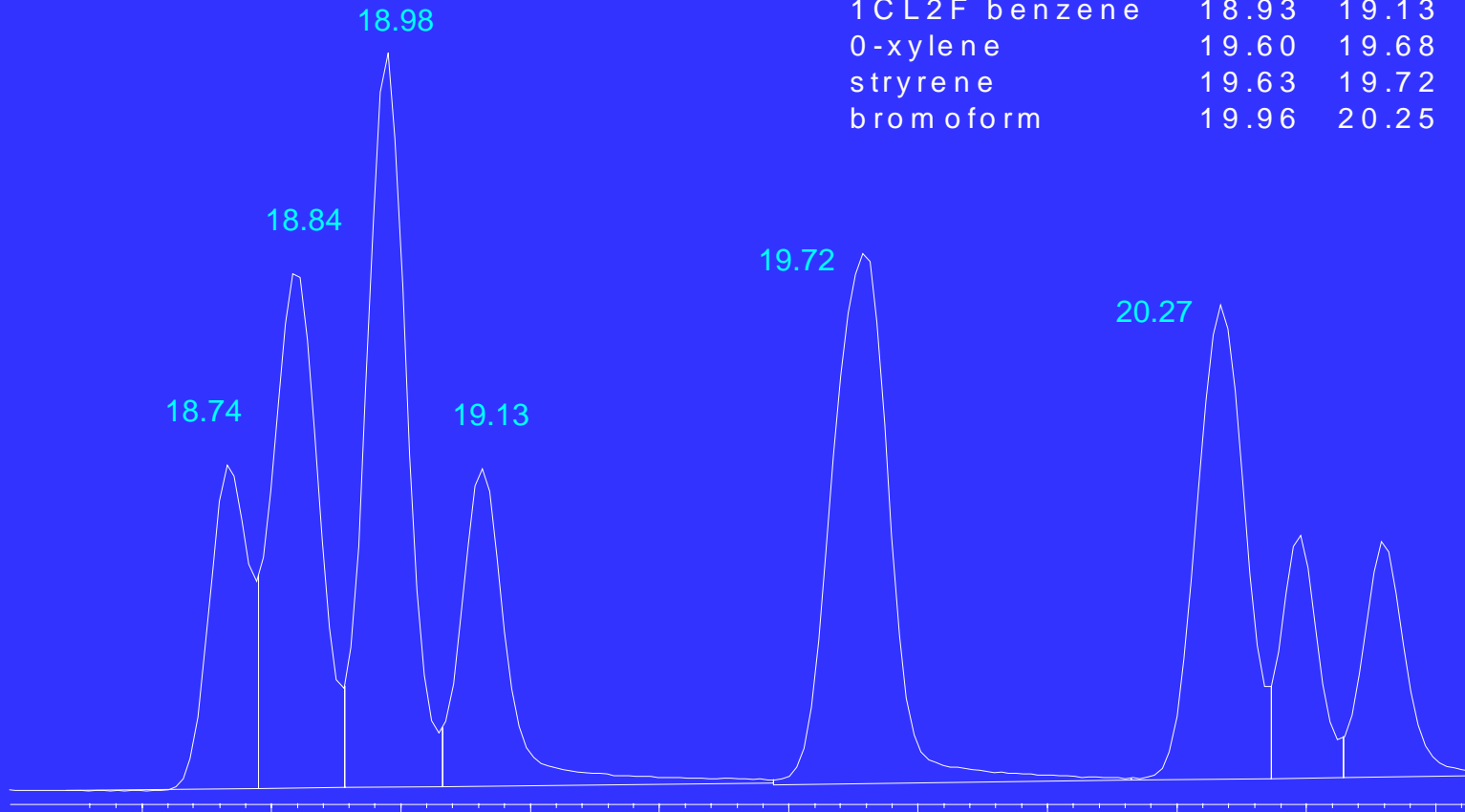
Stationary Phases Used for Modeling
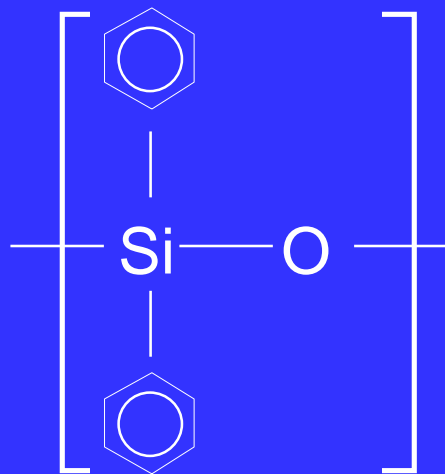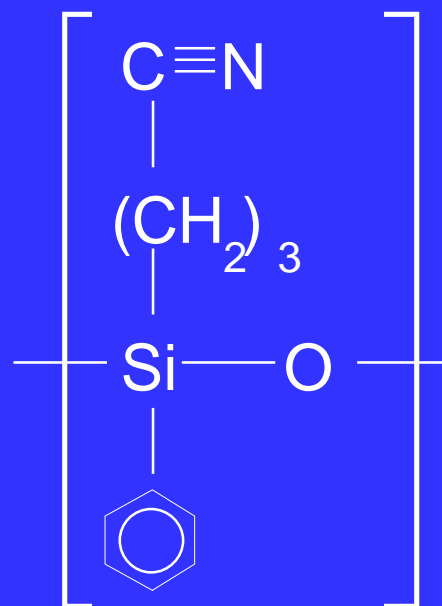
trifluoropropylmethyl
polysiloxane
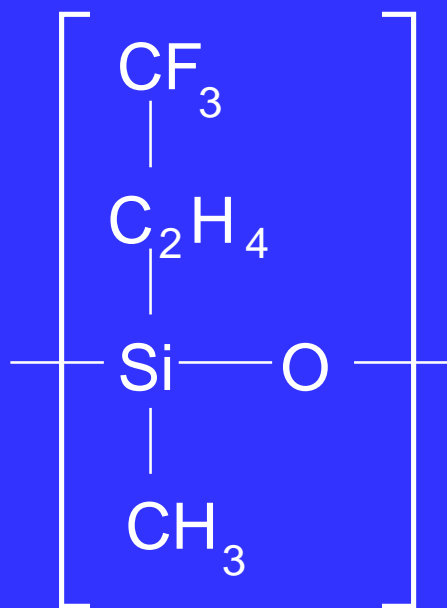
dimethyl
polysiloxane

Stationary Phases Used for Modeling

diphenyl
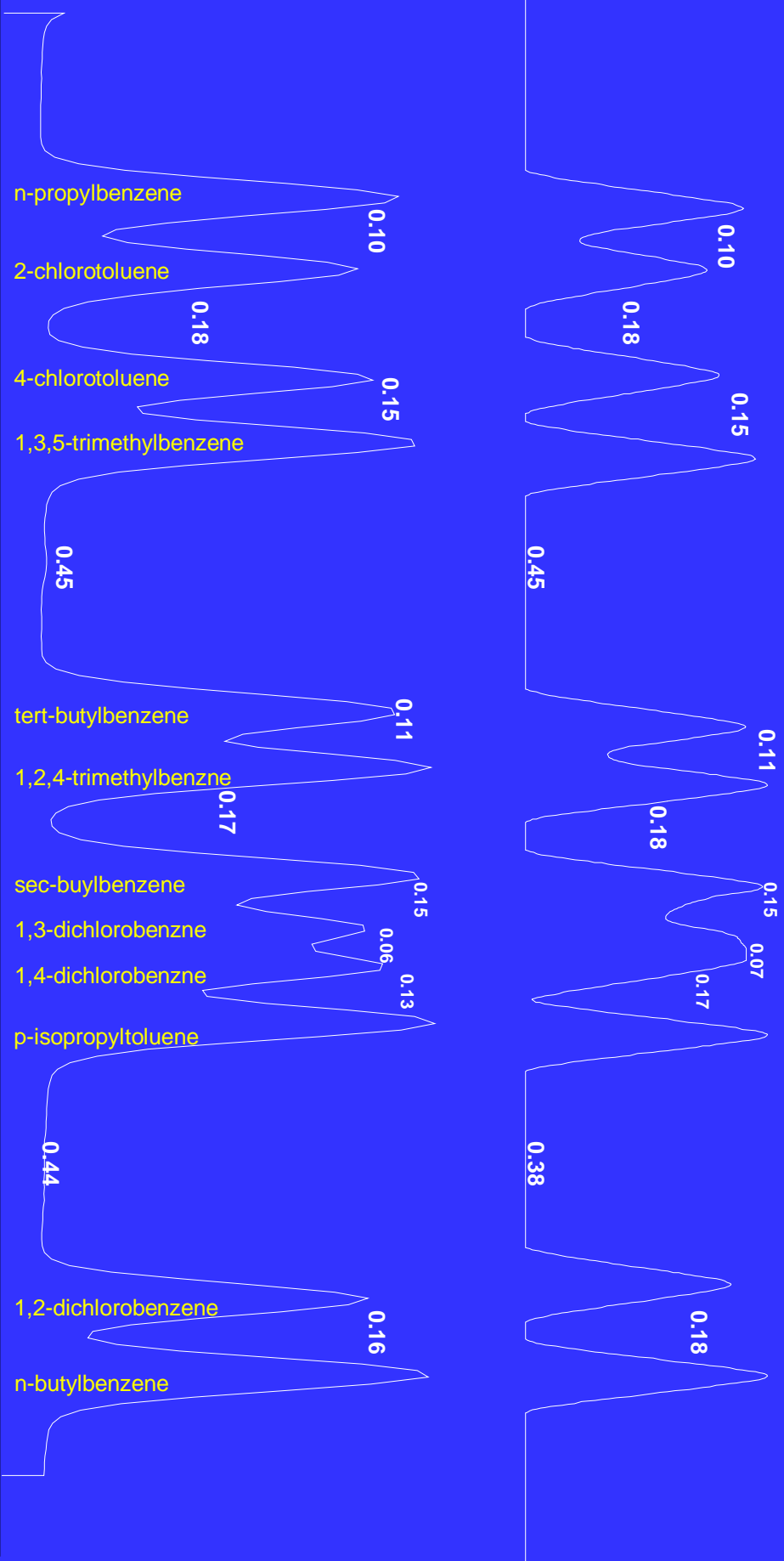polysiloxane

cyanopropylphenyl
polysiloxane

Predicted vs. Actual 4 Dimensional Phase

n-propylbenzene — 0.10
2-chlorotoluene — 0.18
4-chlorotoluene — 0.15
1,3,5-trimethylbenzene — 0.45
tert-butylbenzene — 0.11
1,2,4-trimethylbenzne — 0.17
sec-buylbenzene — 0.15
1,3-dichlorobenzne — 0.06
1,4-dichlorobenzne — 0.13
p-isopropyltoluene — 0.44
1,2-dichlorobenzene — 0.16
n-butylbenzene

0.10
0.18
0.15
0.45
0.11
0.18
0.15
0.07
0.17
0.38
0.18

Actual Phase - Rtx®-VGC
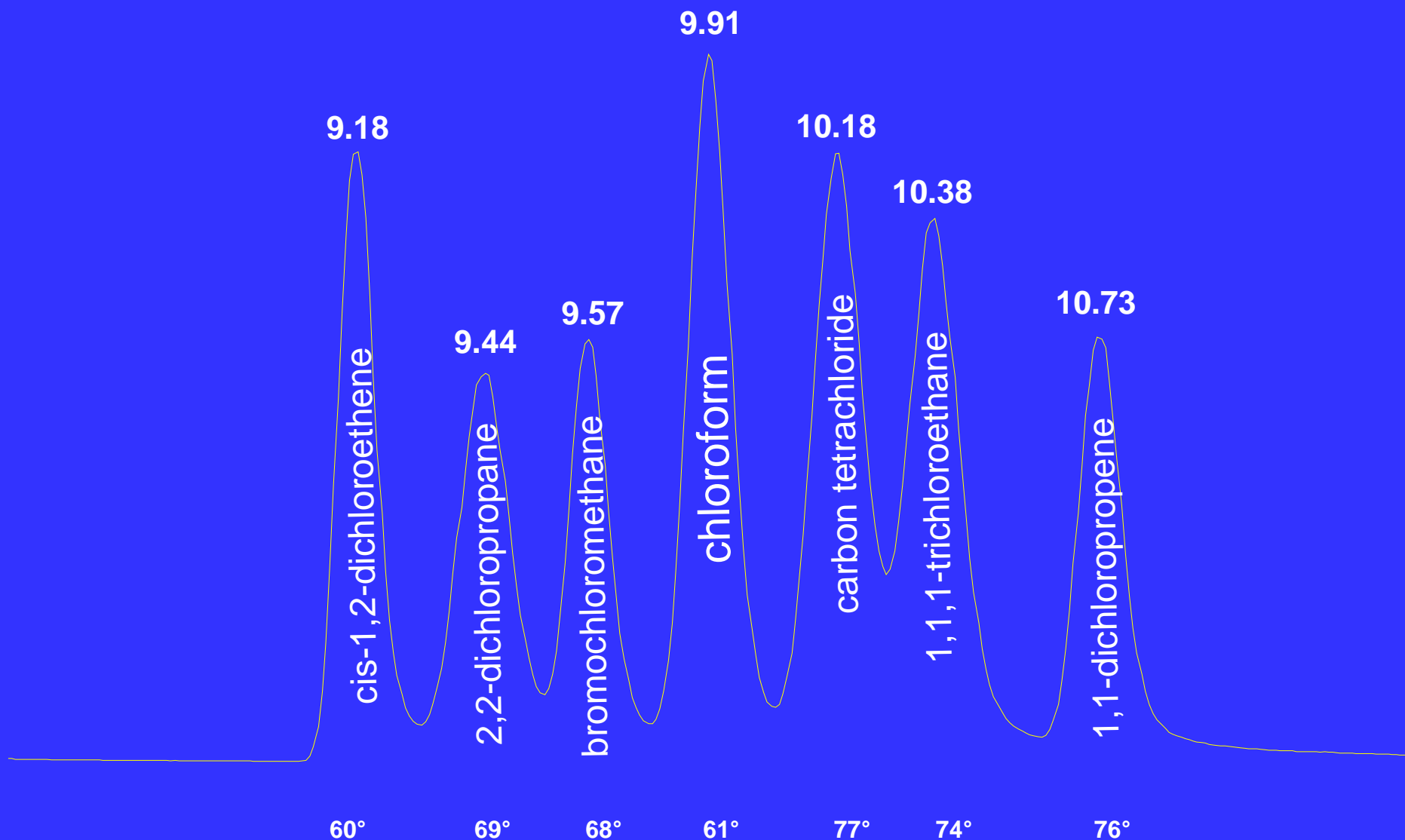
USP <467> Method I

Method I: G27 30m x 0.53mm x 5.0μm df, w/5m PM guard

Inj: Direct Aqueous, 1/10 dilution, 70°C, 1μL

Oven Temp: 35(5)8/175 (0) 35/260

Detector: FID, 260°C, 1 x 10^{-12} AFS

Carrier: helium, 4.1psi const., 35cm/sec @ 35°C

methylene chloride	600ppm
chloroform	60ppm
benzene	2ppm
trichloroethylene	80ppm
1,4-dioxane	380ppm

Rtx®-VGC
USP <467> Method I

methylene chloride

chloroform

benzene

trichloroethylene

1,4-dioxane

5

10
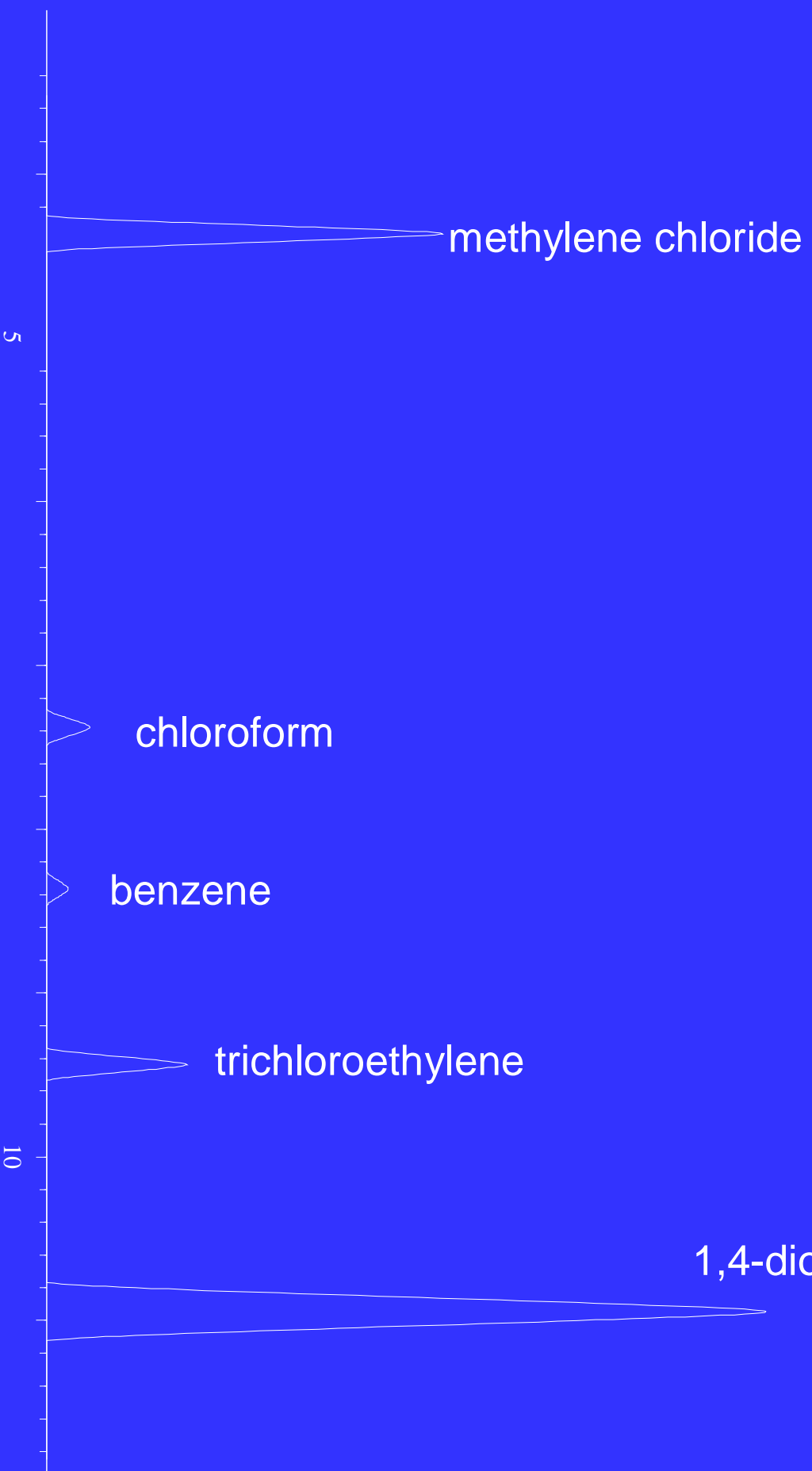
USP <467> Method IV

Method IV: G43 30m x 0.53mm x 3.0µm df

Inj: 100µL cat#36007 in 5mL water, 1g sodium sulphate in 20mL headspace vial

Oven Temp: 40(20)35/240(20)

Detector: FID, 260°C, 1.25 x 10^{-11} AFS

Carrier: helium, 3.5psi const., 35cm/sec @ 40°C

Split Ratio: 2:1

Concentrator: ThermoQuest HS2000 Headspace Autosampler Vial 80°C, 60 min. shaker on

USP <467> Method IV

USP <467> Calibration Mix #5 (cat# 3007)

Prepared in dimethylsulfoxide, 1mL/ampul

methylene chloride	600ppm
chloroform	60ppm
benzene	2ppm
trichloroethylene	80ppm
1,4-dioxane	380ppm

Rtx®-VGC
USP <467> Method IV

35°C (5) @ 8°C/min to 175°C   Inlet Pressure : 24.1 kPa

mV

methylene chloride

chloroform

benzene

trichloroethylene

1,4-dioxane

TRACE-FID
36007

Minutes
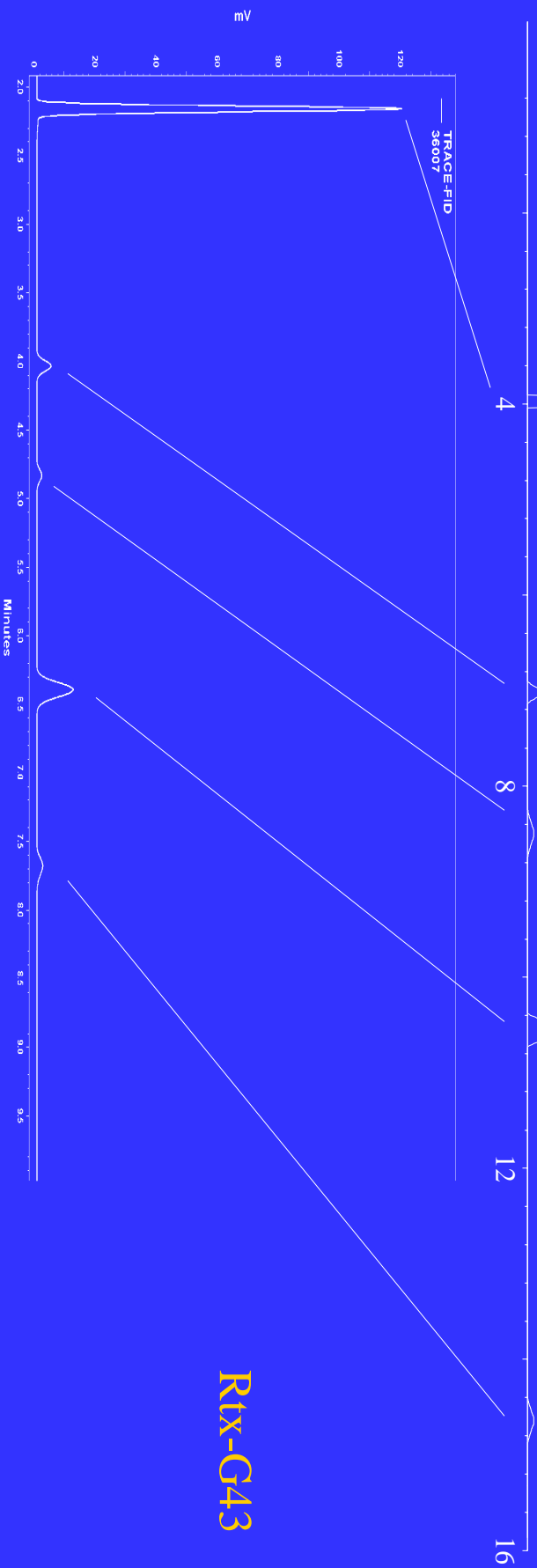
Rtx-G43

USP <467> Method V

Method V: G43 30m x 0.53mm x 5.0µm df, w/5m PM guard

Inj: Direct Aqueous, 1/10 dilution, 70°C, 1µL

Oven Temp: 40(20)35/240(10)

Detector: FID, 260°C, 1 x 10^{-12} AFS

Carrier: helium, 4.1psi const., 35cm/sec @ 35°C
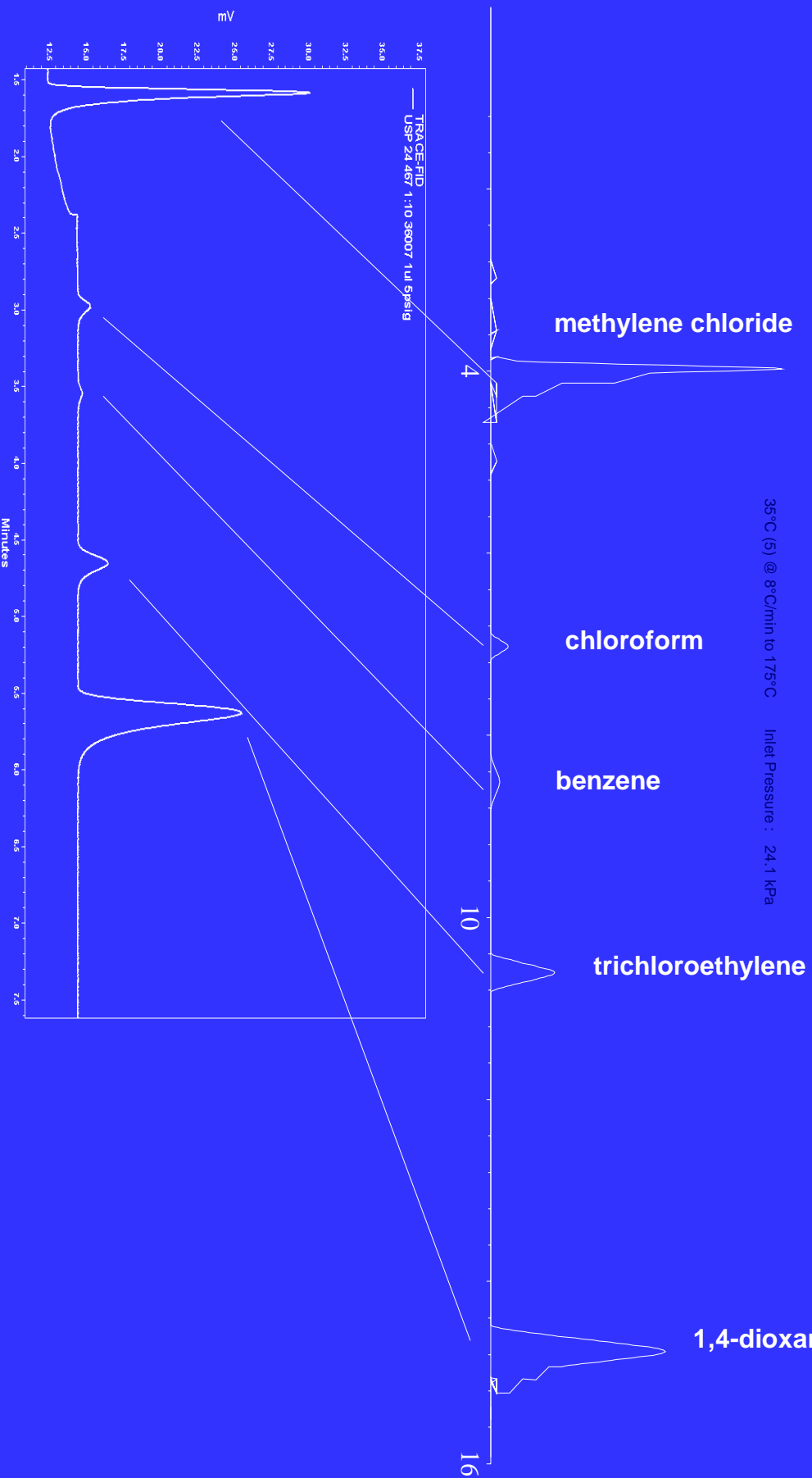
USP <467> Method V

USP <467> Calibration Mix #5 (cat# 3007)

Prepared in dimethylsulfoxide, 1mL/ampul

methylene chloride	600ppm
chloroform	60ppm
benzene	2ppm
trichloroethylene	80ppm
1,4-dioxane	380ppm

Rtx®-VGC
USP <467> Method V

35°C (5) @ 8°C/min to 175°C   Inlet Pressure :   24.1 kPa

mV

methylene chloride

chloroform

benzene

trichloroethylene

1,4-dioxane

—— TRACE-FID
USP 24 467 1:10 36007 1ul 5psig

Minutes

USP <467> Common solvents

Method I: G27 30m x 0.53mm x 5.0μm df, w/5m PM guard

Inj: Headspace at 500ppm in bulk pharm. 2:1 split

Oven Temp: 35(10)5/100 (0) 25/240(5)

Detector: FID, 260°C, 1 x 10^{-11} AFS

Carrier: helium, 4.1psi const., 35cm/sec @ 35°C

Samples shaken and heated at 90°C for 15 minutes, 1mL headspace injection.

Rtx®-G27
USP <467>
Common Solvents

benzene/C-tet/n-butanol
1,2-DCA
1,1,1-TCA
chloroform
ethyl ace
MEK / C-6
n-propanol
methylene chloride
1,1-dichloroethene
diethyl ether
cetonitrile/ aceteone/ isopropanol
ethanol
ethylene oxide
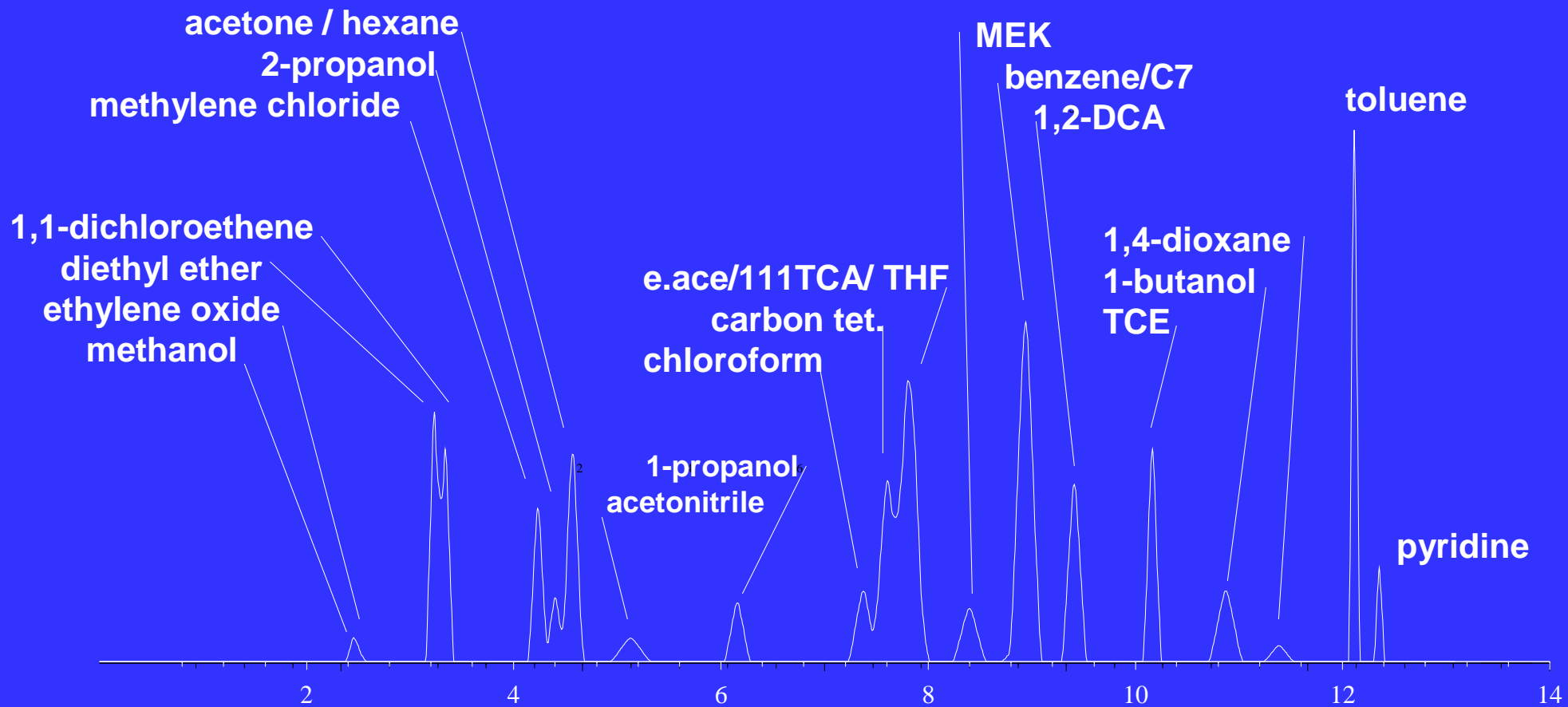methanol
THF
toluene
1,4-dioxane
C7
TCE
pyridine

20 minutes

Rtx®-VGC
USP <467> Common Solvents

Rtx®-VGC

- New stationary phase
- Unique selectivity
- Low bleed
- Confirm G27, G43

Conclusions

- First in a series of application-specific columns
- Define customer needs
- Computer modeling
- Stationary phase predictions
- Resolution of critical compounds
- Most stable polymer functionalities

For More Information...

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