Derivatization of some carboxylic and hydroxy acids with the chiral fluorescent tag R-DBD-APy

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Brown University

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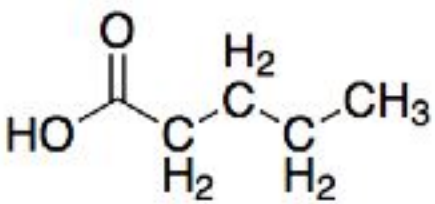
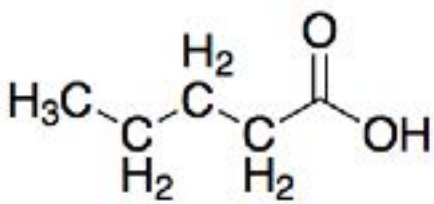
Chirality

Achiral
(can superimpose mirror images)

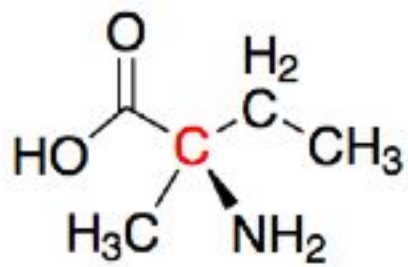
Chiral
(cannot superimpose mirror images)



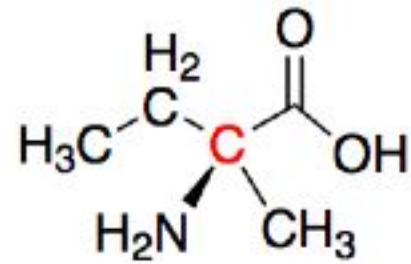
Valeric acid



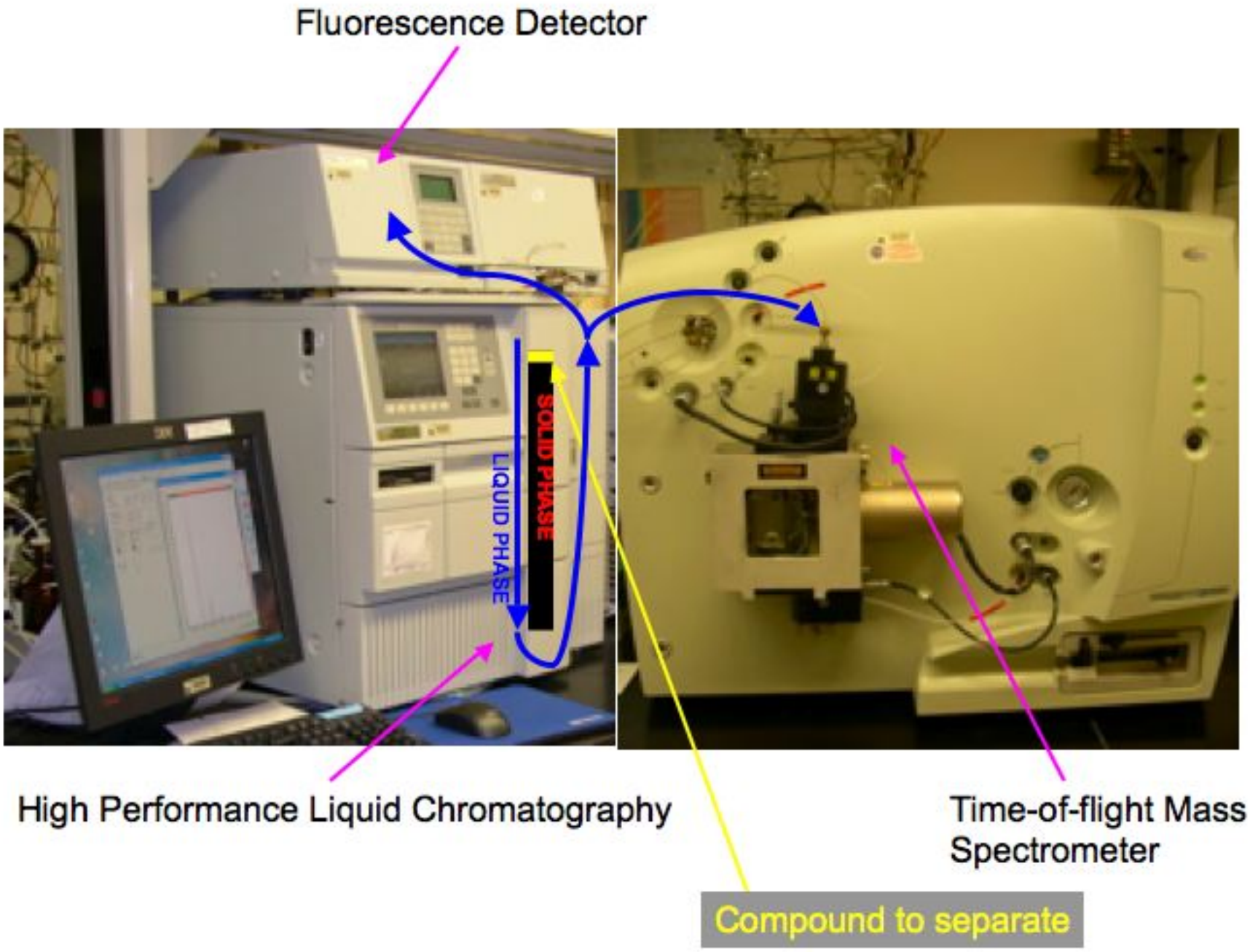
Valeric acid



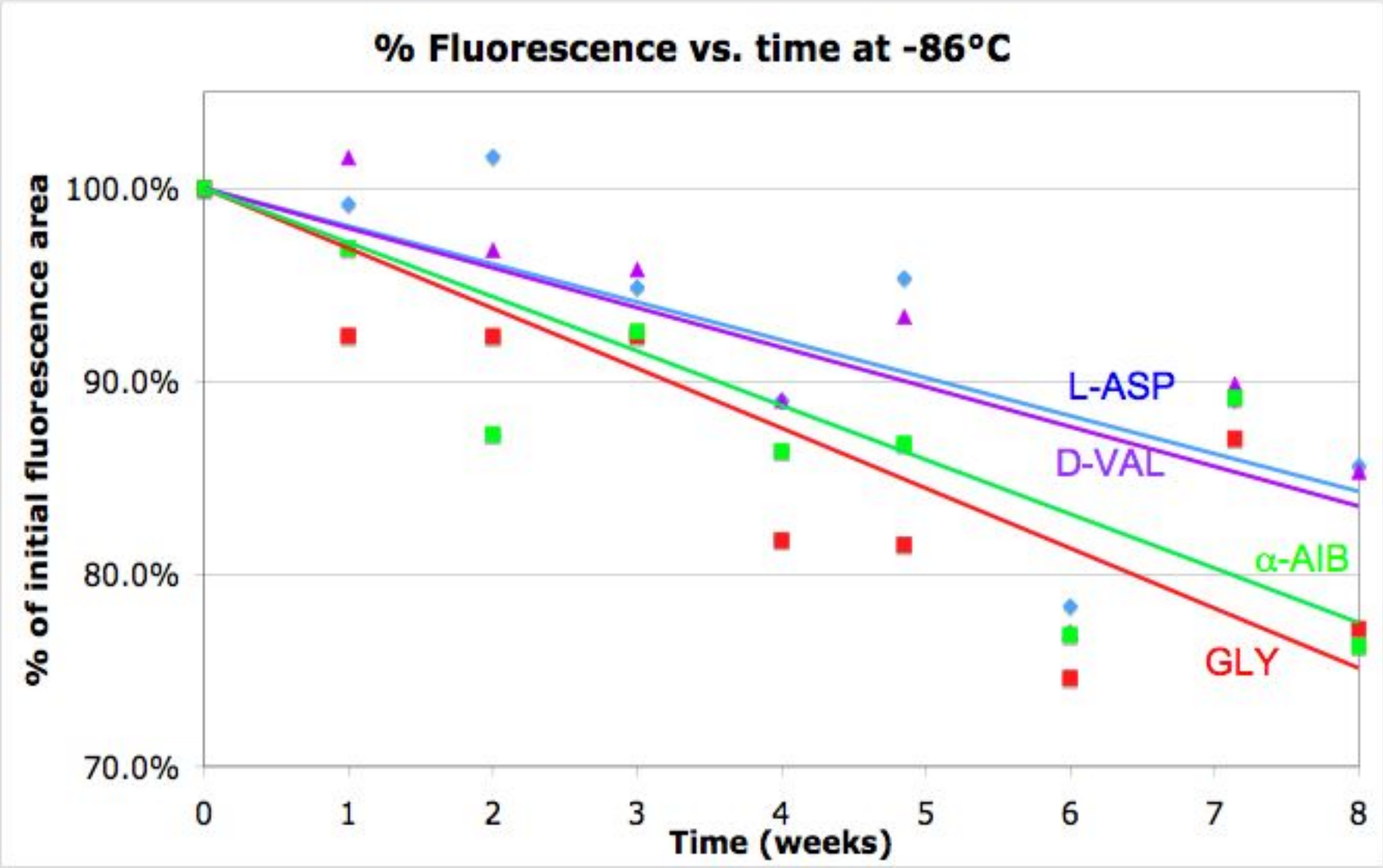
L-isovaline



D-isovaline

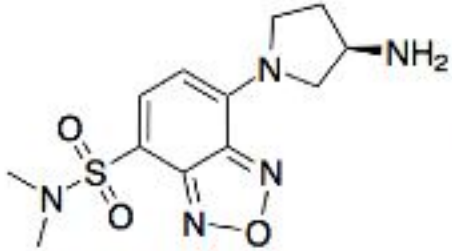

Fluorescence Detector
SOLID PHASE
LIQUID PHASE
High Performance Liquid Chromatography
Time-of-flight Mass Spectrometer
Compound to separate

Decomposition of Amino acids derivatized with OPA/NAC



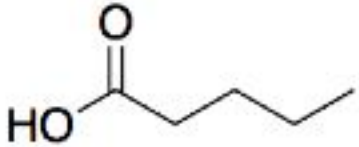
R-4-(N,N-dimethylaminosulfonyl)-7-(3-aminopyrrolidin-1-yl)-2,1,3-benzoxadiazole

$$\frac{[\text{R - DBD - APy}]}{[\text{acid}]} = 200$$

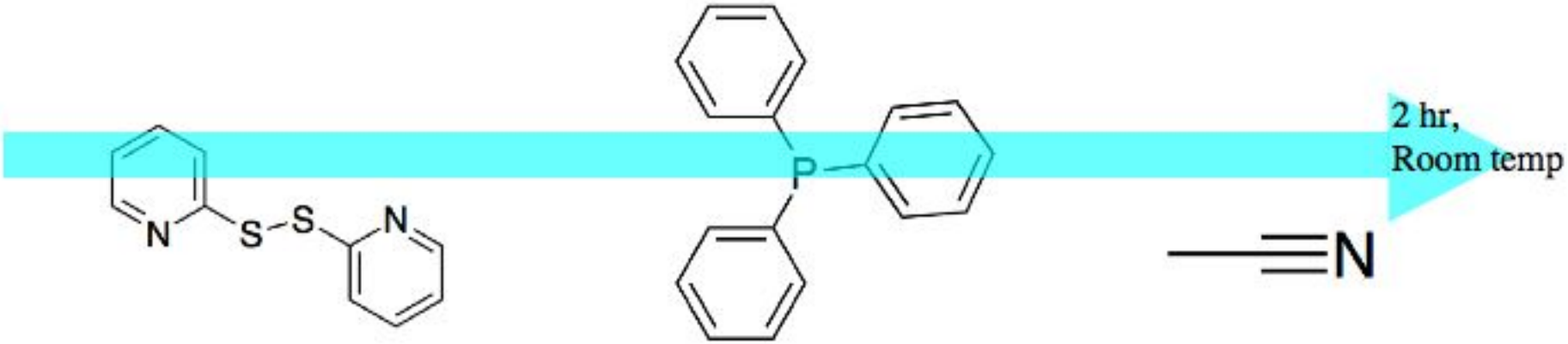


R-DBD-Apy (excess)

+



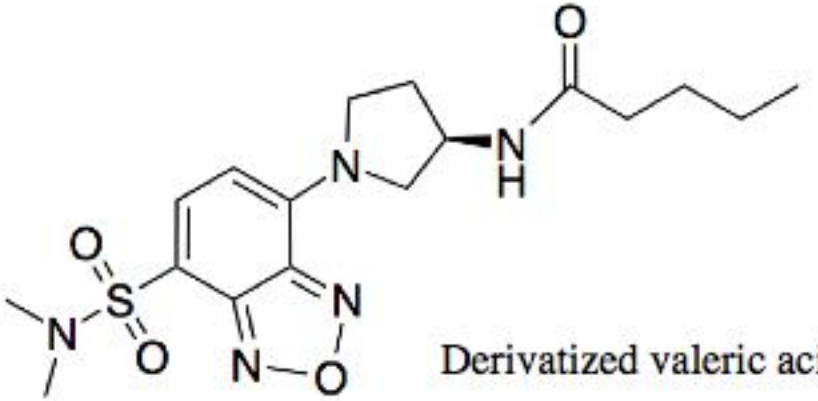
Valeric acid



2,2'-dipyridyl disulfide (DPDS)

Triphenylphosphine (TPP)

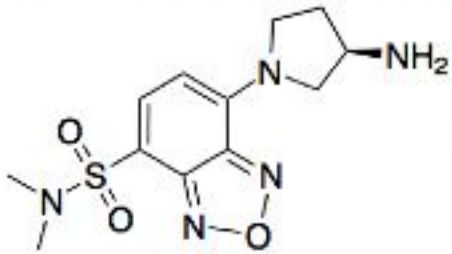
Acetonitrile (ACN)



Derivatized valeric acid

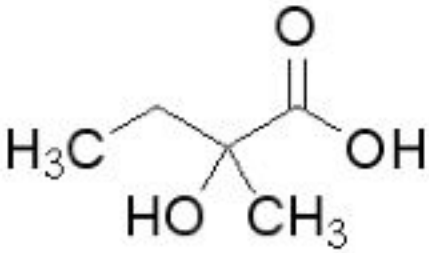
R-4-(N,N-dimethylaminosulfonyl)-7-(3-aminopyrrolidin-1-yl)-2,1,3-benzoxadiazole

$$\frac{[\text{R - DBD - APy}]}{[\text{acid}]} = 200$$

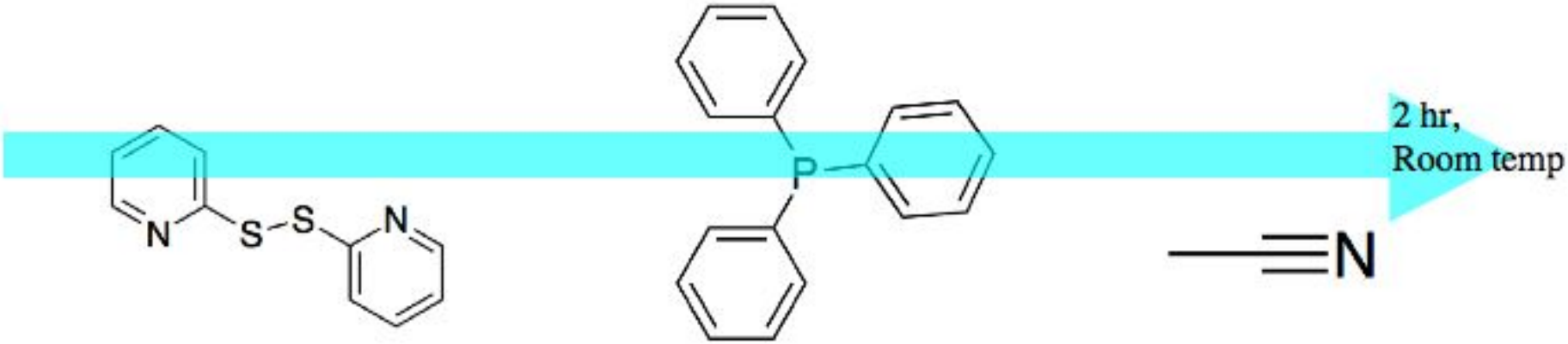


R-DBD-Apy (excess)

+



2-hydroxy-2-methylbutyric acid



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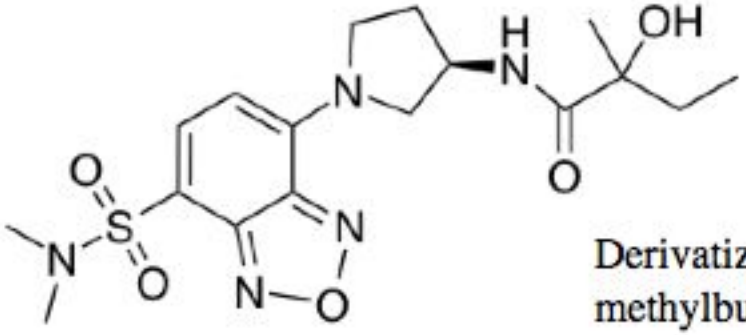
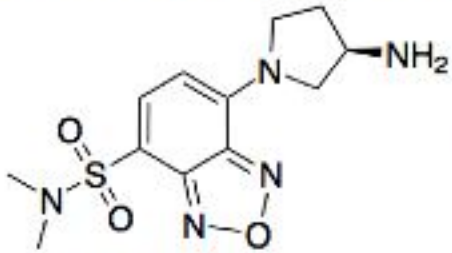


Derivatized 2-hydroxy-2-methylbutyric acid

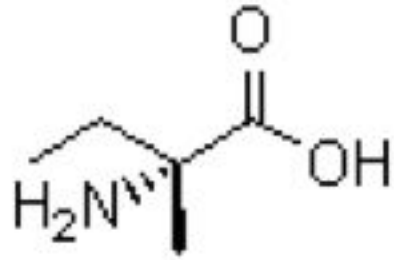
R-4-(N,N-dimethylaminosulfonyl)-7-(3-aminopyrrolidin-1-yl)-2,1,3-benzoxadiazole

$$\frac{[\text{R - DBD - APy}]}{[\text{acid}]} = 200$$

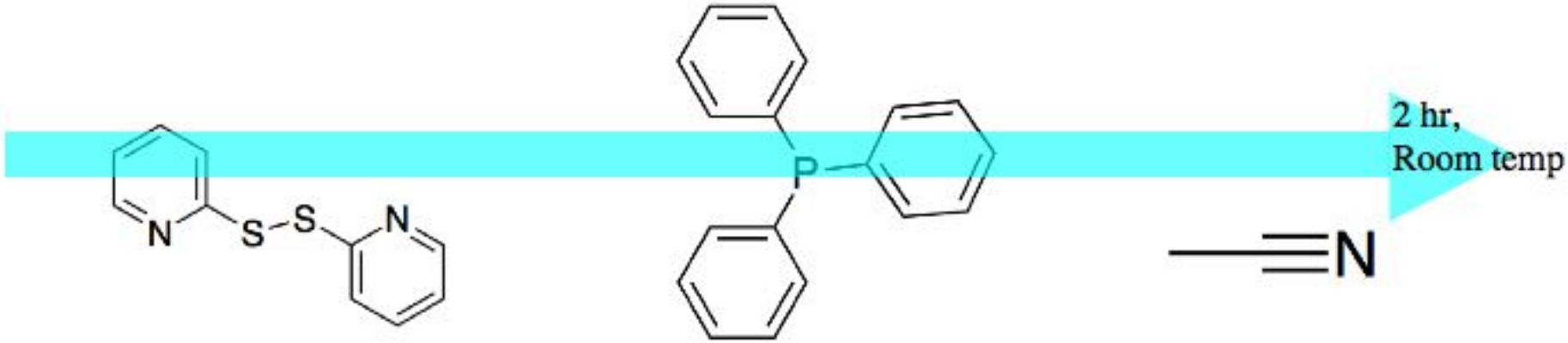


R-DBD-Apy (excess)

+



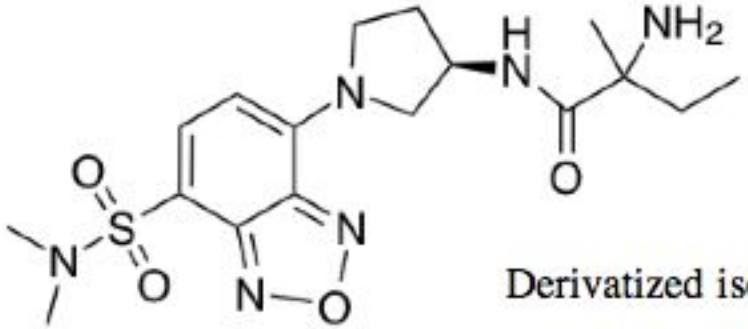
isovaline



2,2'-dipyridyl disulfide (DPDS)

Triphenylphosphine (TPP)

Acetonitrile (ACN)



Derivatized isovaline

The Strecker synthesis is the oldest organic synthesis of amino acids.

$$R-\overset{\overset{O}{\|}}{C}-H + NH_3 \rightleftarrows R-\underset{\underset{NH_2}{|}}{\overset{\overset{OH}{|}}{C}}-H \rightleftarrows R-\underset{\underset{NH}{\|}}{CH} + H_2O \qquad (1)$$

$$R-\underset{\underset{NH}{\|}}{C}-H + HCN \rightleftarrows R-\underset{\underset{NH_2}{|}}{CH}-C\equiv N \qquad (2)$$

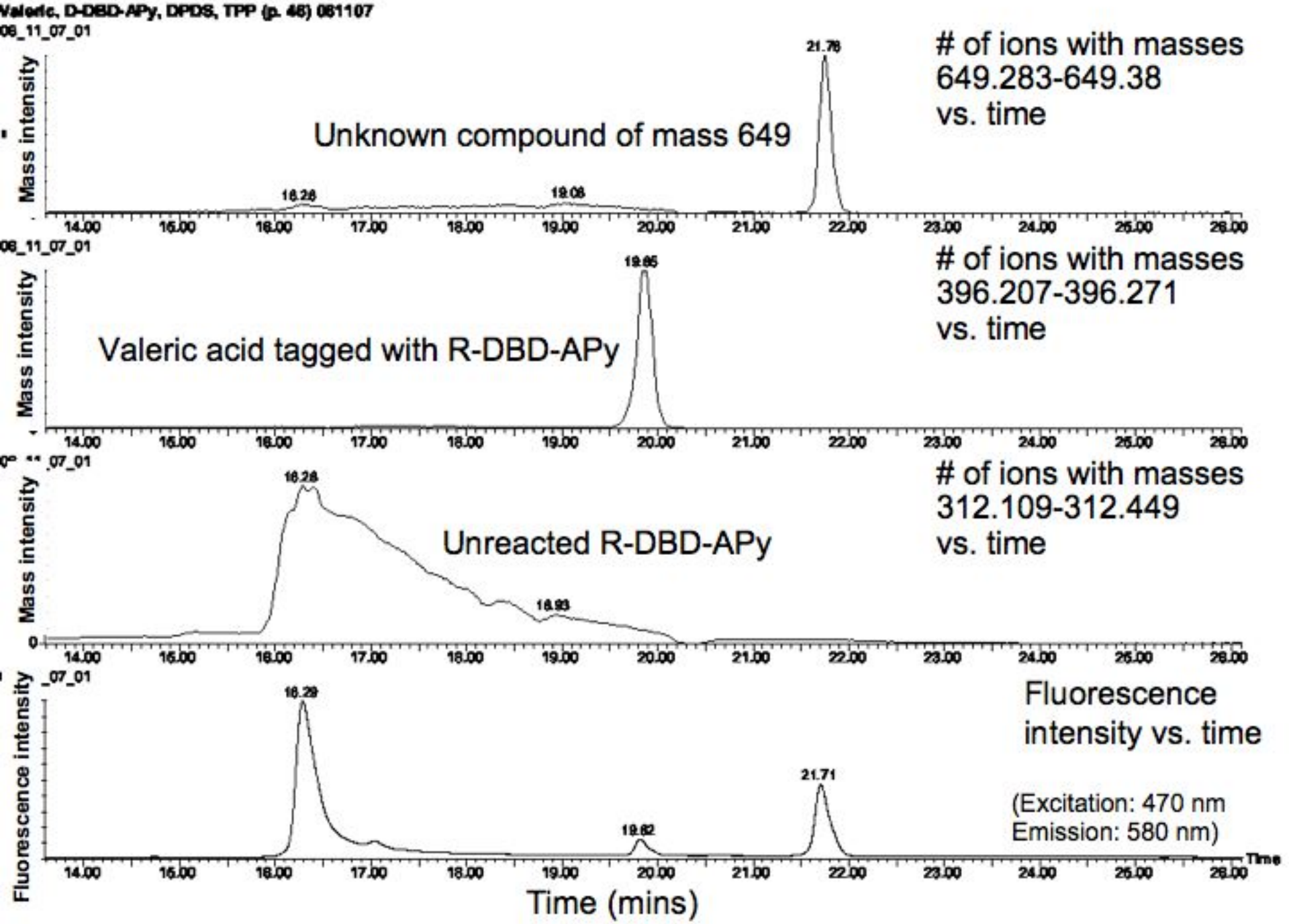
$$R-\underset{\underset{NH_2}{|}}{CH}-C\equiv N \xrightarrow{H_2O} R-\underset{\underset{NH_2}{|}}{CH}-\overset{\overset{O}{\|}}{C}-NH_2 \xrightarrow{H_2O} \boxed{R-\underset{\underset{NH_2}{|}}{CH}-COOH + NH_3 \qquad (3)}$$

A parallel series of reactions leads to the formation of hydroxy-acids.

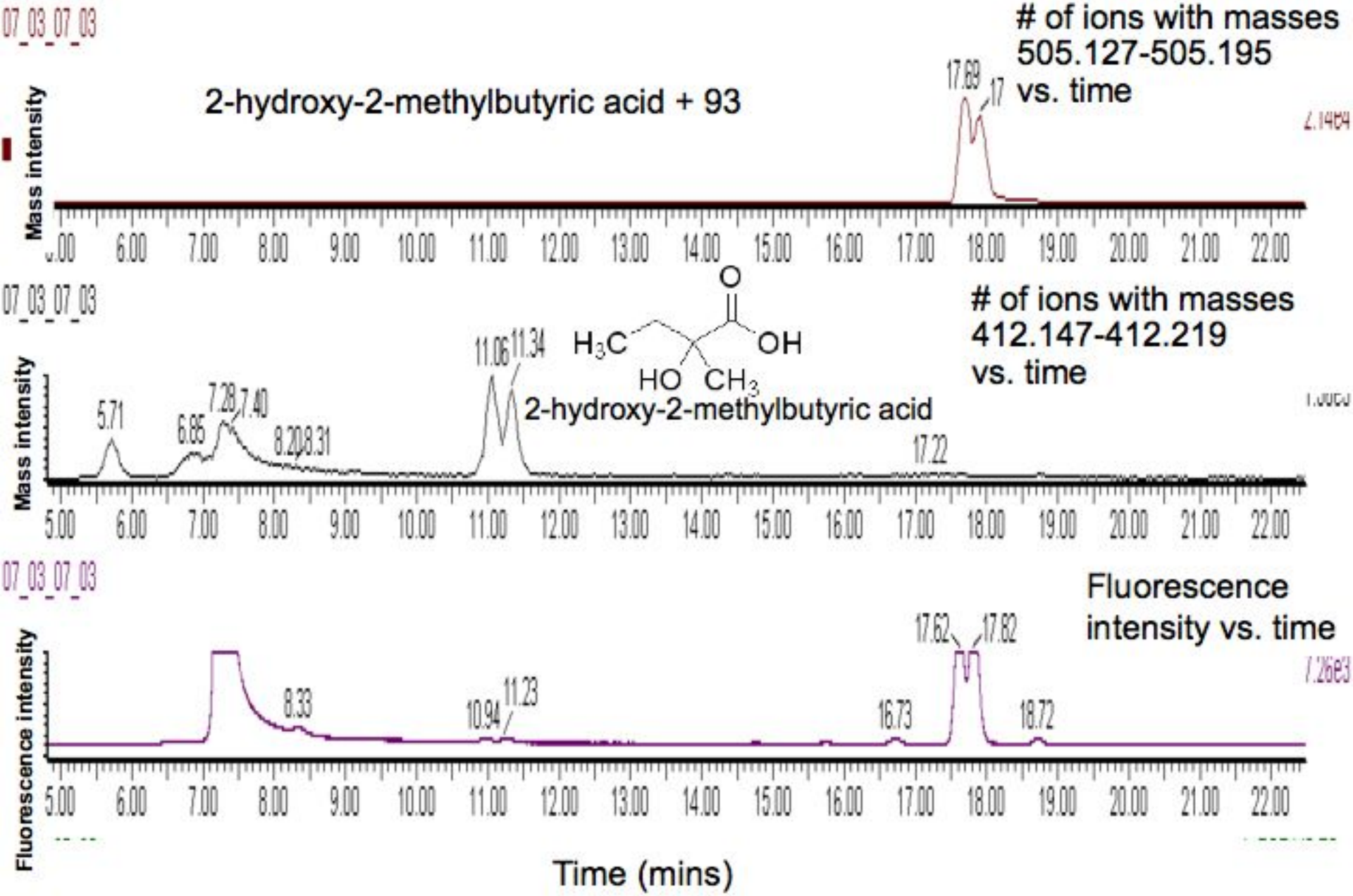
$$R-\underset{\underset{O}{\|}}{C}-H + HCN \rightleftarrows R-\underset{\underset{OH}{|}}{CH}-C\equiv N \qquad (2')$$

$$R-\underset{\underset{OH}{|}}{CH}-C\equiv N \xrightarrow{H_2O} R-\underset{\underset{OH}{|}}{CH}-\overset{\overset{O}{\|}}{C}-NH_2 \xrightarrow{H_2O} \boxed{R-\underset{\underset{OH}{|}}{CH}-COOH + NH_3 \qquad (3')}$$

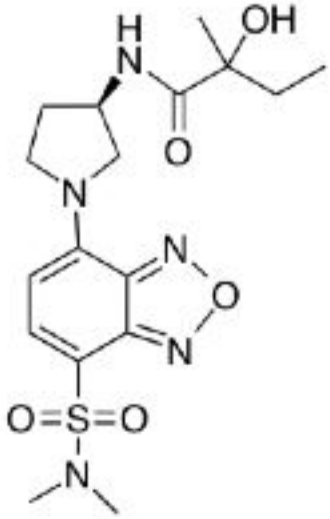
Source: The Origins of Life on the Earth, S. L. Miller & L. E. Orgel, p. 88


Valeric, D-DBD-APy, DPDS, TPP (p. 46) 061107
Mass intensity
Unknown compound of mass 649
# of ions with masses
649.283-649.38
vs. time
Valeric acid tagged with R-DBD-APy
# of ions with masses
396.207-396.271
vs. time
Unreacted R-DBD-APy
# of ions with masses
312.109-312.449
vs. time
Fluorescence intensity
Fluorescence intensity vs. time
(Excitation: 470 nm
Emission: 580 nm)
Time (mins)

xs 2-hydroxy-2-methylbutyric acid, toyo'oka, pg. 70



Derivatized 2-hydroxy-2-methylbutyric (412 amu)

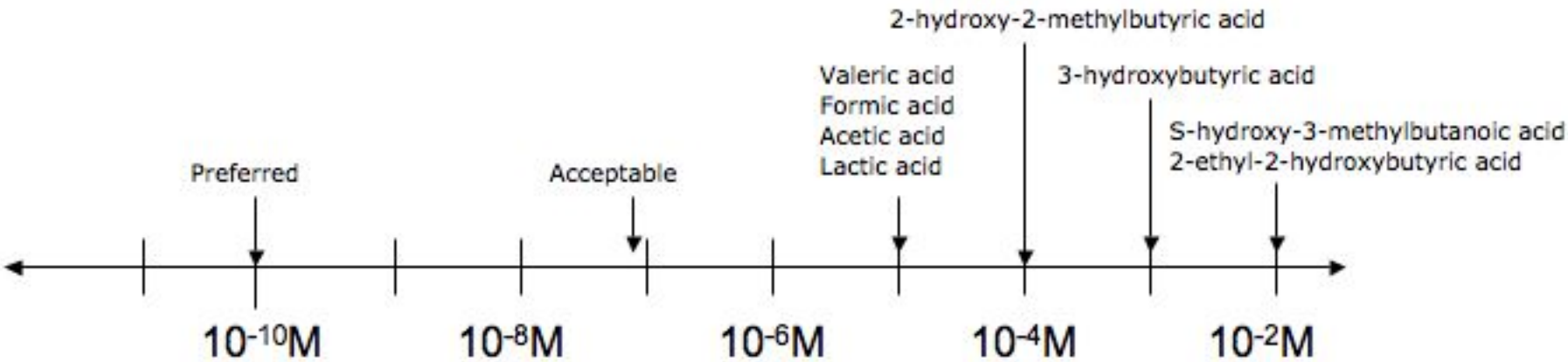


+

1-Dodecanethiol? ($C_{12}H_{26}S$) (202 amu)

→ ?? (505 amu)

Derivatizing carboxylic acids had very limited success



Sample concentration at start of reaction, moles/L

Alternative approaches: different mobile phase, longer reaction time, different fluorescent reagent, different wavelength, different catalyst

Acknowledgements
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