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RÉPUBLIQUE FRANÇAISE

MINISTÈRE  
DE  
L'INTÉRIEUR

# Cannabinoïdes de synthèse et situation française



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Lyon

Marseille

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## Cathinones : classement par famille de molécules (2012)

« Toute molécule dérivée de la cathinone, ses sels et ses stéréoisomères, avec :

- un substituant alkyl, phényl, alkoxy, alkylenedioxy, haloalkyl, halogéné sur le cycle phényl,
- un substituant alkyl en position 3,
- un substituant alkyl ou dialkyl ou cyclique sur l'azote,

à l'exception du bupropion.

- Toute structure dérivée du 2-amino-1-one propane par substitution en position 1 avec tout système monocyclique ou polycyclique, ainsi que ses sels et ses stéréoisomères. » (34)

## Cannabinoïdes de synthèse : classement nominatif (2009)

«Les cannabinoïdes suivants, ainsi que leurs isomères, stéréo-isomères, esters, éthers et sels :

JWH-018 – 1-Pentyl-3-(1-Naphthoyl)Indole ou (Naphtalen-1-yl)(1-Pentyl-1H-Indol-3-yl)Méthanone) ;

CP 47,497 – (5-(1,1-Diméthylheptyl)-2-[(R,3S)-3 –hydroxycyclohexyl]-phénol ;

CP 47,497-C6 – (5-(1,1-Diméthylhexyl)-2-[(1R,3S)-3 – hydroxycyclohexyl]-phénol ;

CP 47,497-C8 – (5-(1,1-Diméthyl-octyl)-2-[(1R,3S)-3 – hydroxycyclohexyl]-phénol ;

CP 47,497-C9 – (5-(1,1-Diméthyl-nonyl)-2-[(1R,3S)-3 – hydroxycyclohexyl]-phénol ;

HU - 210 - (6aR) - trans - 3 - (1,1 - Diméthylheptyl) - 6a, 7, 10, 10a- tétrahydro-1 – hydroxy-6,6-diméthyl-6H-dibenzo[b,d]pyran-9-méthanol » (28)

Peu de saisies... officiellement !

↳ Pas de chiffres disponibles au niveau de l'OCRTIS



↳ Chiffres fournis par la Douane



35 kg dont 2kg classés stupéfiants





# Cannabinoïdes de synthèse... fabrication



# Cannabinoides de synthèse... fabrication



## CANNABINOIDS JWH-250

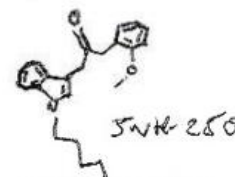
> Dosage antérieur  $50 \text{ mg/g}$

> Nouveau dosage  $37,5 \text{ mg/g}$

Soit  $1500 \text{ mg}$  pour  $40 \text{ g}$

FABRICATION  $1,5 \text{ g}$  JWH-250 en solution d'acétone.

Évaporation  $\rightarrow$   $40 \text{ g}$  Tabac Amsterdamer  
+ JWH dissout



PRIX:  $2,50 \text{ €}$  / g

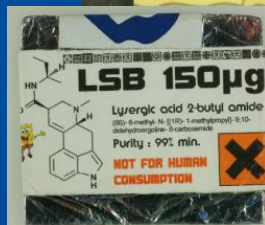
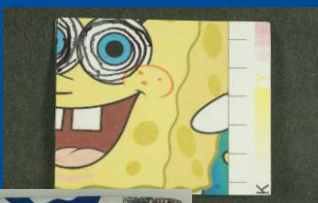
BENEFICES:  $2,5 \times 40 = 100,00 \text{ €}$

Technique  $\rightarrow$  évaporation  
solution d'alcool/acétone  
récepteur  
plaque de surface

Le produit fini par se fixer de façon homogène suite à l'évaporation du solvant. Les herbes sont ainsi imbibées de manière équilibrée.

COMPTES: ET PREVISIONS

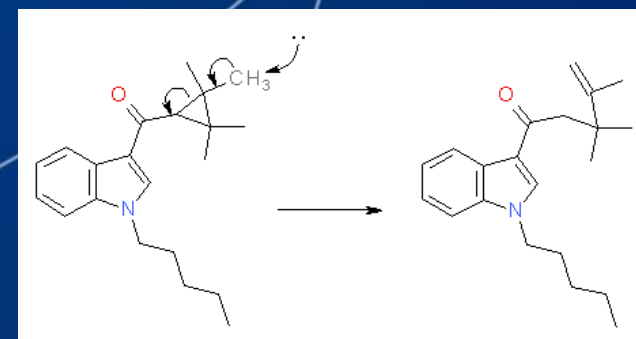
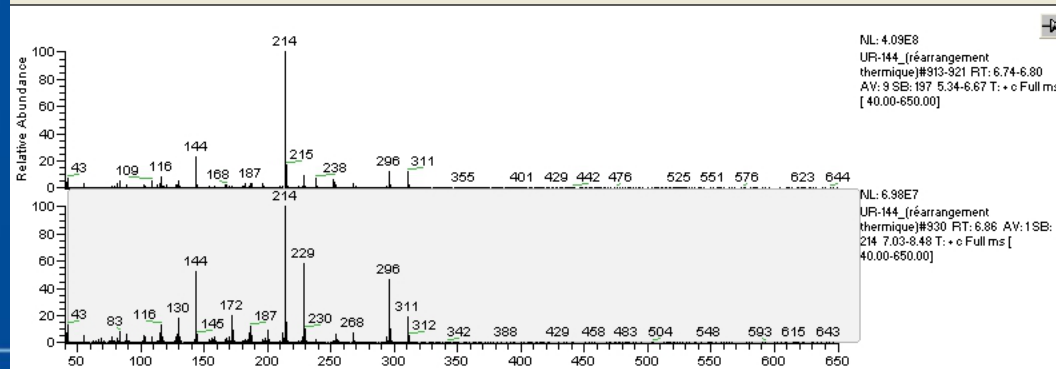
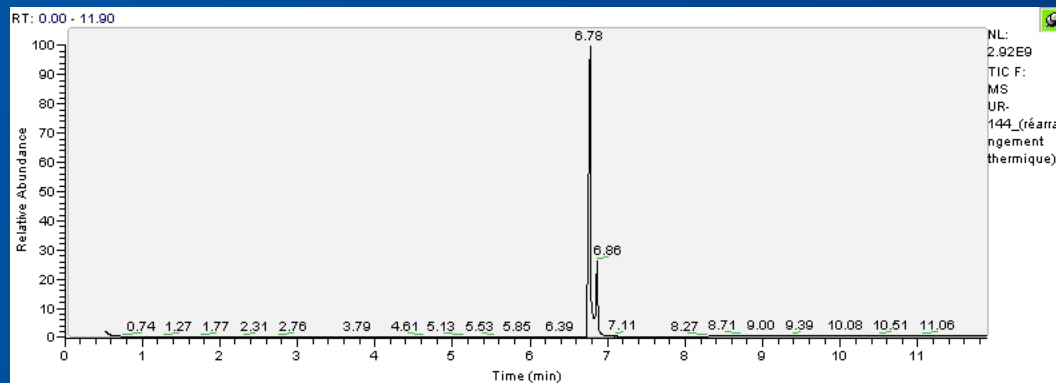
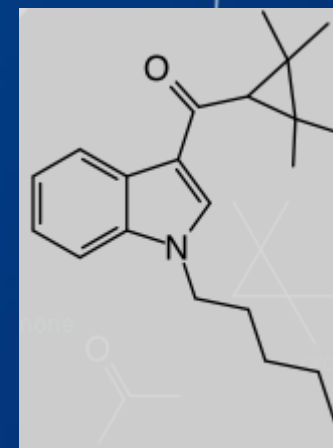
Actuel:  $200 + 270 = 470 \text{ €}$  (à rev.)  
bases +  $460 \text{ €}$  de 2012  $\approx 930 \text{ €}$   
(-) les dépenses: env.  $180 \text{ €}$



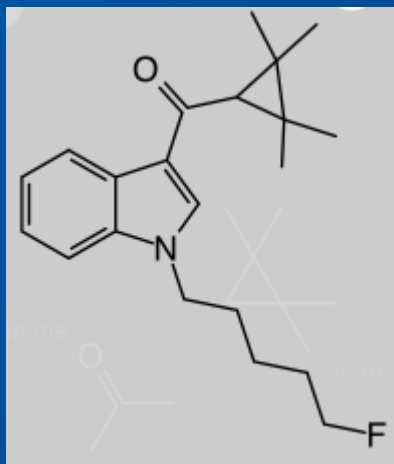
V. Ladroue, F. Besacier, M. Hologne  
Annales de Toxicologie Analytique 2013, 25(4): 175-184



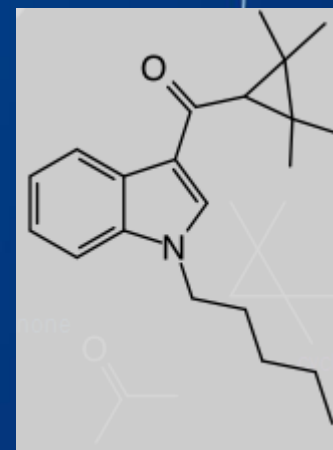
# Cannabinoides de synthèse... fabrication



# Cannabinoides de synthèse... fabrication



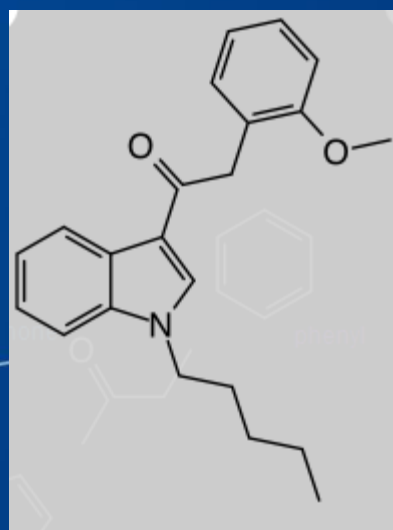
UR-144



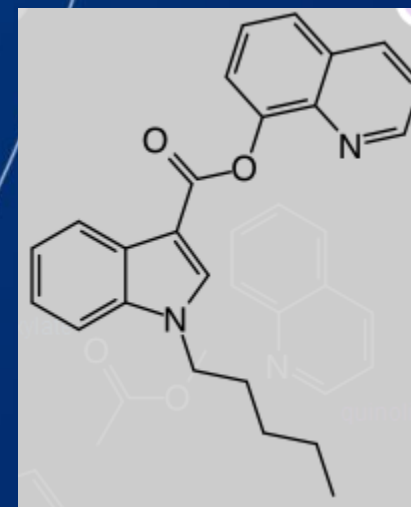
5F-UR-144 (XLR11)



PB-22 (QUPIC)



JWH-250

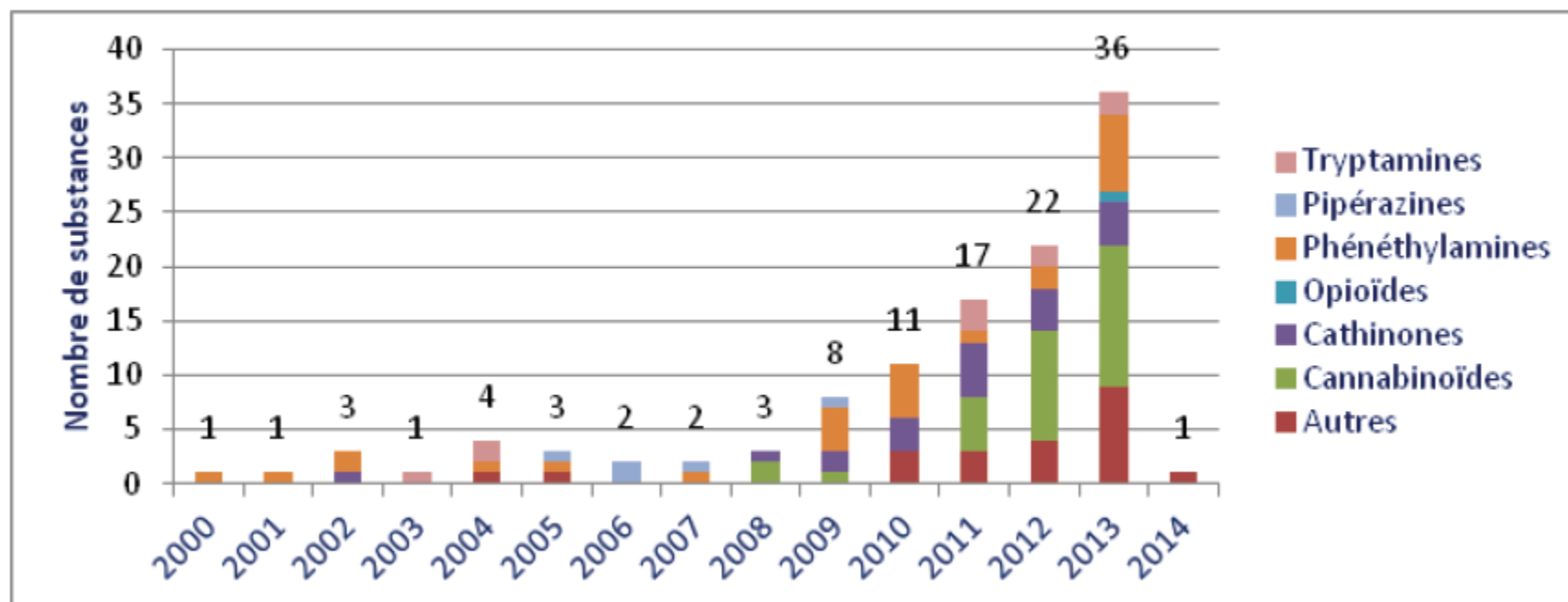


# Cannabinoïdes de synthèse... historique des apparitions



Nouveaux produits de synthèse identifiés en France depuis 2000  
OFDT – Note d'information SINTES 7 mars 2014

Graphique 1- Nombre de substances identifiées en France par famille et par année depuis 2000 jusqu'en mars 2014

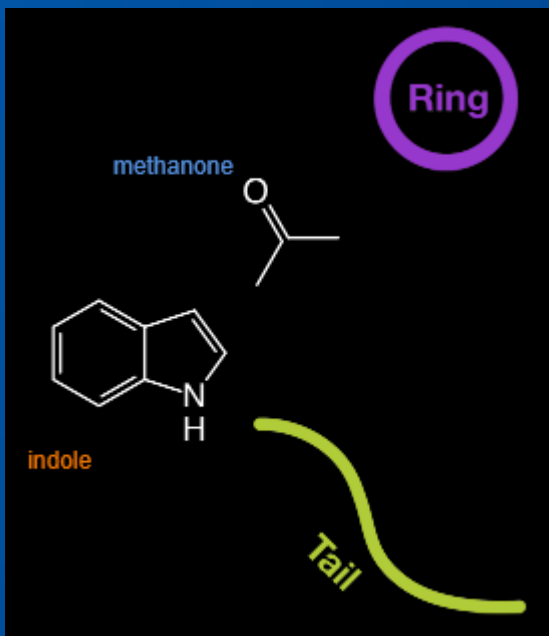




# Cannabinoides de synthèse... historique des apparitions



## Aminoalkylindoles



## Naphthoylindoles

## Phénylacétylindoles

## Benzoylindoles

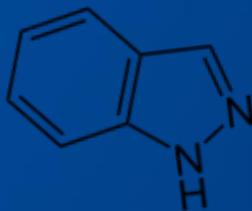
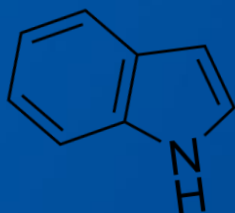
## Cyclopropoylindoles

## Indole carboxamides

Cannabinoides
<b>2008</b>
CP47,497 (C8+C10)* JWH-018*
<b>2009</b>
JWH-073
<b>2011</b>
AM-2201 JWH-019 JWH-122 JWH-210 JWH-250
<b>2012</b>
5FUR-144 (XLR-11) HU-331 JWH-081 JWH-122 [5-fluoropentyl] JWH-122 N[4-pentenyl] JWH-200 RCS-4 UR-144 UR-144 (-2H) Méthanandamide
<b>2013</b>
5F-AB-PINACA 5F-PB22 AB-FUBINACA AB-PINACA AKB-48 AKB-48F APICA JWH-203 JWH-307 PB-22 Quchic RH-34 STS-135

# Cannabinoides de synthèse... historique des apparitions

Aminoalkylindoles → Aminoalkylindazoles

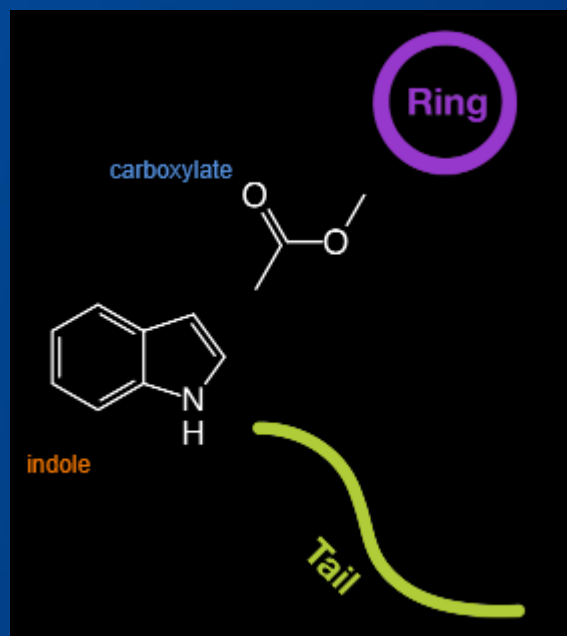
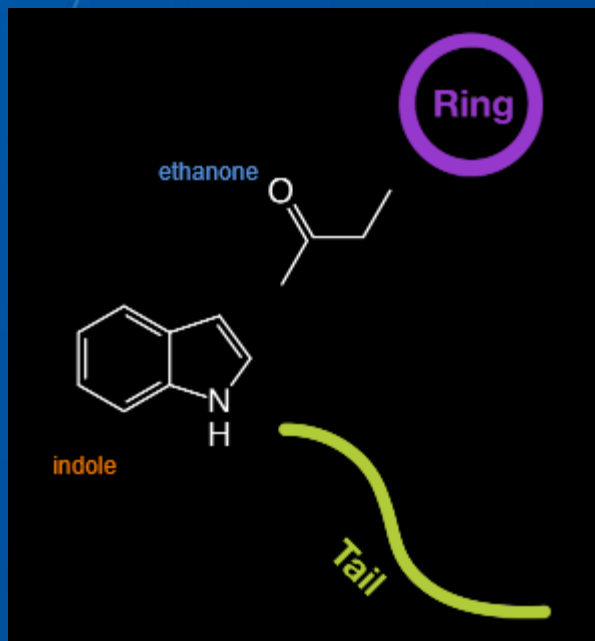


THJ Series : AM-2201 => THJ-2201  
JWH-018 => THJ-018

APICA => APINACA (AKB-48)

Cannabinoides
<b>2008</b>
CP47,497 (C8+C10)* JWH-018*
<b>2009</b>
JWH-073
<b>2011</b>
AM-2201 JWH-019 JWH-122 JWH-210 JWH-250
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# Cannabinoides de synthèse... historique des apparitions



PB-22 (QUPIC), BB-22 (QUCHIC)

Cannabinoides	
<b>2008</b>	CP47,497 (C8+C10)* JWH-018*
<b>2009</b>	JWH-073
<b>2011</b>	AM-2201 JWH-019 JWH-122 JWH-210 JWH-250
<b>2012</b>	5FUR-144 (XLR-11) HU-331 JWH-081 JWH-122 [5-fluoropentyl] JWH-122 N[4-penteny] JWH-200 RCS-4 UR-144 UR-144 (-2H) Méthanandamide
<b>2013</b>	5F-AB-PINACA 5F-PB22 AB-FUBINACA AB-PINACA AKB-48 AKB-48F APICA JWH-203 JWH-307 PB-22 Quchic RH-34 STS-135

# Cannabinoides de synthèse... historique des apparitions

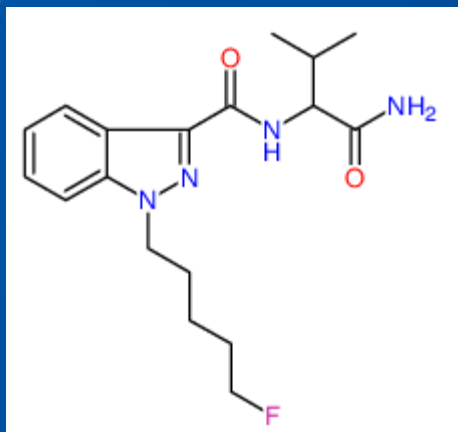


	A	B	C	D	E
1	18/06/2014				
2	Substance	Created	Updated	Type	Group
4	<a href="#">5F-AMB</a>	juin-14	juin-14	Narcotic dr	Cannabinoi
11	<a href="#">AM-2201 benzimidazole analogue / FUBIMINA</a>	avr-14	avr-14	Narcotic dr	Cannabinoi
13	<a href="#">AB-CHMINACA</a>	avr-14	avr-14	Narcotic dr	Cannabinoi
14	<a href="#">5F-AMBICA</a>	avr-14	avr-14	Narcotic dr	Cannabinoi
27	<a href="#">JWH-018 indazole analogue</a>	févr-14	mai-14	Narcotic dr	Cannabinoi
28	<a href="#">Mepirapim</a>	févr-14	mars-14	Narcotic dr	Cannabinoi
33	<a href="#">EDU-PB-22</a>	févr-14	févr-14	Narcotic dr	Cannabinoi
38	<a href="#">5F-PB-22 indazole analogue</a>	janv-14	mars-14	Narcotic dr	Cannabinoi
39	<a href="#">PB-22 indazole analogue</a>	janv-14	févr-14	Narcotic dr	Cannabinoi
44	<a href="#">N,N-Diethyl-2-(1-pentyl-1H-indol-3-yl)-4-thiazol-methana</a>	déc-13	avr-14	Narcotic dr	Cannabinoi
45	<a href="#">N-(2-Methoxyethyl)-N-(1-methylethyl)-2-(1-pentyl-1H-ind</a>	déc-13	avr-14	Narcotic dr	Cannabinoi
46	<a href="#">1-(Cyclohexylmethyl)-2-[(4-ethoxyphenyl)methyl]-N,N-d</a>	déc-13	avr-14	Narcotic dr	Cannabinoi
47	<a href="#">SDB-006</a>	déc-13	avr-14	Narcotic dr	Cannabinoi
48	<a href="#">FUB-PB-22</a>	déc-13	avr-14	Narcotic dr	Cannabinoi
49	<a href="#">M5FPIC</a>	déc-13	févr-14	Narcotic dr	Cannabinoi
51	<a href="#">5F-SDB-006</a>	déc-13	févr-14	Narcotic dr	Cannabinoi
54	<a href="#">A-796.260 isomer</a>	déc-13	déc-13	Narcotic dr	Cannabinoi

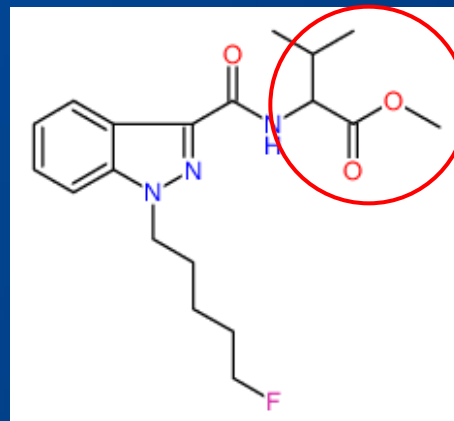
European Database  
On New Drugs



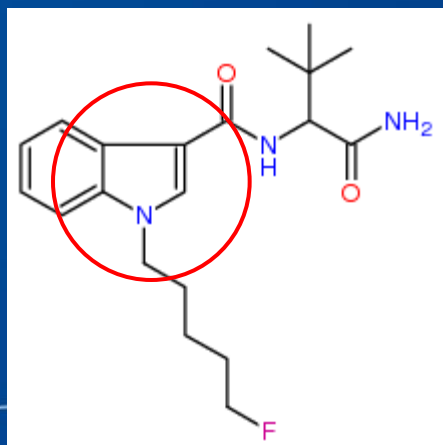
# Cannabinoides de synthèse... historique des apparitions



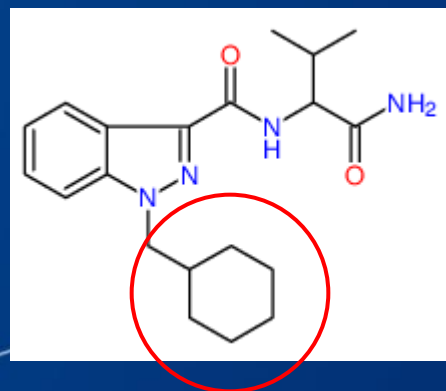
5F-AB-PINACA



5F-AMB (ou 5F-AMP)

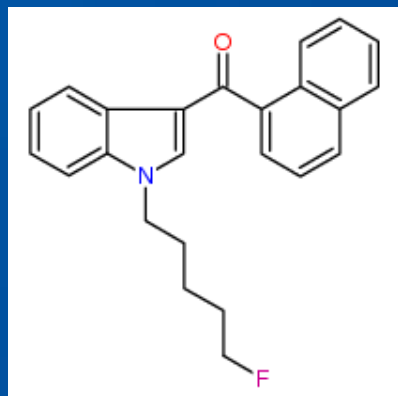


5F-AMBICA (5F-ADBICA)

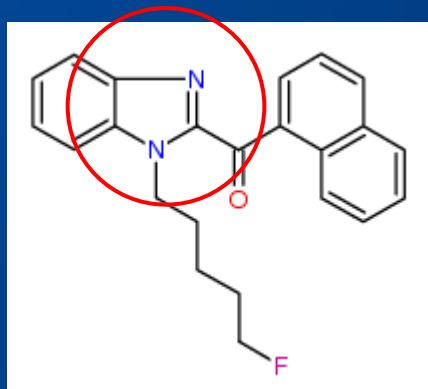


AB-CHMINACA

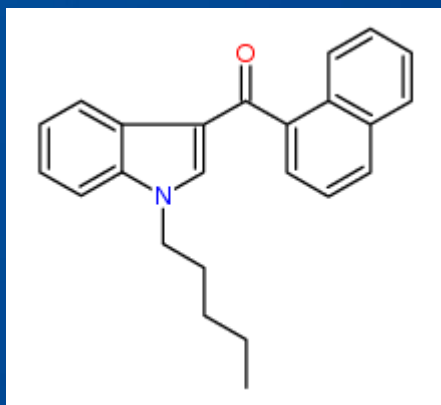
# Cannabinoides de synthèse... historique des apparitions



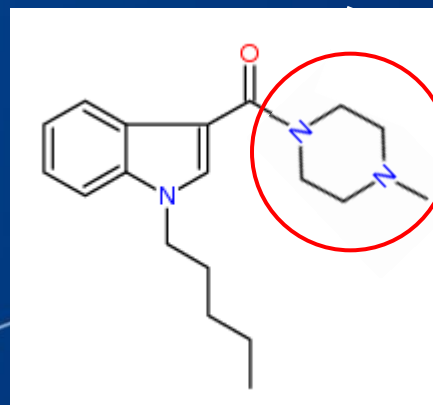
AM-2201



FUBIMINA



JWH-018



MEPIRAPIM

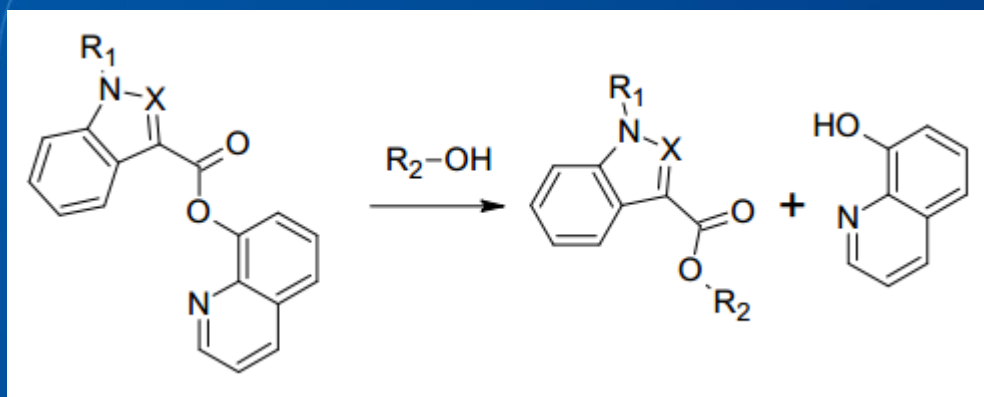
# Cannabinoides de synthèse... difficulté des identifications



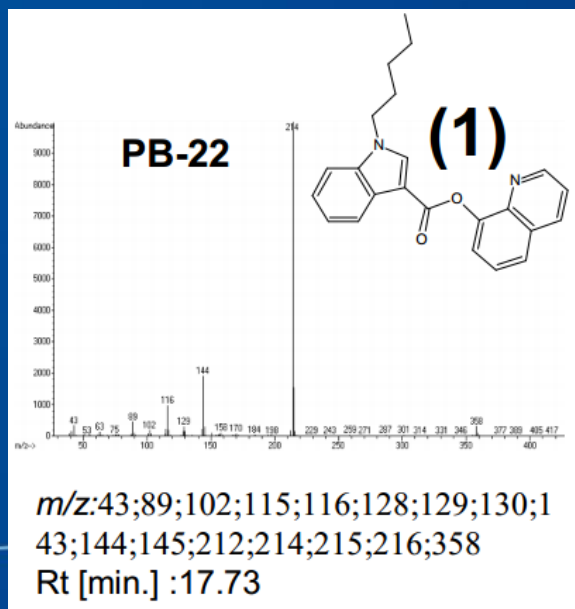
- Manque de matériaux de référence (coûts !)  
*pour identifier, et doser*
- Spectres de masse non disponibles dans les bibliothèques classiques  
*swgdrug, cayman, etc.*
- Problème de décomposition de certains composés en GC-MS  
*transestérification*
- Problème pour distinguer des analogues / isomères  
*technique analytique complémentaire*
- Problème des mélanges de composés
- Etiquette sur le sachet saisi pas souvent fiable (!)



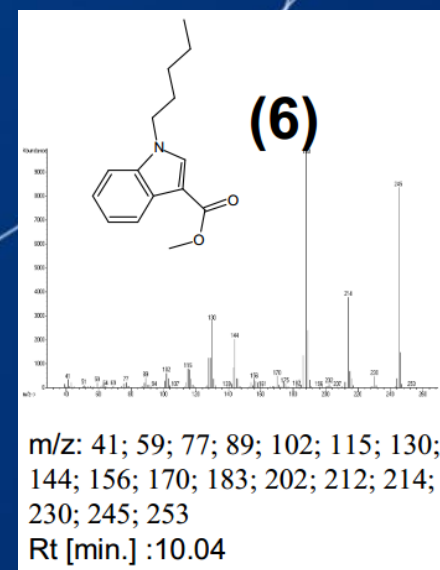
# Cannabinoides de synthèse... difficulté des identifications



Transestérification dans les alcools primaires



Methanol

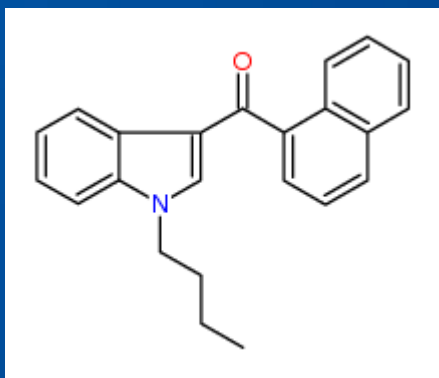




# Cannabinoides de synthèse... difficulté des identifications

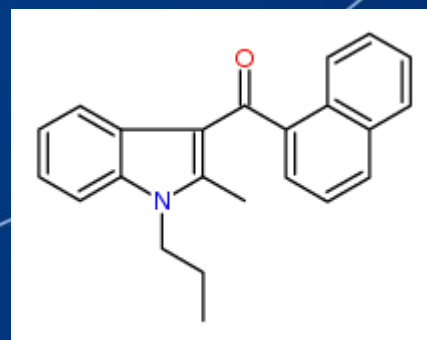


Analogues posant problème d'identification sans les matériaux de référence

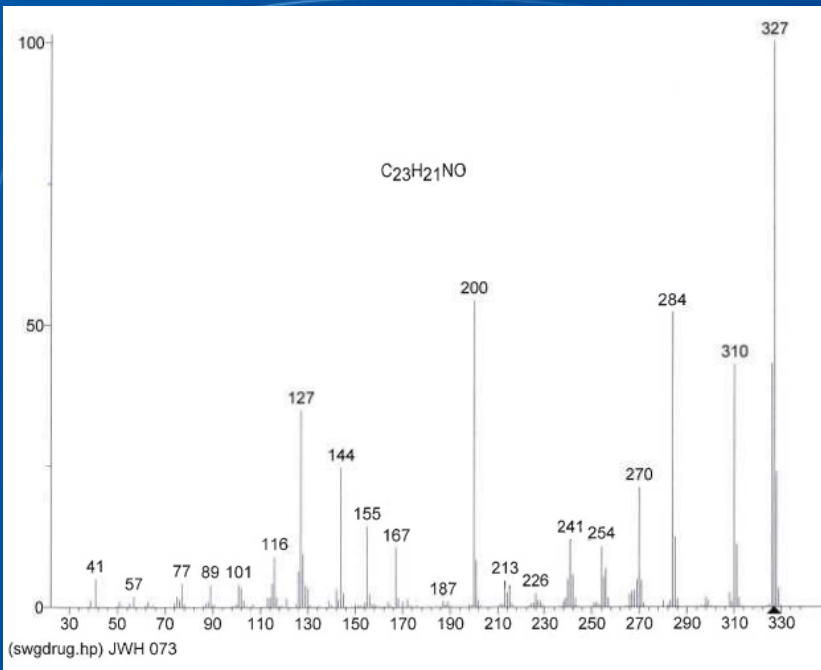


JWH-073

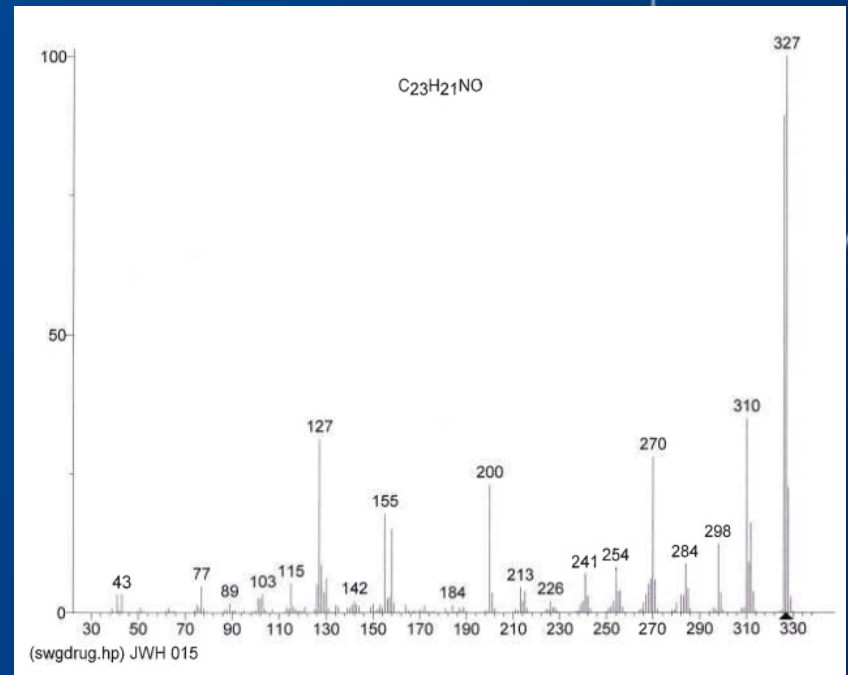
M = 327 g/mol



JWH-015



JWH-073



JWH-015

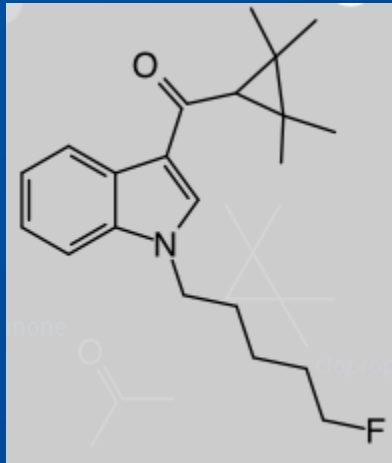
RT différents mais MS proches (et masse exacte inutile)...

=> Matériaux de référence, ou  $MS^2$ , ou autre technique (!)

# Cannabinoides de synthèse... difficulté des identifications



Isomères posant problème d'identification

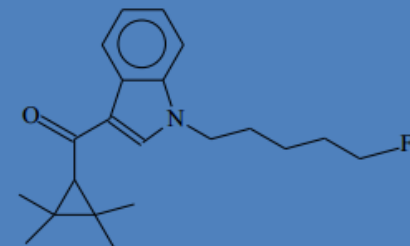
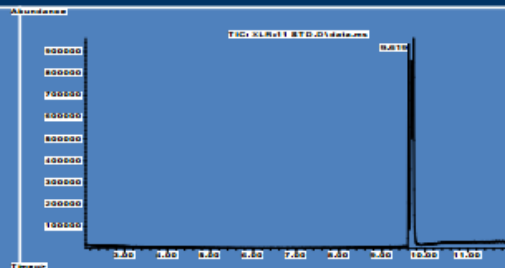
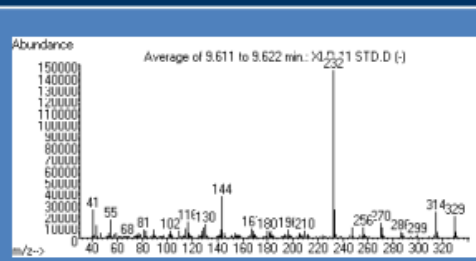


5F-UR-144 (XLR11)

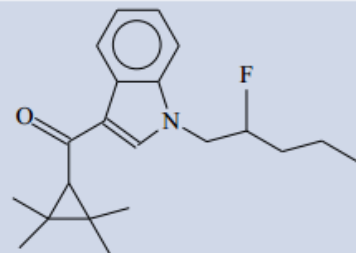
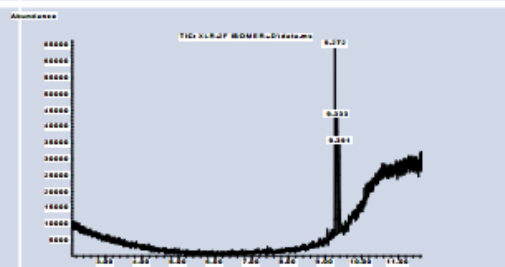
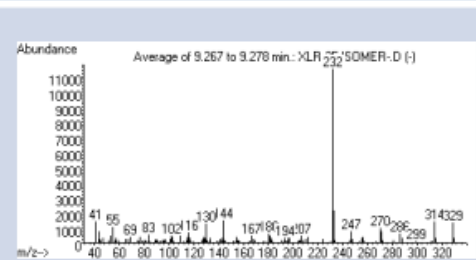


Position du fluor ?

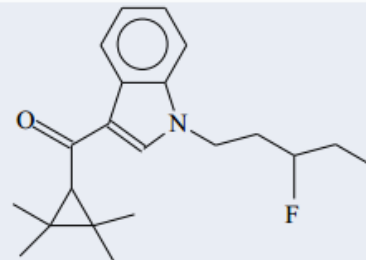
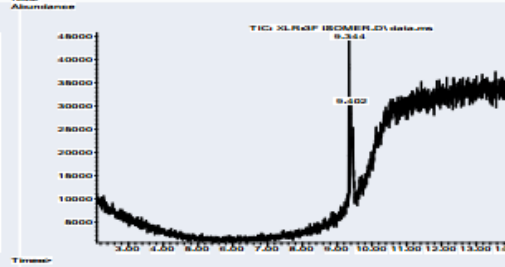
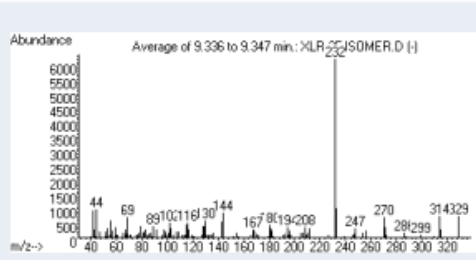
5F



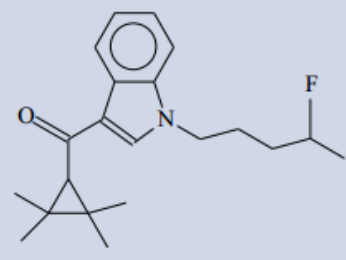
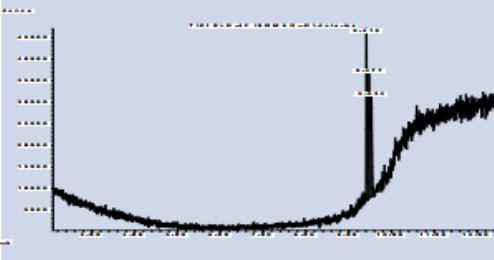
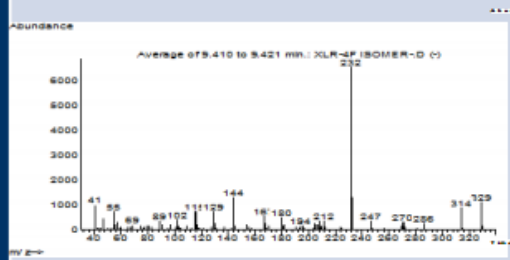
2F



3F



4F

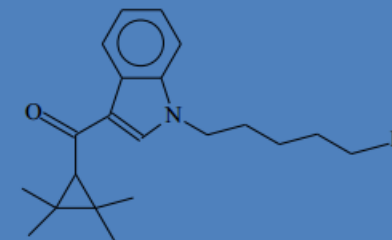
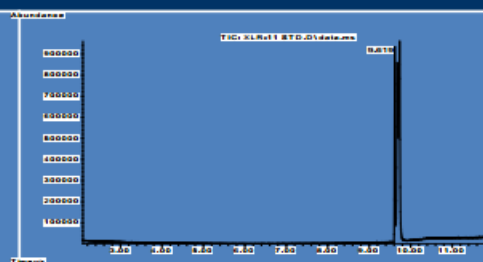


U. Wolf, Israel



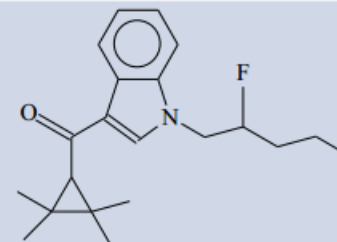
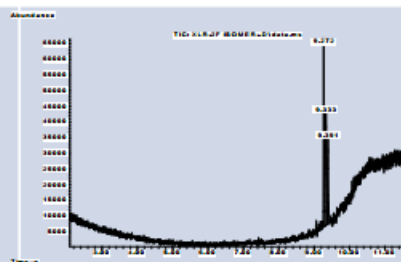
**5F**

RT = 9.62 min.  
Closest isomer 4F  
2.1% dif.  
(RT1-RT2)/RT1



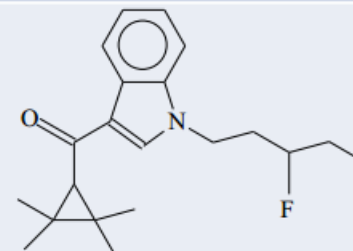
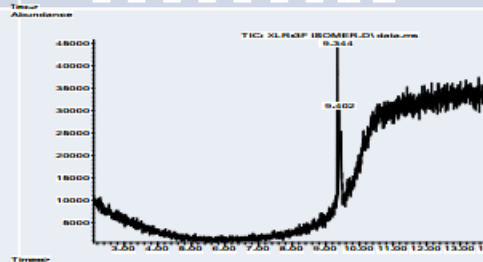
**2F**

RT = 9.27 min.  
Closest isomer 3F  
0.75% dif.



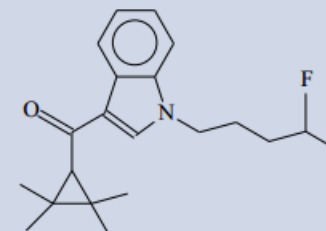
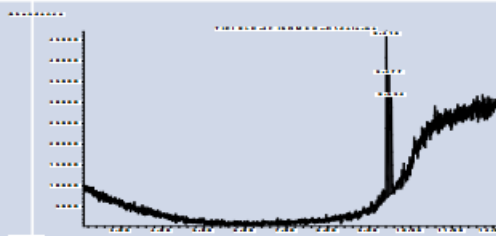
**3F**

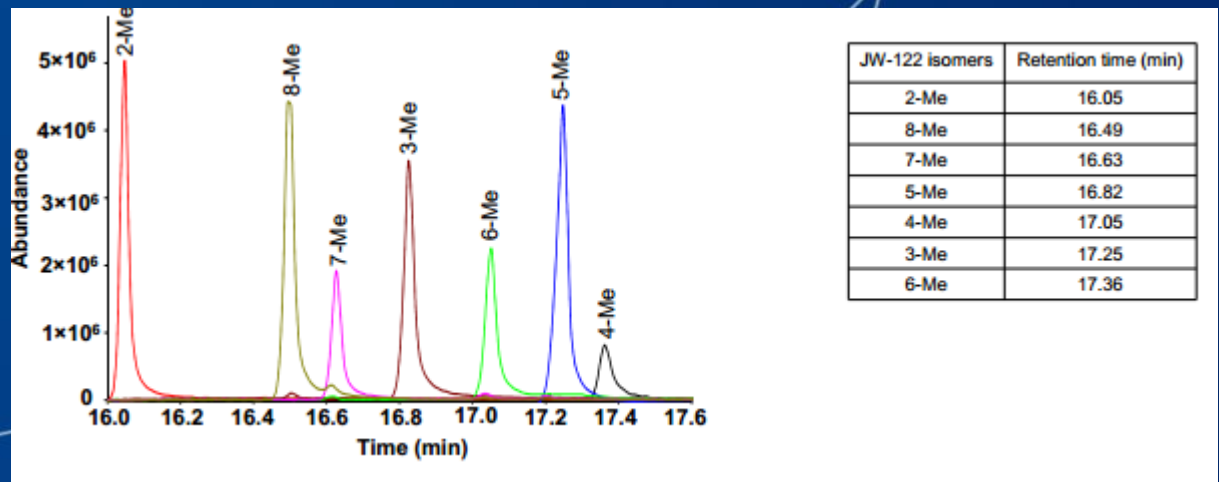
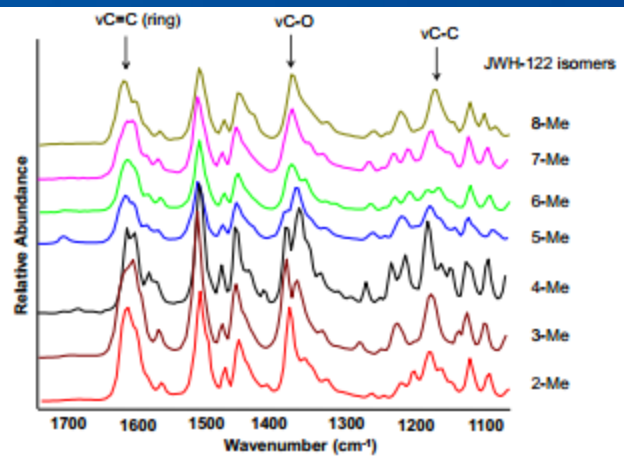
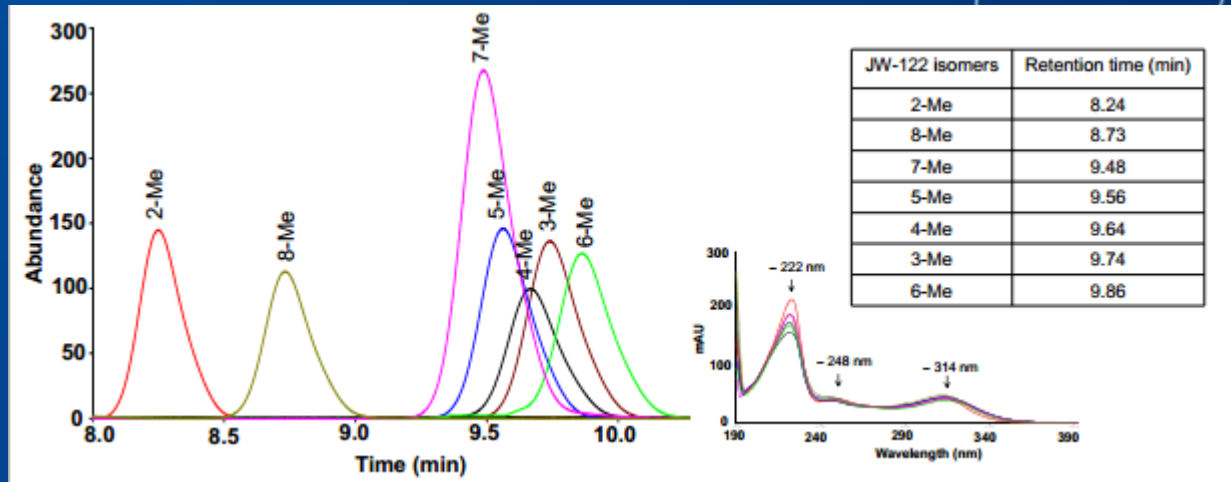
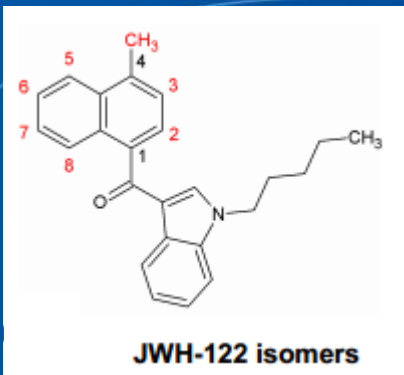
RT = 9.34 min.  
Closest isomer 2F  
0.75% dif.



**4F**

RT = 9.42 min.  
Closest isomer 3F  
0.85% dif.





# Cannabinoïdes de synthèse... difficulté des identifications



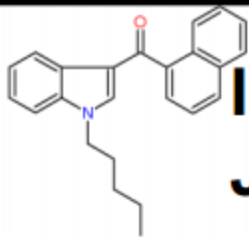
GC-IR comme technique complémentaire !



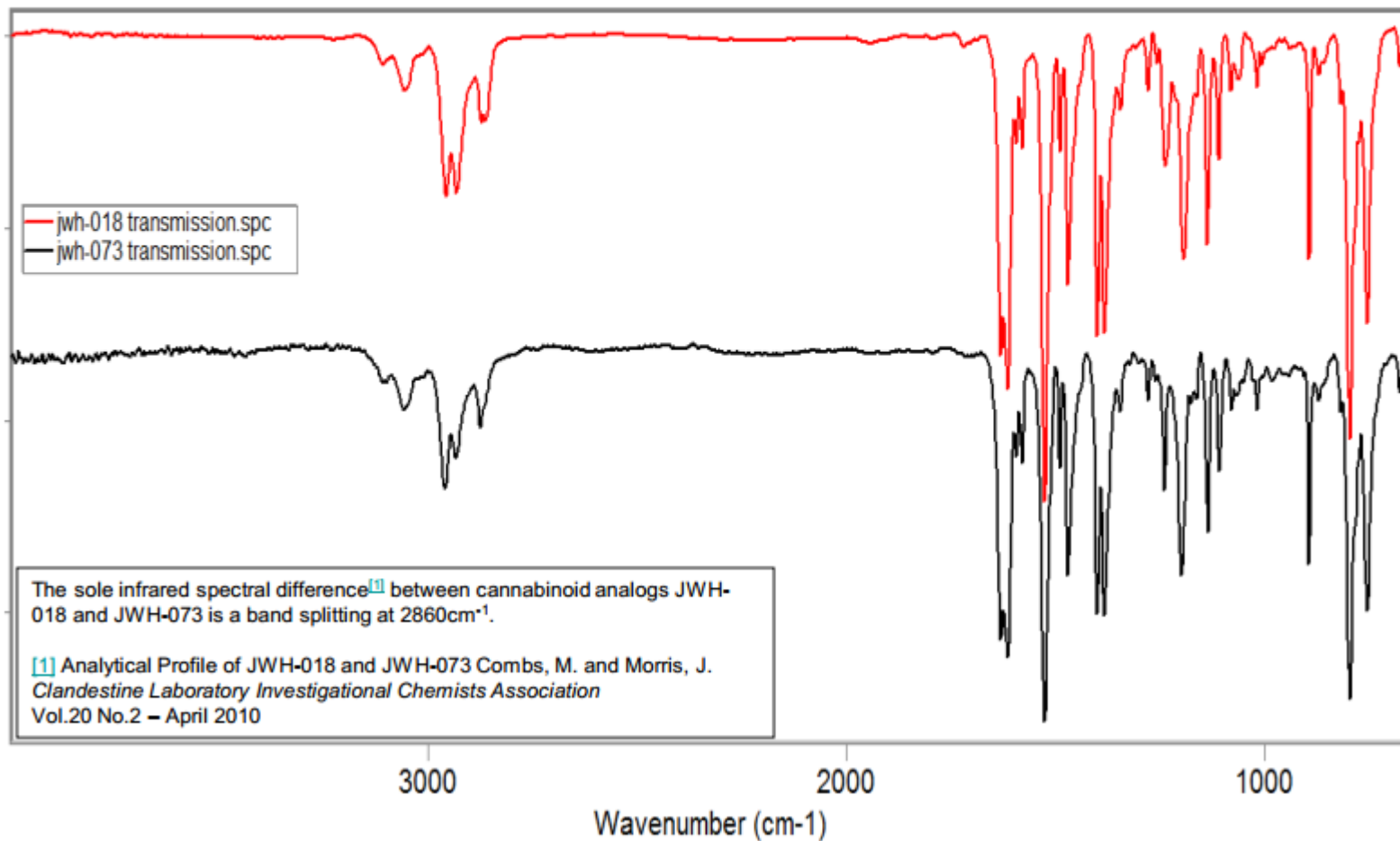
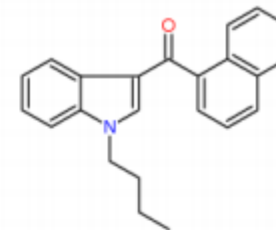
DiscovIR



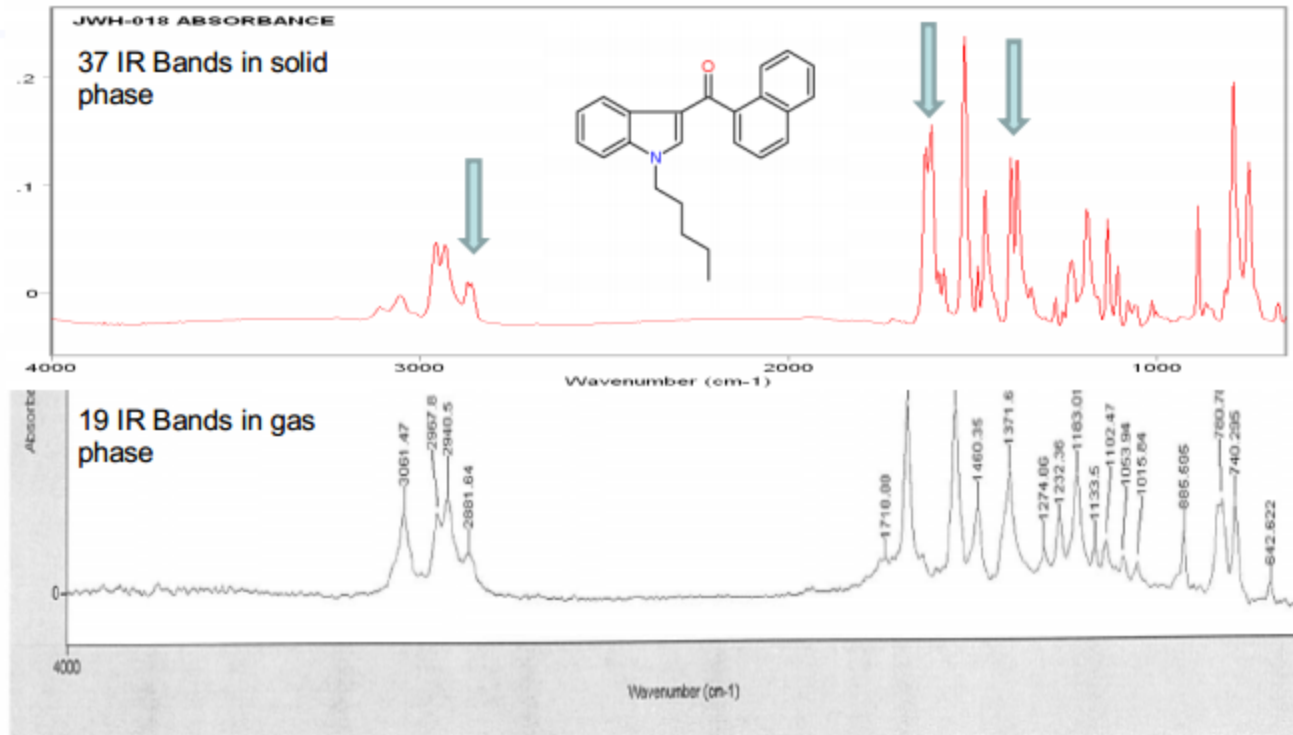
GC-IRD



# Infrared Spectral Comparison of JWH-18 (red) and JWH-073 (black)

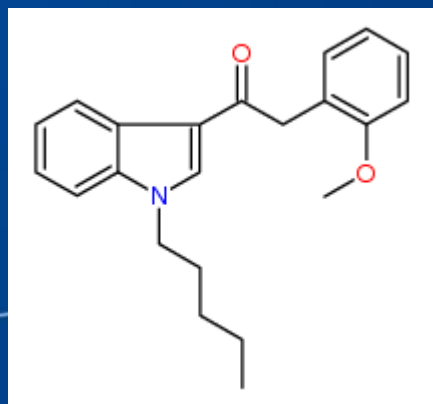
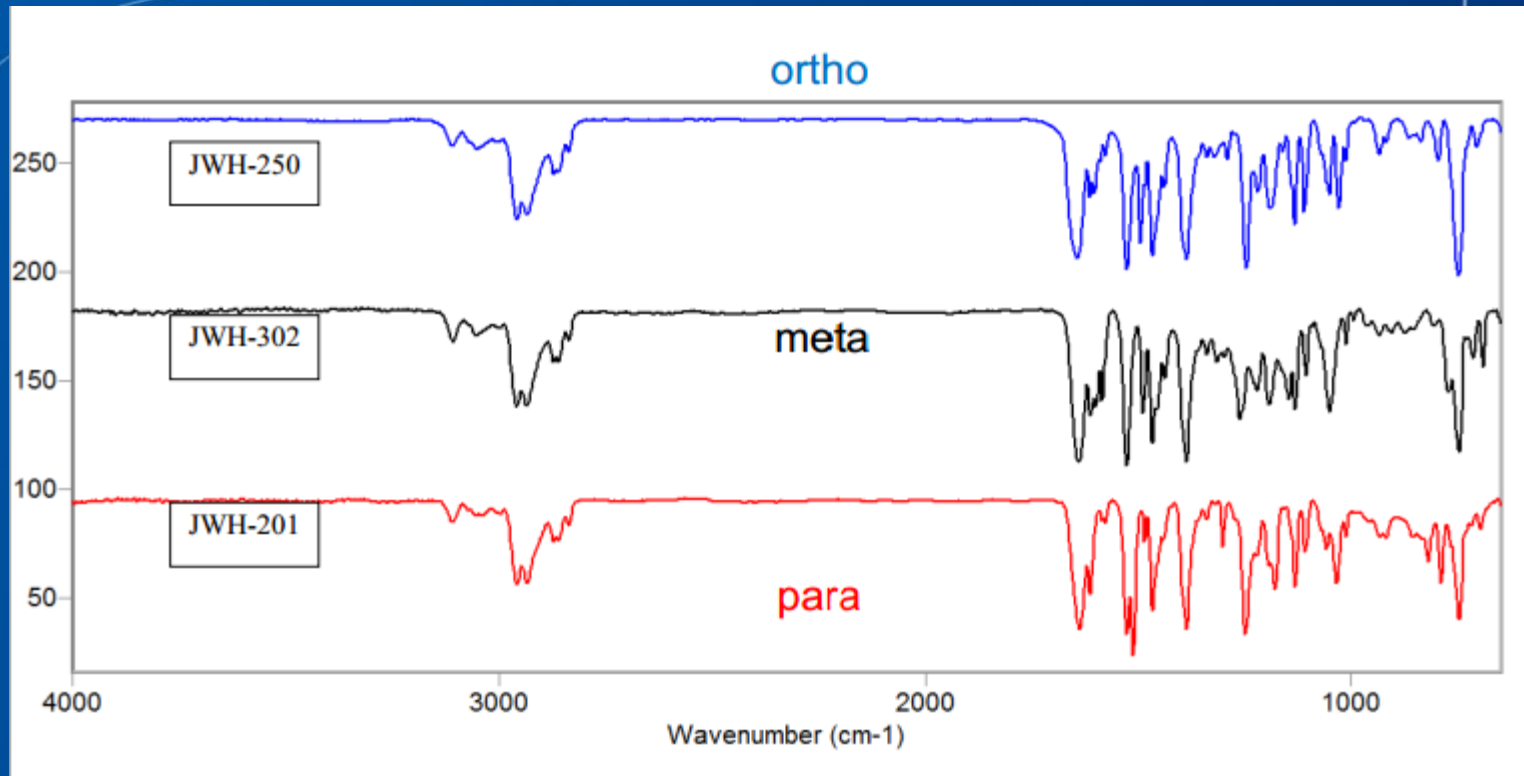


## JWH-018 Solid phase (Red) vs. Gas phase FTIR Spectra



Molecules are free to rotate in the gas phase. Centrifugal distortion causes broad infrared bands. Therefore less spectral resolution is observed in gas phase GC-IR so the IR band at 2860 cm<sup>-1</sup> which distinguishes JWH-018 from JWH-073 is not detected. The other two doublets highlighted signal the attachment is at the 1'naphthyl position, vs. the 2' naphthyl position.

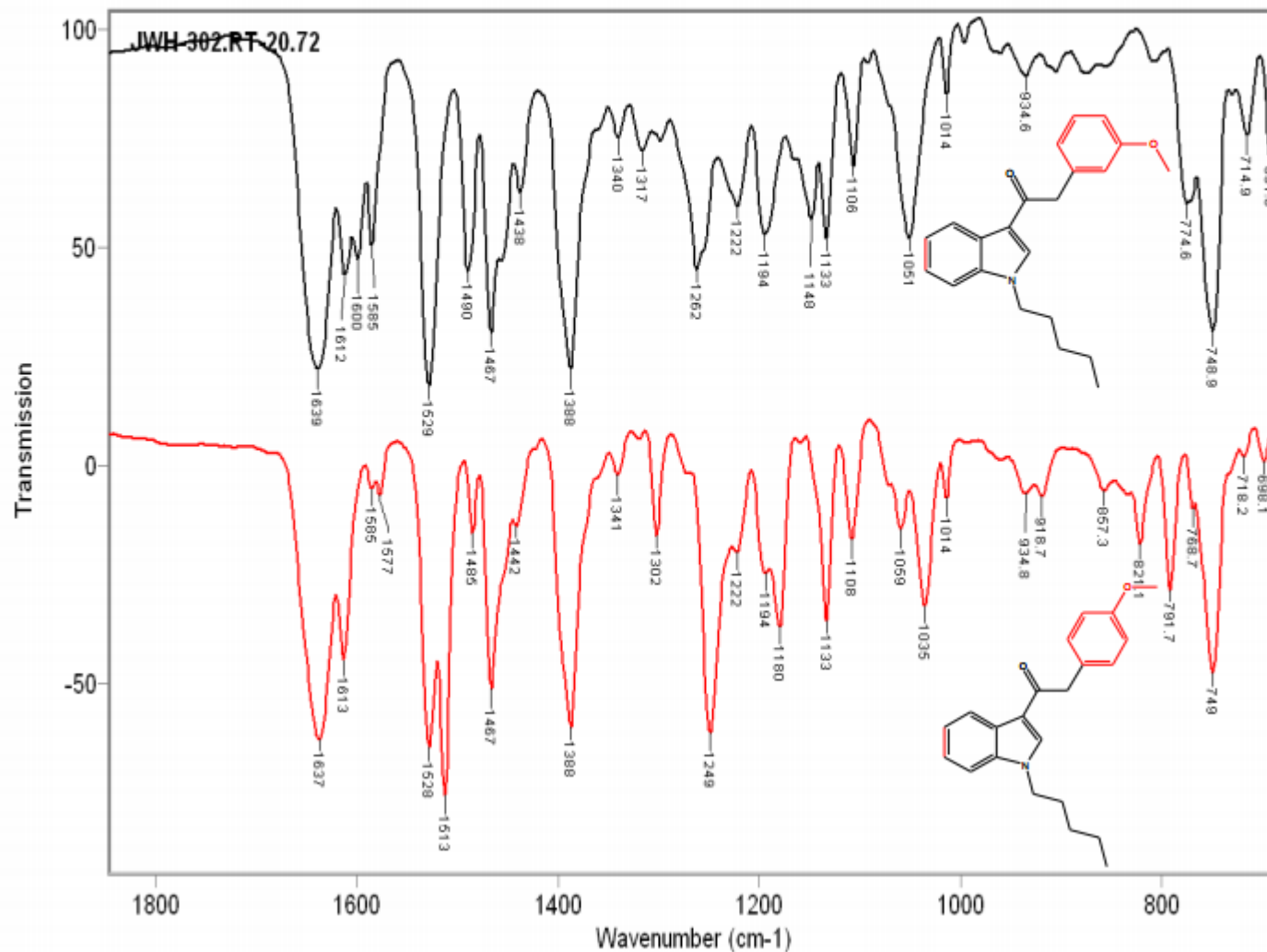




Distinction d'isomères de position

# JWH-302 vs JWH-201

4cm<sup>-1</sup> resolution



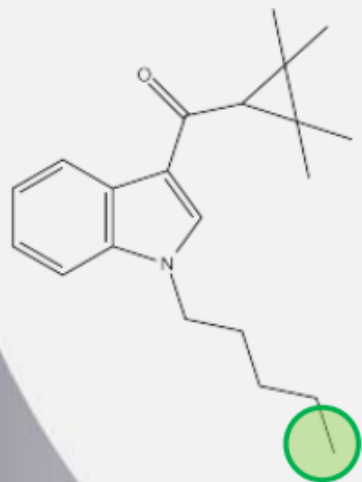
# Cannabinoides de synthèse... difficulté des identifications



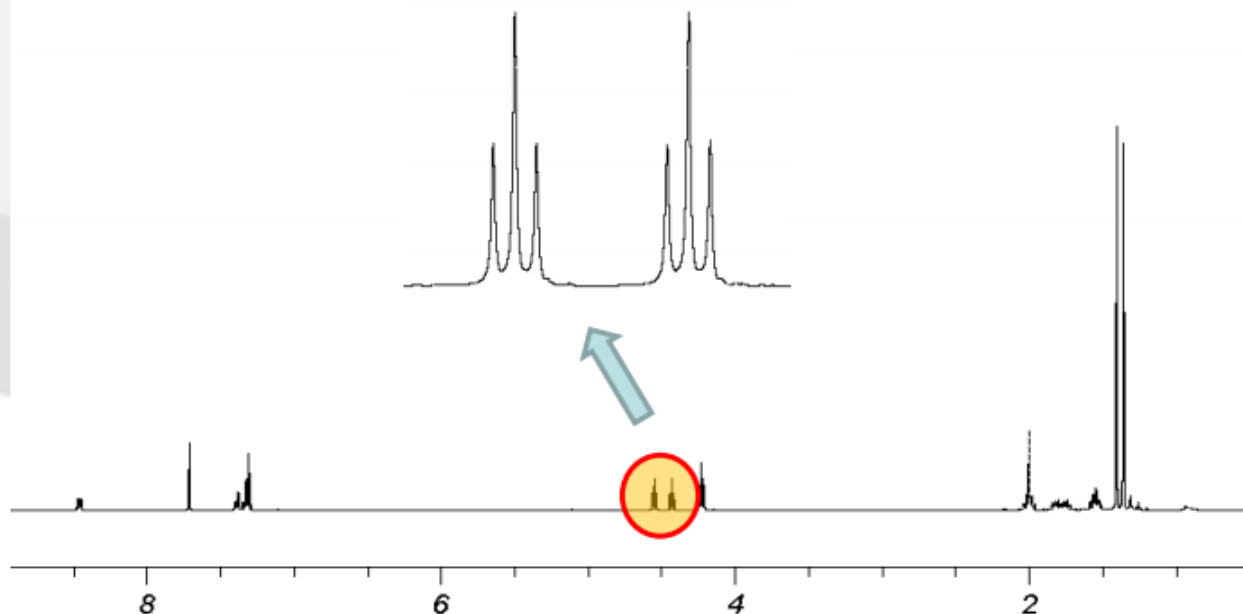
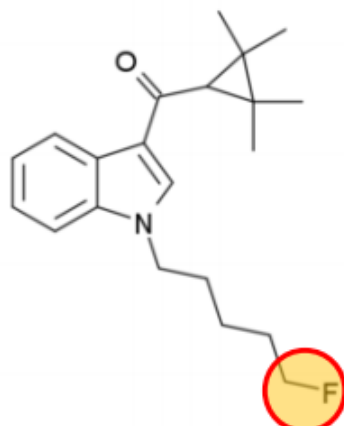
RMN comme technique complémentaire !



➤ UR 144

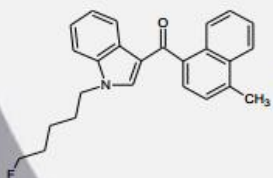


➤ XLR 11



34

MAM2201

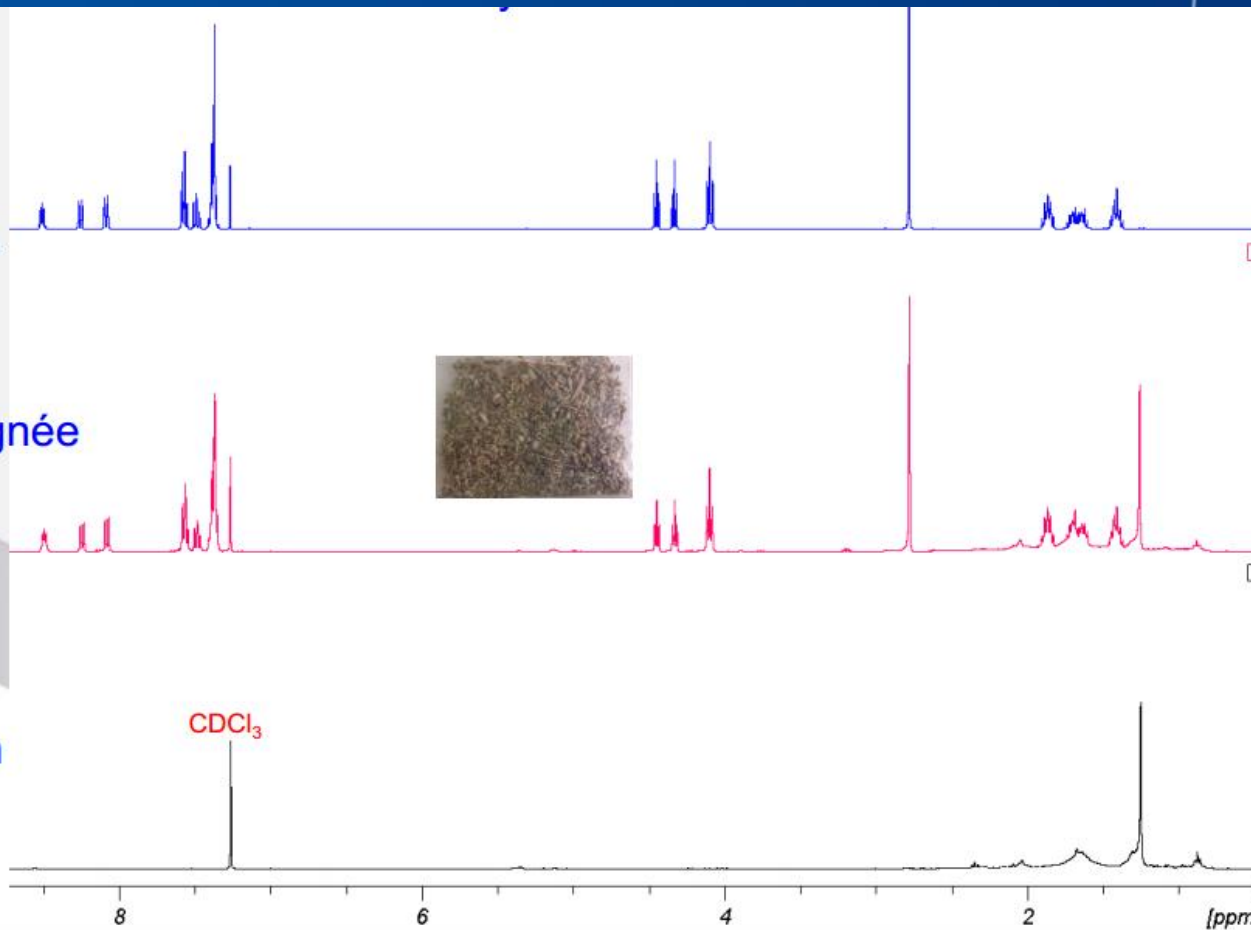


Herbe imprégnée



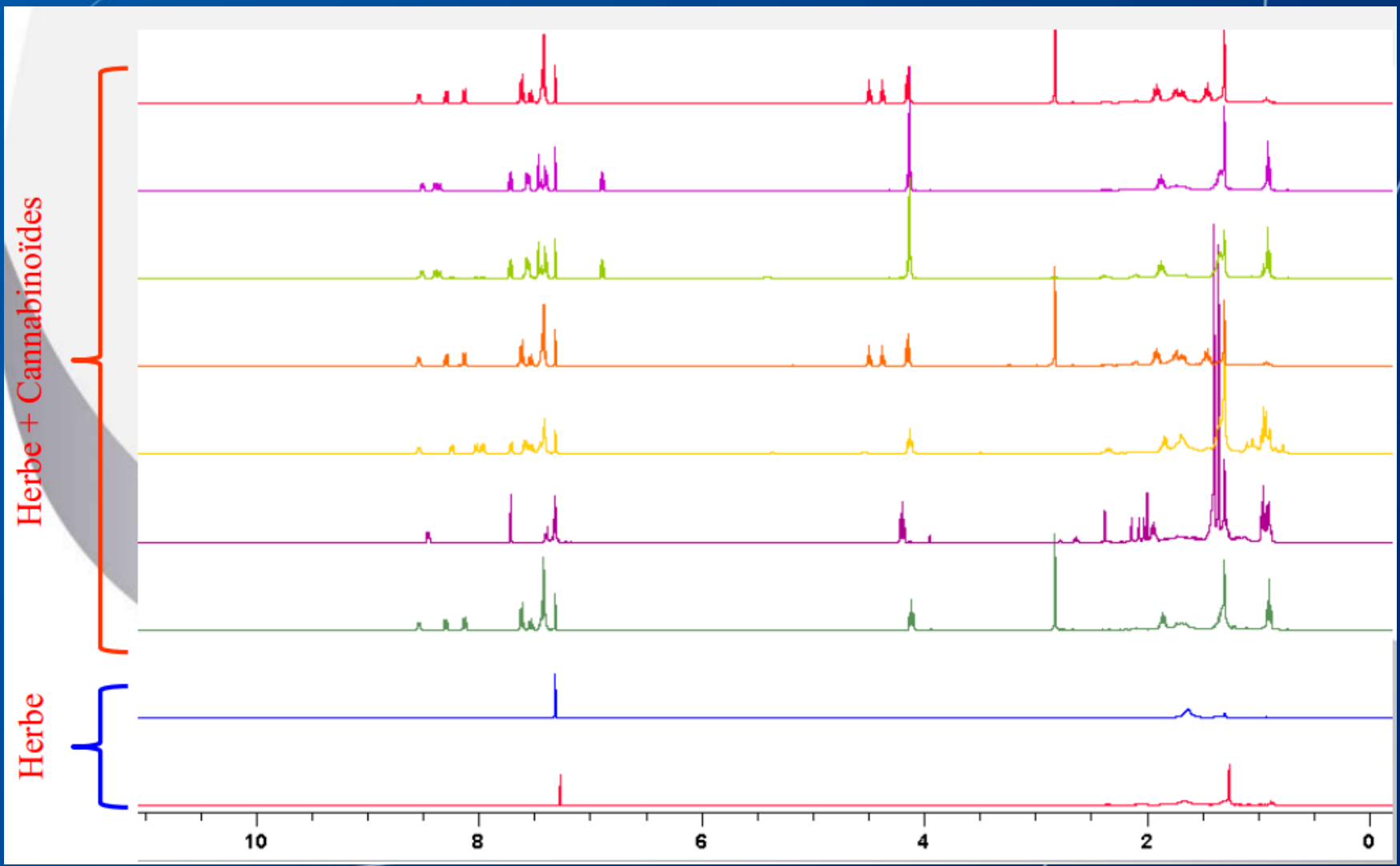
Herbe témoin

CDCl<sub>3</sub>



39





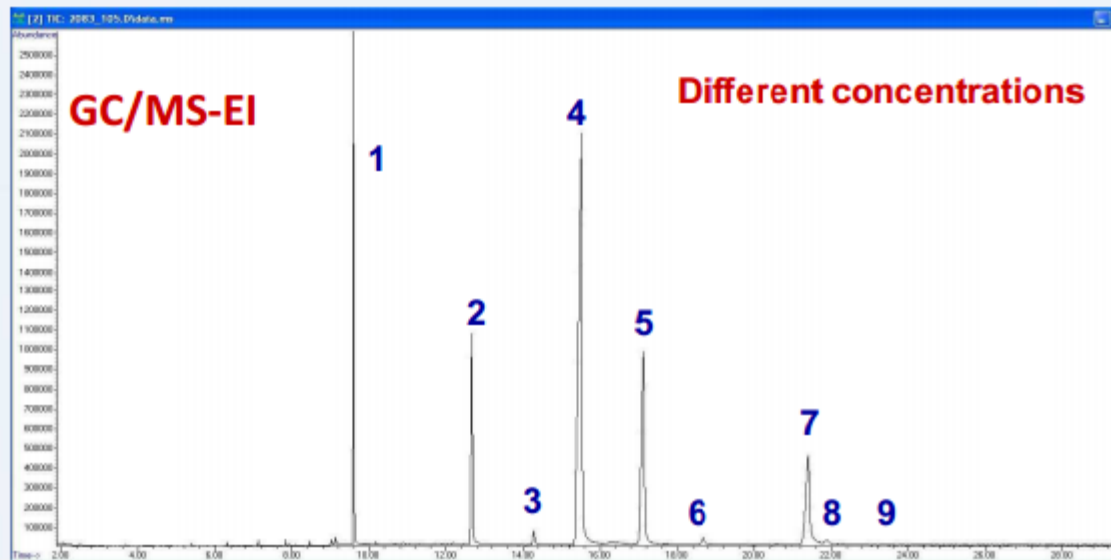
# Cannabinoides de synthèse... difficulté des identifications



Problème des mélanges...

Dry plant matter (0.09 g) and a pipe contained:

- 1 - Dimethocaine
- 2 - Fenazepam
- 3 - (1-butyl-1H-indol-3-yl)(4-methoxyphenyl)methanone
- 4 - RCS-4
- 5 - JWH-073
- 6 - JWH-018
- 7 - AM-2201
- 8 - JWH-122
- 9 - JWH-081



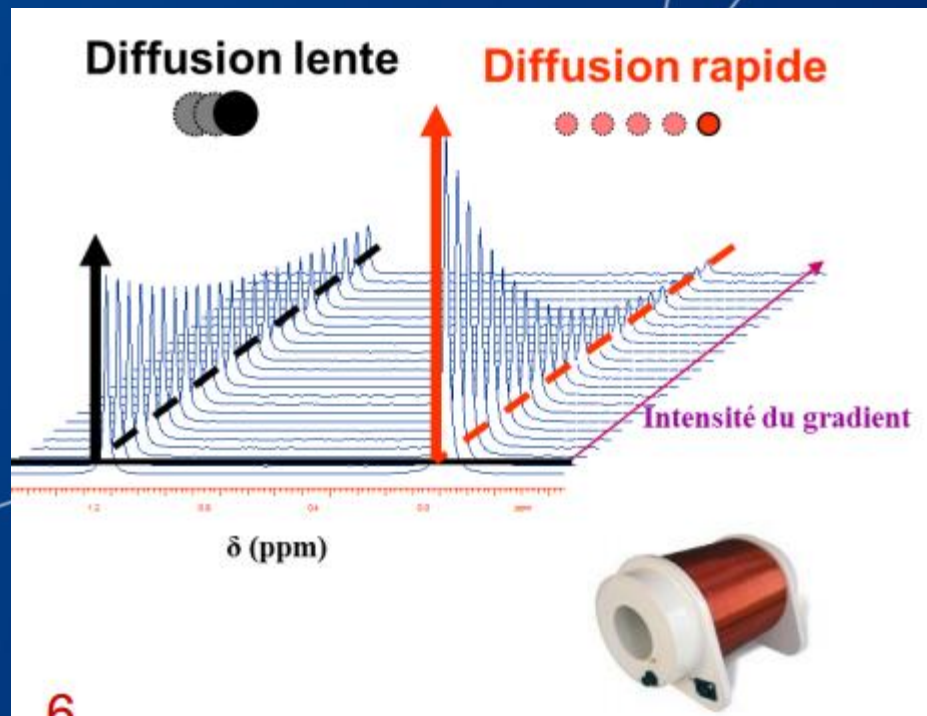
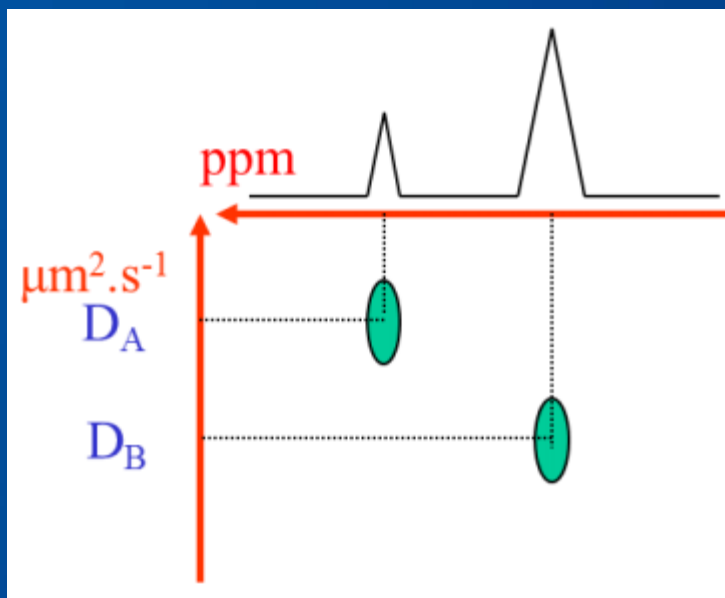
**E 2083/2012/TA evidence no 5 – dry plant matter and a pipe**

# RMN 2D DOSY (Diffusion Ordered Spectroscopy)

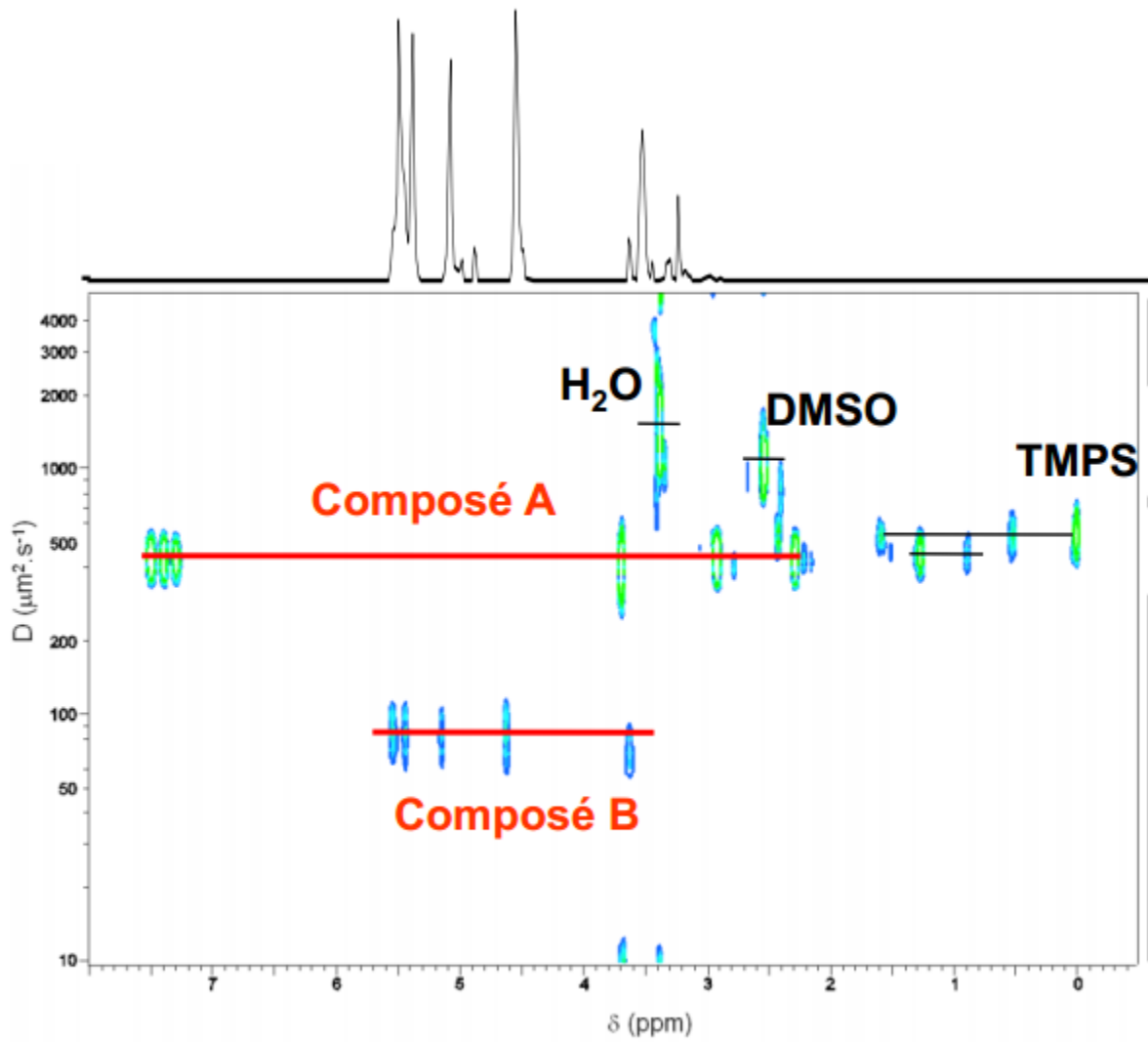


$$D = \frac{k_B T}{6 \pi \eta R_H}$$

D : Coefficient de diffusion  
 η : Viscosité dynamique  
 R<sub>H</sub> : Rayon hydrodynamique de la molécule considérée sphérique.  
 k<sub>B</sub> : Cte de Boltzmann



# Coefficient de Diffusion



# Déplacement Chimique





**Merci pour votre attention**