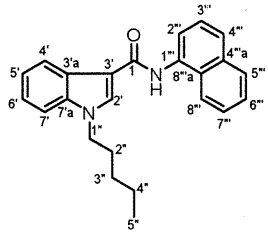
Shimokawa Y., Kikura-Hanajiri R., Aritake K., Urade Y., Goda Y.: Characterization of four new designer drugs, 5-chloro-NNEI, NNEI indazole analog, α-PHPP and α-POP, with 11 newly distributed designer drugs in illegal products. Forensic Sci. Int., (2014) 243, 1-13.

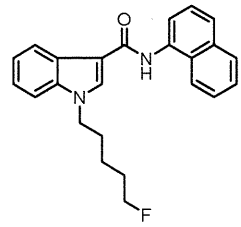
4. Uchiyama N., Shimokawa Y., Matsuda S., Kawamura M., Kikura-Hanajiri R., Goda Y.: Two new synthetic cannabinoids, AM-2201 benzimidazole analog (FUBIMINA) and (4-methylpiperazin-1-yl) (1-pentyl-1H-indol-3-yl)methanone (MEPIRAPIM), and three phenethylamine derivatives, 25H-NBOMe 3,4,5-trimethoxybenzyl analog, 25B-NBOMe, and 2C-N-NBOMe, identified in illegal products identified in illegal products. Forensic Toxicol. (2013) 32, 105–117.
5. 内山奈穂子：違法ドラッグ（脱法ドラッグ）の正体は？和漢薬, 723, 10-11 (2013).

H. 知的財産権の出願・登録状況

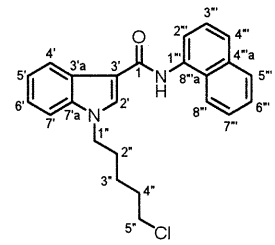
特になし.



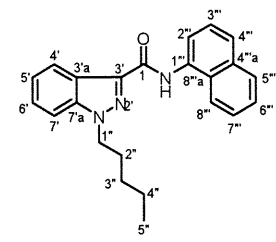
NNEI (MN-24, **1**)
$C_{24}H_{24}N_2O$: 356



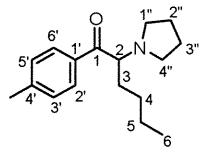
5-Fluoro-NNEI (5-Flouro-MN-24, **2**)
$C_{24}H_{23}FN_2O$: 374



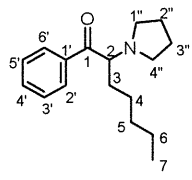
5-Chloro-NNEI (**3**)
$C_{24}H_{23}ClN_2O$: 391



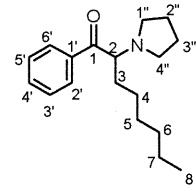
NNEI indazole analog (**4**)
[*N*-(Naphthalen-1-yl)-1-pentyl-1 *H*-indazole-3-carboxamide]
$C_{23}H_{23}N_3O$: 357



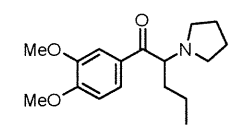
MPHP
(4-Methyl-α-pyrrolidinohexylphenone, **5**)
$C_{17}H_{25}NO$: 259



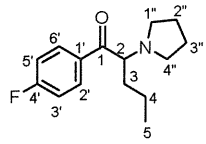
α-PHPP
(α-Pyrrolidinoheptanophenone, **6**)
$C_{17}H_{25}NO$: 259



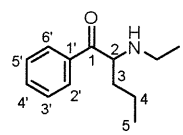
α-POP
(α-Pyrrolidino-octanophenone, **7**)
$C_{18}H_{27}NO$: 273



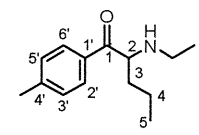
3,4-Dimethoxy-α-PVP (**8**)
$C_{17}H_{25}NO_3$: 291



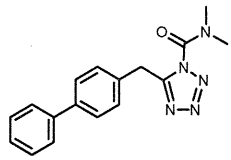
4-Fluoro-α-PVP (**9**)
$C_{15}H_{20}FNO$: 249



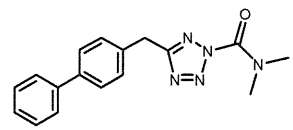
α-Ethylaminopentiophenone
(α-EAPP, **10**)
$C_{13}H_{19}NO$: 205



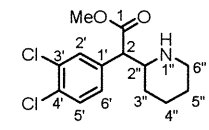
2-(Ethylamino)-1-(*p*-tolyl)pentan-1-one
(*N*-Ethyl-4-methyl-pentedrone,
4-Methyl-α-ethylaminopentiophenone, **11**)
$C_{14}H_{21}NO$: 219



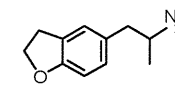
LY2183240 (**12**)
$C_{17}H_{17}N_5O$: 307



LY2183240 2'-isomer (**13**)
$C_{17}H_{17}N_5O$: 307



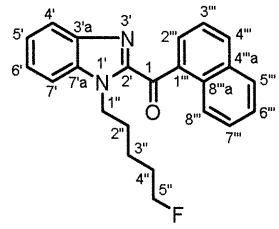
3,4-Dichloromethylphenidate (**14**)
$C_{14}H_{17}Cl_2NO_2$: 302



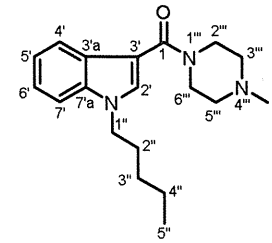
5-APDB (**15**)
$C_{11}H_{15}NO$: 177

Fig. 1a. 平成 25 年度前半買い上げ違法ドラッグ製品より検出された新規流通化合物(**1**–**15**)

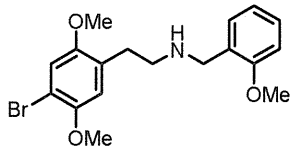
合成カンナビノイド(**1**–**4**), カチノン系化合物(**5**–**11**), 合成カンナビノイド関連化合物(**12** , **13**), その他化合物(**14**)及びフェネチルアミン系化合物(**15**)



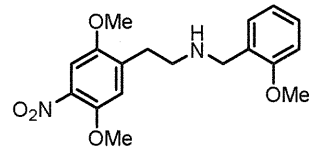
AM-2201 benzimidazole analog
(FUBIMINA, **16**)
(1-(5-Fluoropentyl)-1 *H*-benzo[*d*]imidazol-2-yl)(naphthalen-1-yl)methanone
$C_{23}H_{21}FN_2O$: 360



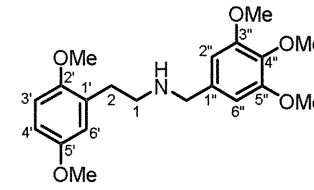
(4-Methylpiperazin-1-yl)(1-pentyl-1*H*-indol-3-yl)methanone
(MEPIRAPIM, **17**)
$C_{19}H_{27}N_3O$: 313



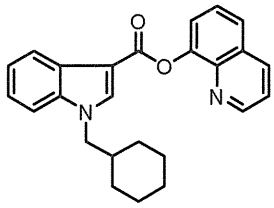
25B-NBOMe (**18**)
$C_{18}H_{22}BrNO_3$: 380



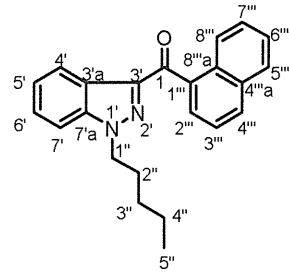
2C-N-NBOMe (**19**)
$C_{18}H_{22}N_2O_5$: 346



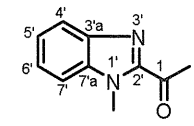
25H-NBOMe 3,4,5-trimethoxybenzyl analog (**20**)
[2-(2,5-Dimethoxyphenyl)- *N*-(3,4,5-trimethoxybenzyl)ethanamine]
$C_{20}H_{27}NO_5$: 361



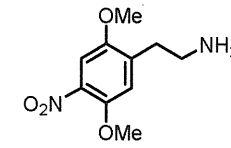
QUCHIC (BB-22)
$C_{25}H_{24}N_2O_2$: 384



JWH-018 indazole analog
$C_{23}H_{22}N_2O$: 342



2-Acetyl-1-methyl-1*H*-benzimidazole



2C-N

Fig. 1b. 平成 25 年度前半買い上げ違法ドラッグ製品より検出された新規流通化合物(**16**–**20**)

合成カンナビノイド(**16** , **17**), フェネチルアミン系化合物(**18**–**20**)及び関連化合物

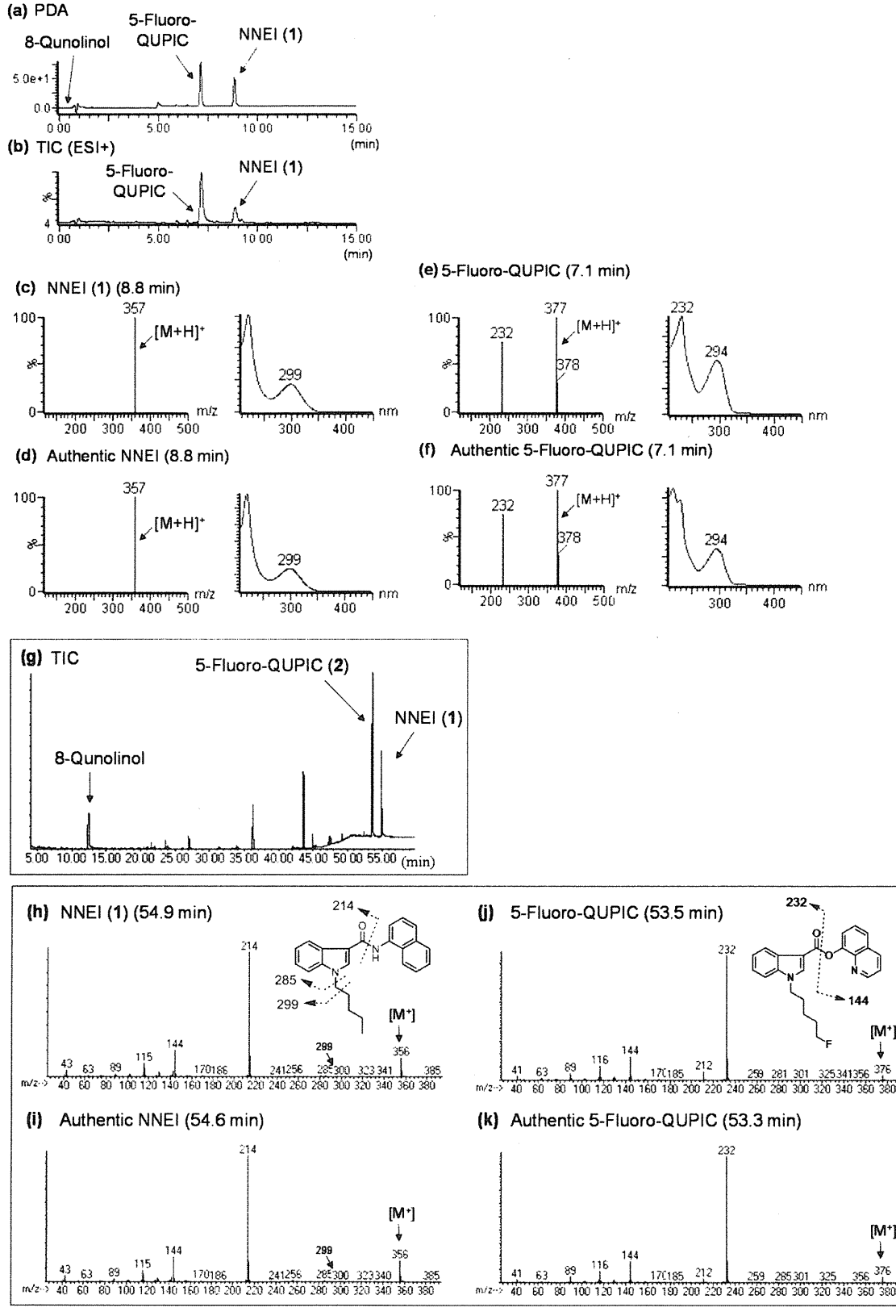


Fig. 2. LC-MS and GC-MS analyses of product A. LC-UV-PDA chromatogram (**a**) and total ion chromatogram (TIC) (**b**). ESI mass and UV spectra of peaks **1** (c), 5-fluoro-QUPIC (e), authentic NNEI and 5-fluoro-QUPIC (d and f, respectively). TIC (**g**) and EI mass spectra of peaks **1** (**h**), 5-fluoro-QUPIC (**j**) and authentic NNEI and 5-fluoro-QUPIC (i and k, respectively) obtained by GC-MS analysis.

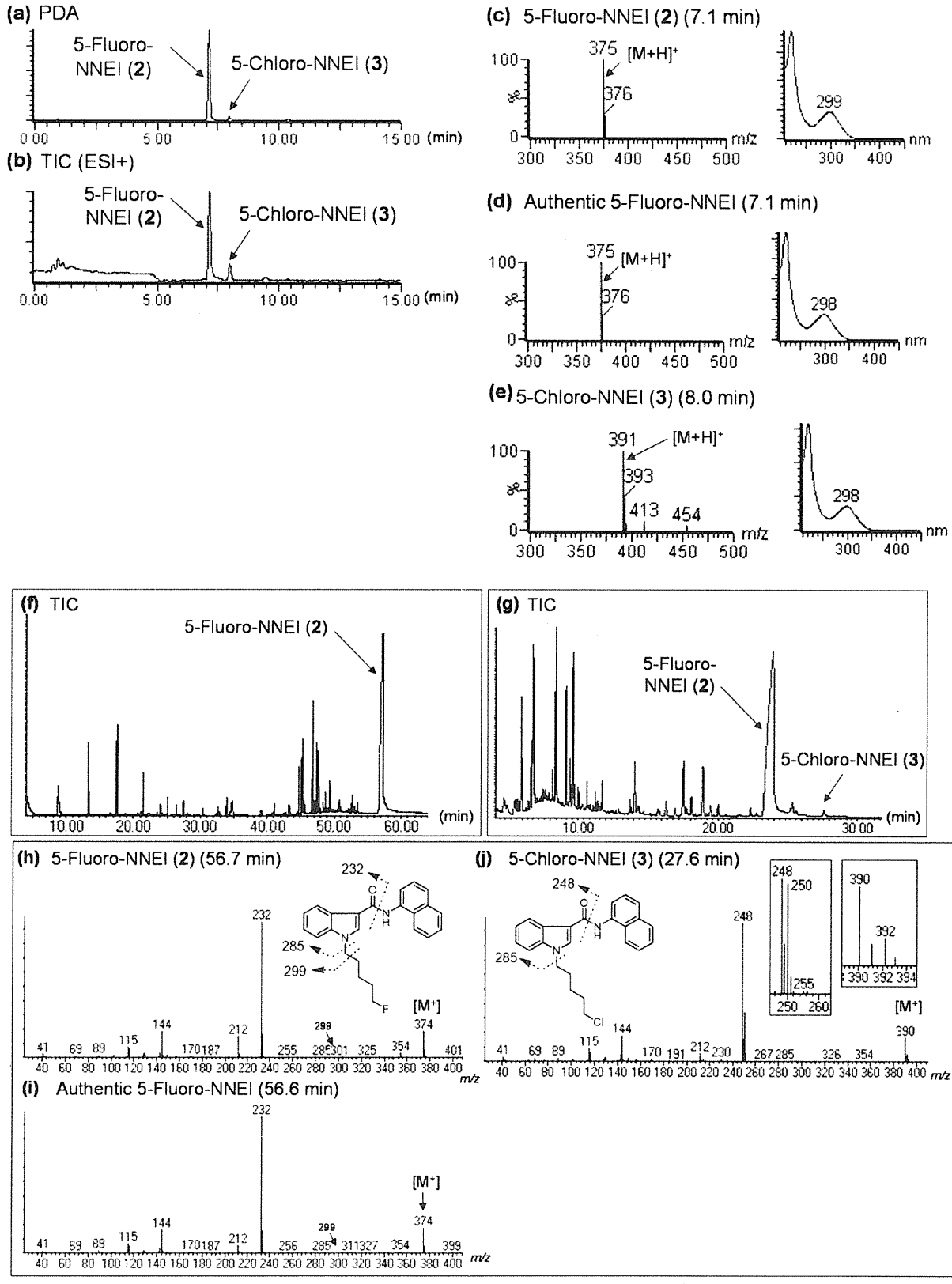


Fig. 3. LC-MS and GC-MS analyses of product B. LC-UV-PDA chromatogram (**a**) and TIC (**b**). ESI mass and UV spectra of peaks **2** (c), **3** (e) and authentic 5-fluoro-NNEI (d). TIC (**f**, **g**) and EI mass spectra of peaks **2** (h), **3** (j) and authentic 5-fluoro-NNEI (i) obtained by the GC-MS analysis.

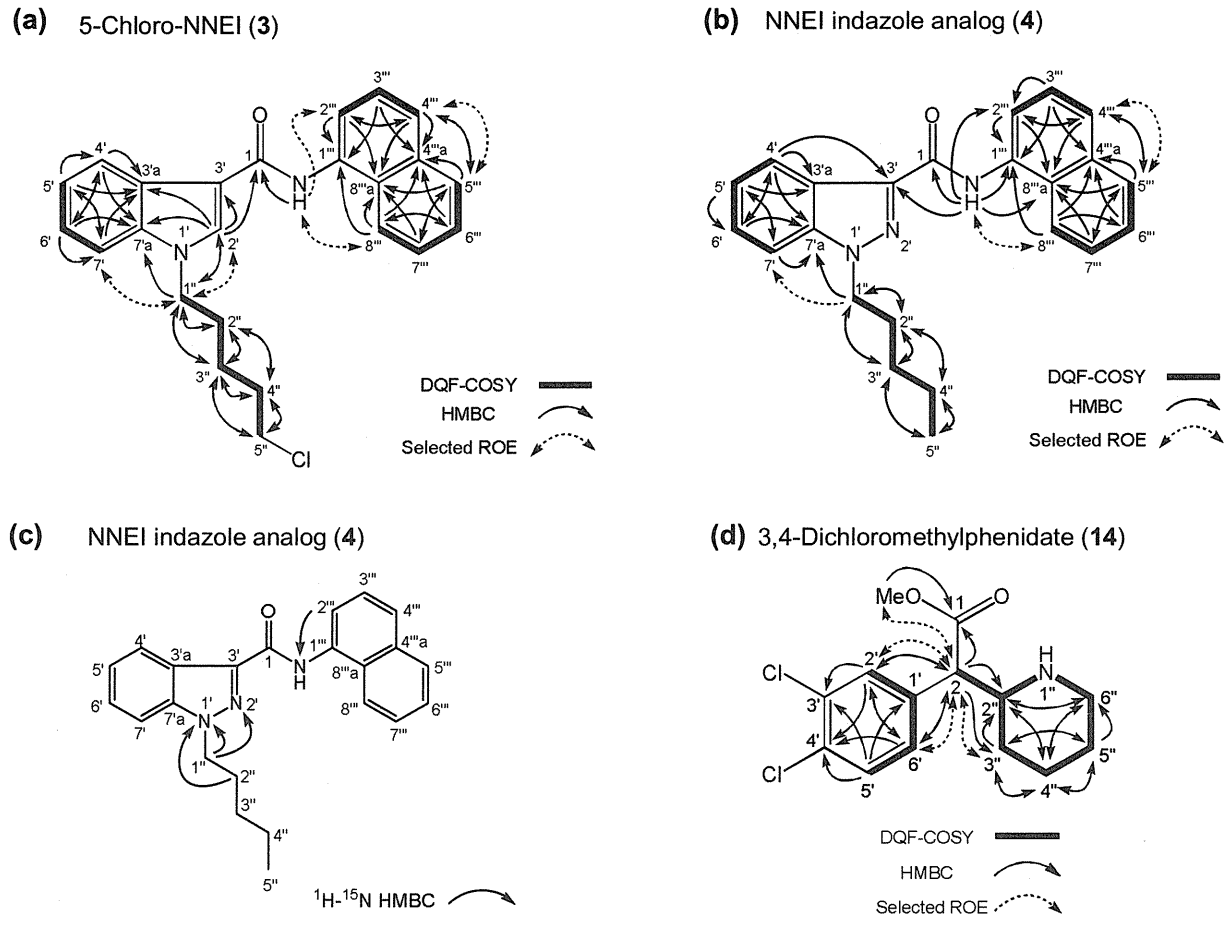


Fig. 4. DQF-COSY, selected HMBC, and selected ROE correlations (**a**) for compound **3** (5-chloro-NNEI), and DQF-COSY, selected HMBC and selected ROE correlations for compound **4** (NNEI indazole analog, **b**) and compound **14** (3,4-Dichloromethylphenidate, **d**). ^{1}H-^{15}N HMBC correlation for compound **4** (NNEI indazole analog, **c**).

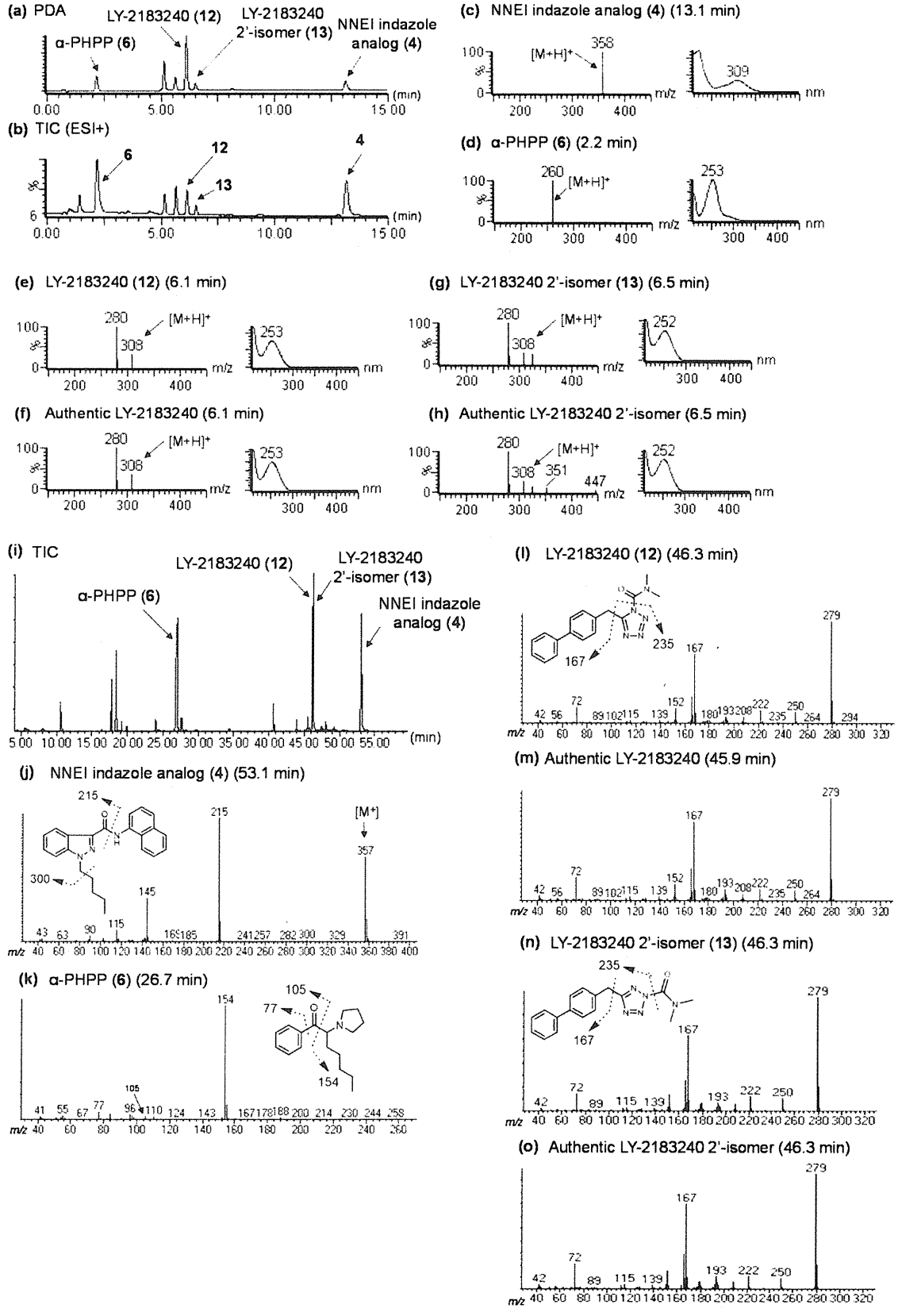


Fig. 5. LC-MS and GC-MS analyses of product C. LC-UV-PDA chromatogram (**a**) and TIC (**b**). ESI mass and UV spectra of peaks **4** (**c**), **6** (**d**), **12** (**e**), **13** (**g**) and authentic LY-2183240 and LY-2183240 2'-isomer (**f** and **h**), respectively. TIC (**i**) and EI mass spectra of peaks **4** (**i**), **6** (**k**), **12** (**l**), **13** (**m**) and authentic LY-2183240 and LY-2183240 2'-isomer (**n** and **o**), respectively, obtained by the GC-MS analysis.

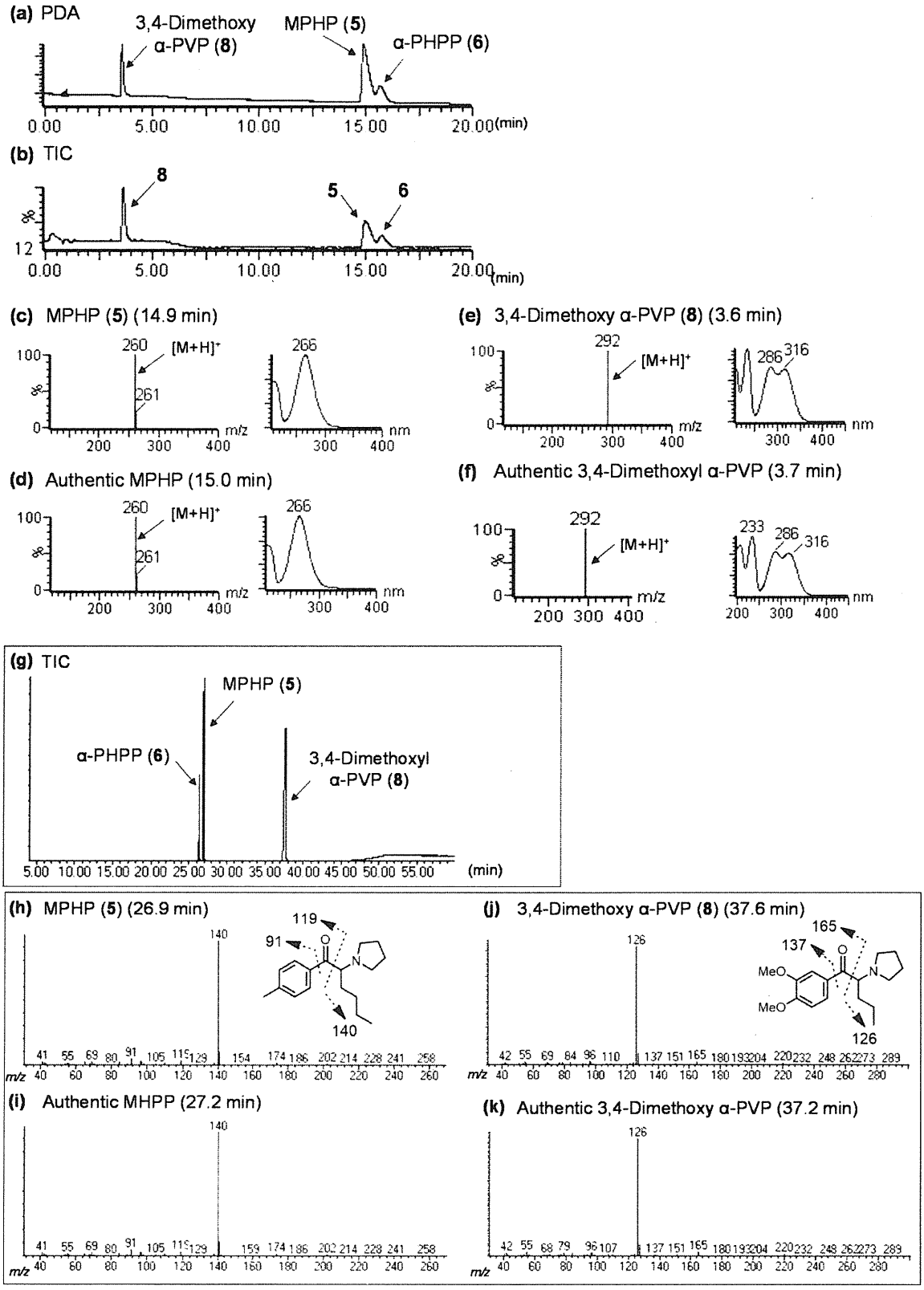


Fig. 6. LC-MS and GC-MS analyses of product D. LC-UV-PDA chromatogram (**a**) and TIC (**b**). ESI mass and UV spectra of peaks **5** (**c**), **8** (**e**) and authentic MPHP and 3,4-dimethoxyl-α-PVP (**d** and **f**), respectively. TIC (**g**) and EI mass spectra of peaks **5** (**h**), **8** (**j**) and authentic MPHP and 3,4-dimethoxyl-α-PVP (**i** and **k**), respectively, obtained by the GC-MS analysis.

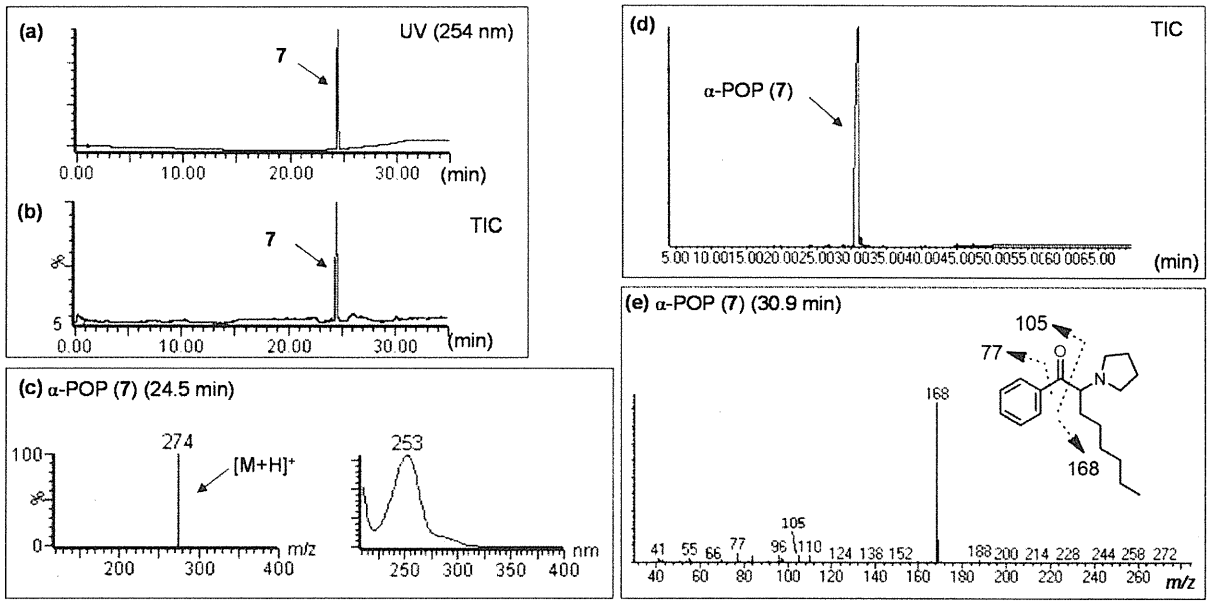


Fig. 7. LC-MS and GC-MS analyses of product E. LC-UV-PDA chromatogram (**a**), TIC (**b**) and ESI mass and UV spectra of peak **7** (**c**). TIC (**d**) and EI mass spectrum of peak **7** (**e**) obtained by the GC-MS analysis.

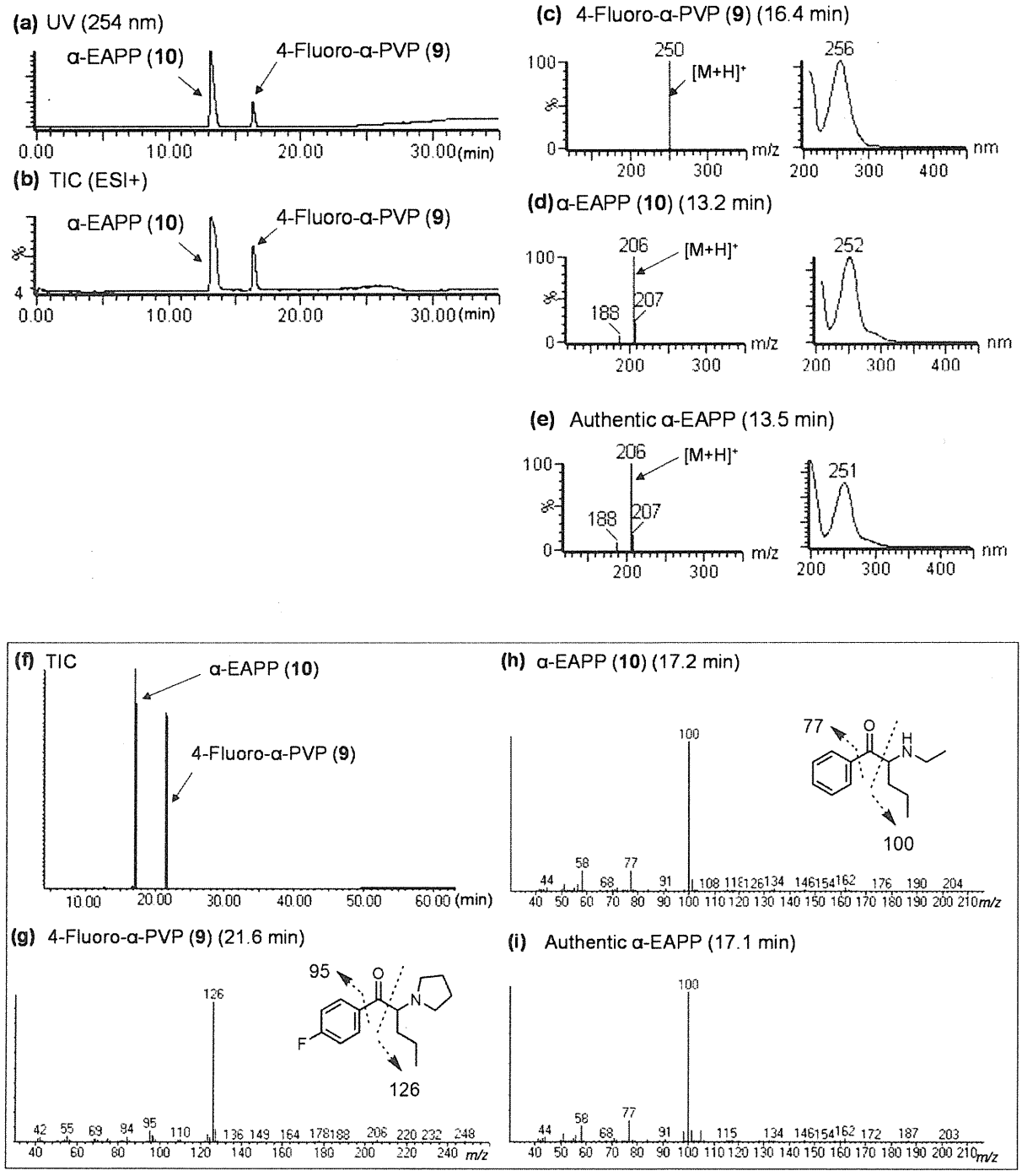


Fig. 8. LC-MS and GC-MS analyses of product F. LC-UV-PDA chromatogram (**a**) and TIC (**b**). ESI mass and UV spectra of peaks **9** (**c**), **10** (**d**) and authentic α-EAHP (**e**), respectively. TIC (**f**) and EI mass spectra of peaks **9** (**g**), **10** (**h**) and authentic α-EAHP (**i**), respectively, obtained by the GC-MS analysis.

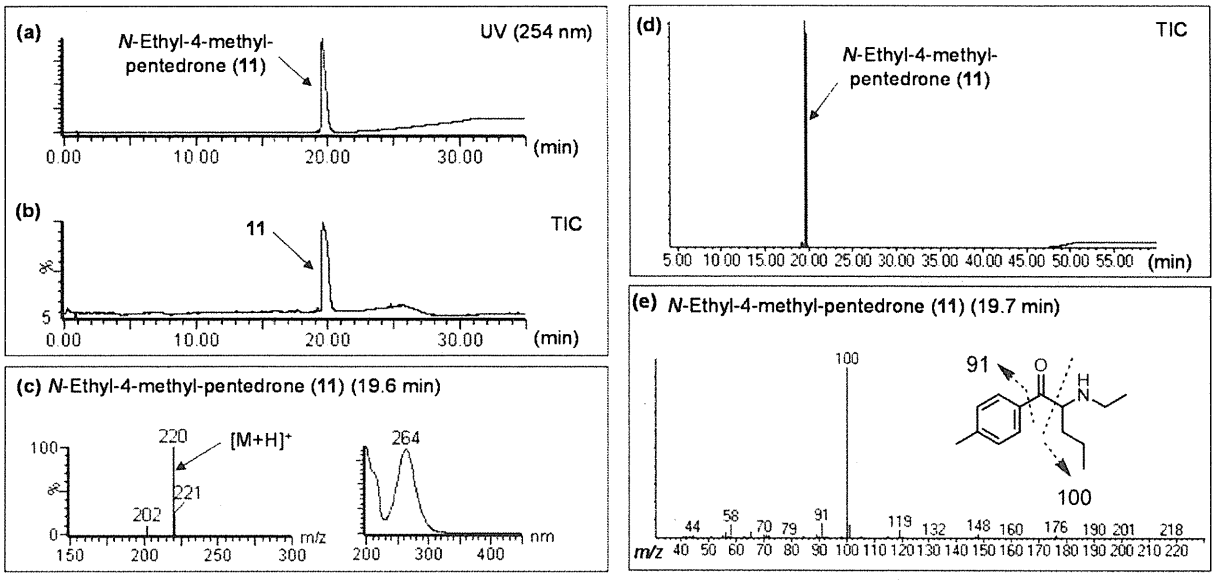


Fig. 9. LC-MS and GC-MS analyses of product G. LC-UV-PDA chromatogram (**a**), TIC (**b**) and ESI mass and UV spectra of peak **11** (**c**). TIC (**d**) and EI mass spectrum of peak **11** (**e**) obtained by the GC-MS analysis.

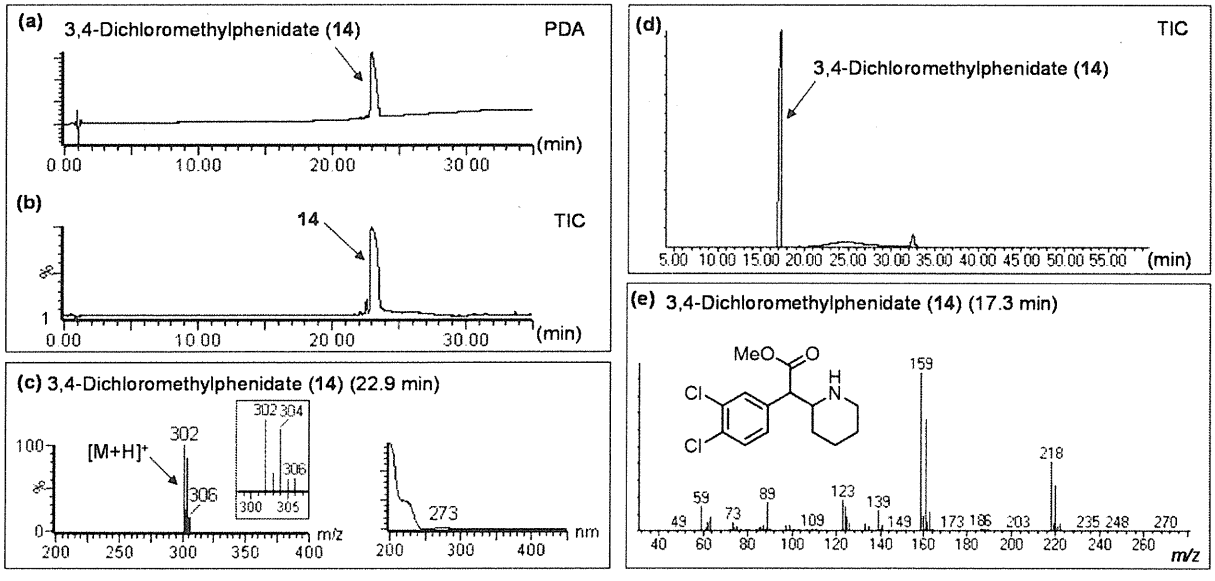


Fig. 10. LC-MS and GC-MS analyses of product H. LC-UV-PDA chromatogram (**a**), TIC (**b**) and ESI mass and UV spectra of peak **14** (**c**). TIC (**d**) and EI mass spectrum of peak **11** (**e**) obtained by the GC-MS analysis.

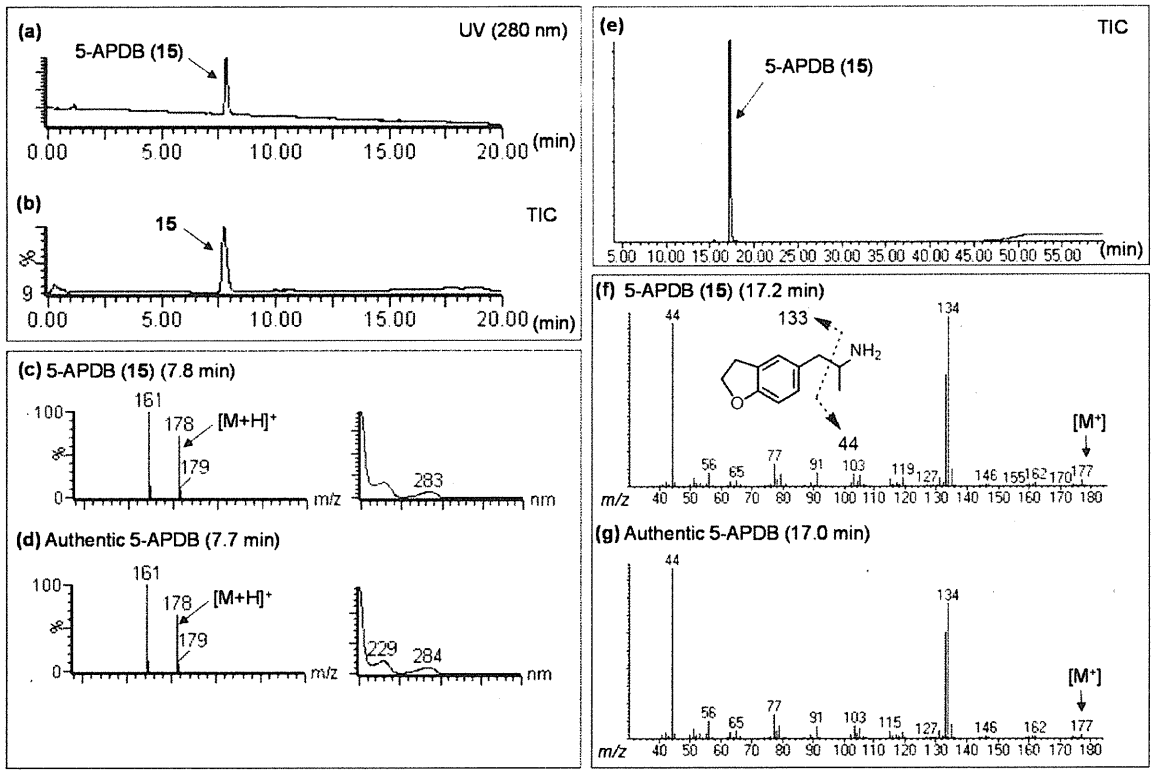


Fig. 11. LC-MS and GC-MS analyses of product I. LC-UV-PDA chromatogram (**a**) and TIC (**b**). ESI mass and UV spectra of peaks **15** (**c**) and authentic 5-APDB (**d**), respectively. TIC (**e**) and EI mass spectra of peaks **15** (**f**) and authentic 5-APDB (**g**), respectively, obtained by the GC-MS analysis.

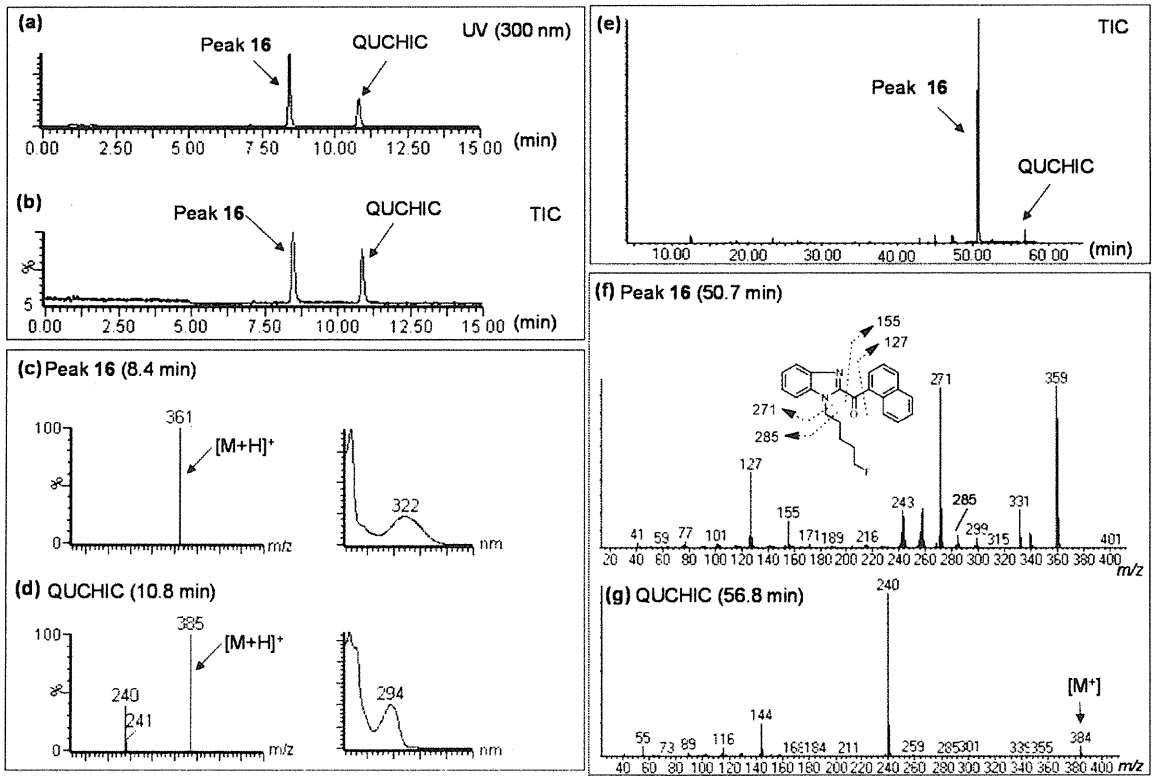
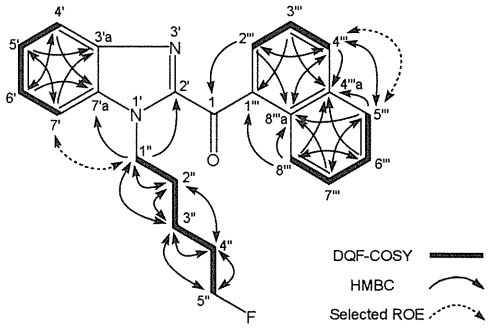
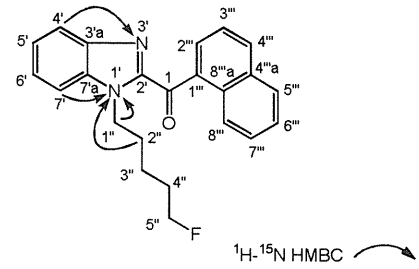


Fig. 12. LC-MS and GC-MS analyses of product J. LC-UV-PDA chromatogram (**a**) and total ion chromatogram (TIC) (**b**). ESI mass and UV spectra of peaks **16** (**c**) and QUCHIC (**d**). TIC (**e**) and EI mass spectra of peaks **16** (**f**) and QUCHIC (**g**) obtained by GC-MS analysis.

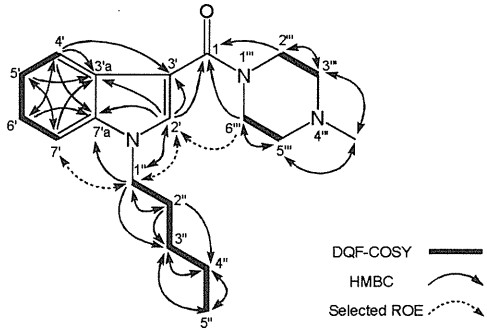
(a) AM-2201 benzimidazole analog (**16**)



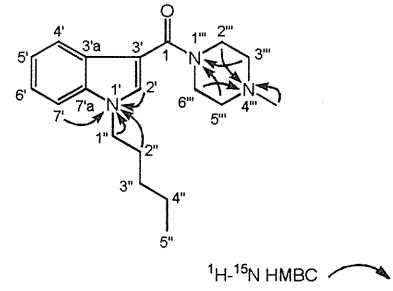
(b) AM-2201 benzimidazole analog (**16**)



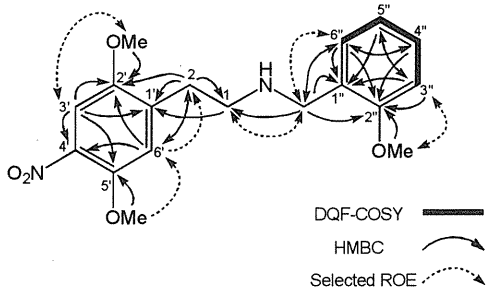
(c) (4-methylpiperazin-1-yl)(1-pentyl-1*H*-indol-3-yl)methanone (**17**)



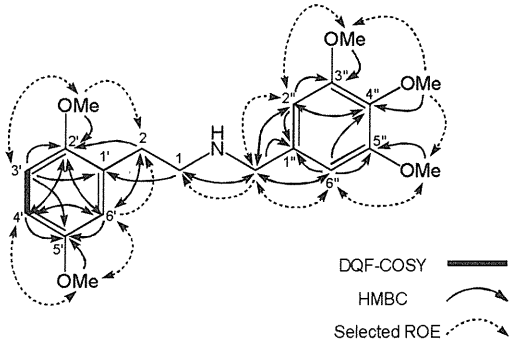
(d) (4-methylpiperazin-1-yl)(1-pentyl-1*H*-indol-3-yl)methanone (**17**)



(e) 2C-N-NBOMe (**19**)



(f) 2-(2,5-Dimethoxyphenyl)-N-(3,4,5-trimethoxybenzyl)ethanamine (**20**)



(g) 2-(2,5-Dimethoxyphenyl)-N-(3,4,5-trimethoxybenzyl)ethanamine (**20**)

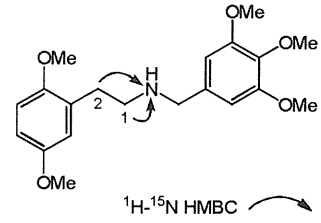


Fig. 13. DQF-COSY, selected HMBC, and selected ROE correlations for compounds **16** (**a**), **17** (**c**), **19** (**e**) and **20** (**f**), and ^{1}H-^{15}N HMBC correlations for compounds **16** (**b**), **17** (**d**), and **20** (**g**), respectively.

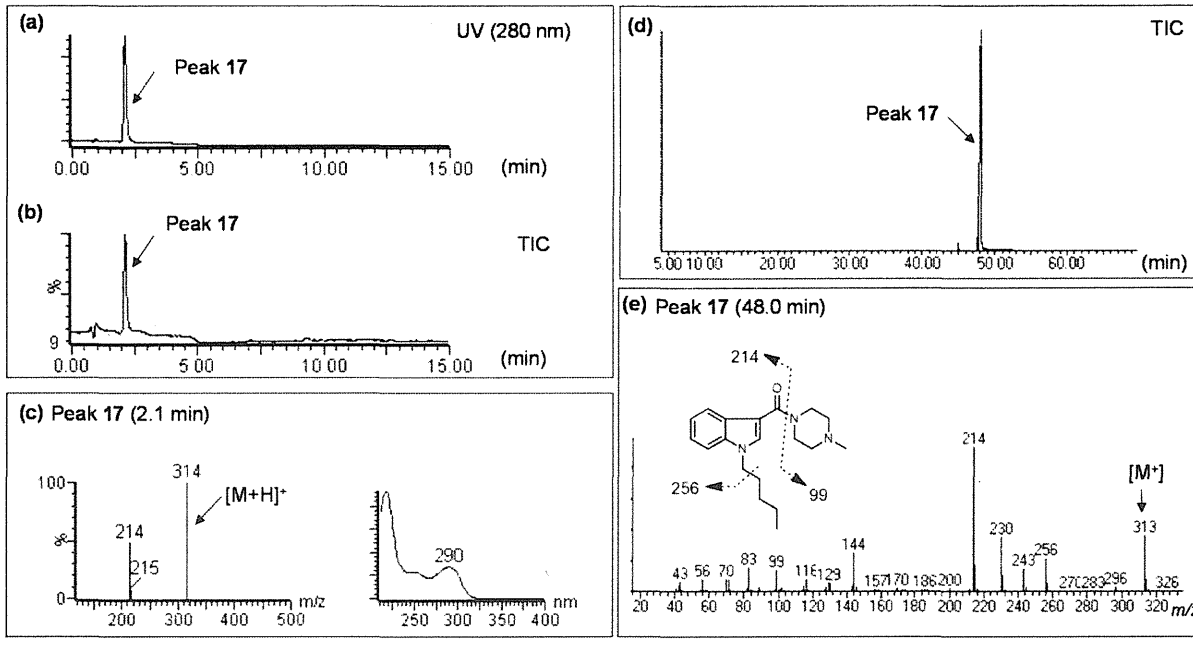


Fig. 14. LC-MS and GC-MS analyses of product K. LC-UV-PDA chromatogram (**a**) and TIC (**b**). ESI mass and UV spectra of peak **17** (**c**). TIC (**d**) and EI mass spectrum of peak **17** (**e**) obtained by the GC-MS analysis.

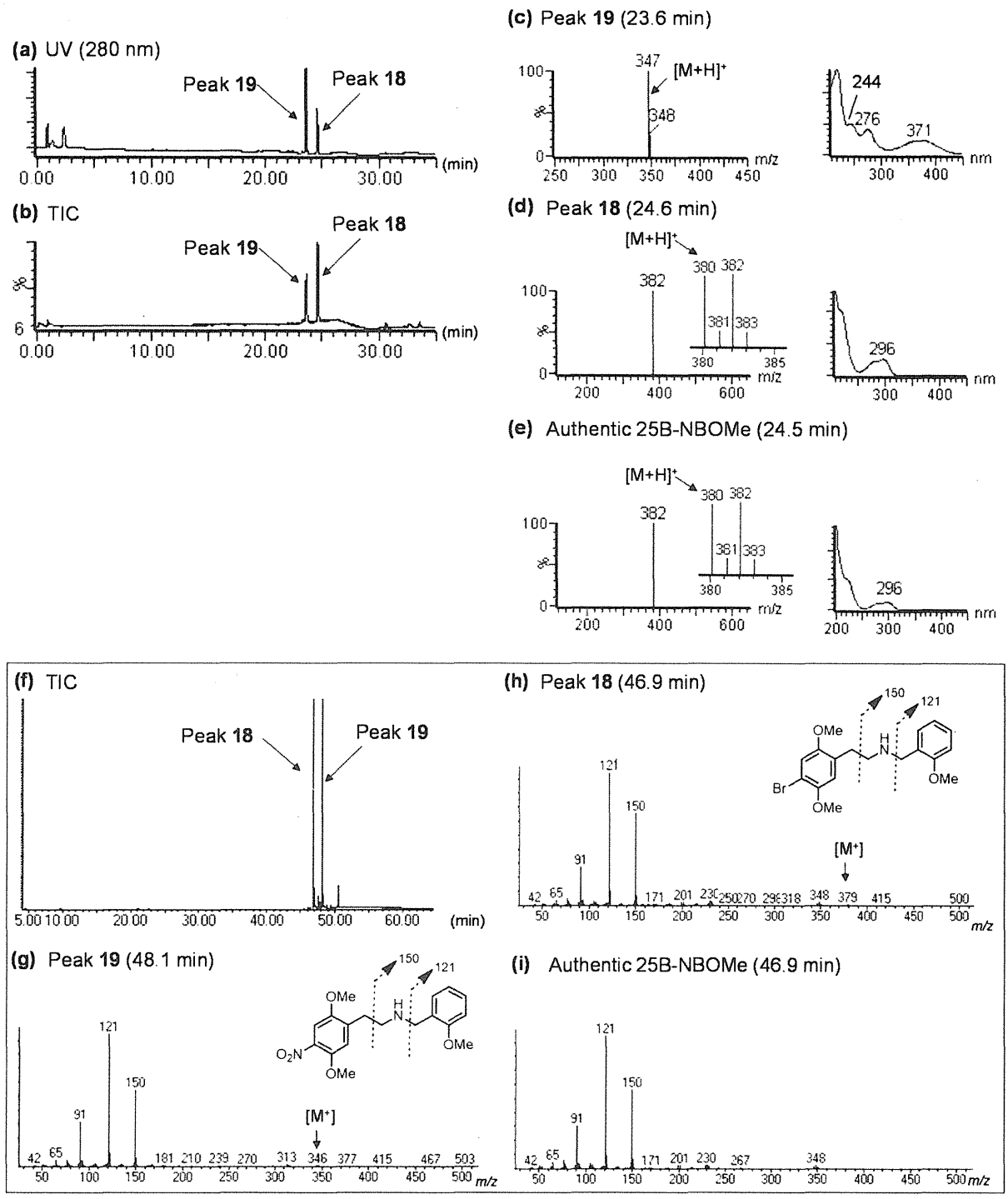


Fig. 15. LC-MS and GC-MS analyses of product L. LC-UV-PDA chromatogram (**a**) and TIC (**b**). ESI mass and UV spectra of peaks **19** (**c**), **18** (**d**) and authentic 25B-NBOMe (**e**), respectively. TIC (**f**) and EI mass spectra of peaks **19** (**g**), **18** (**h**) and authentic 25B-NBOMe (**i**), respectively, obtained by the GC-MS analysis.

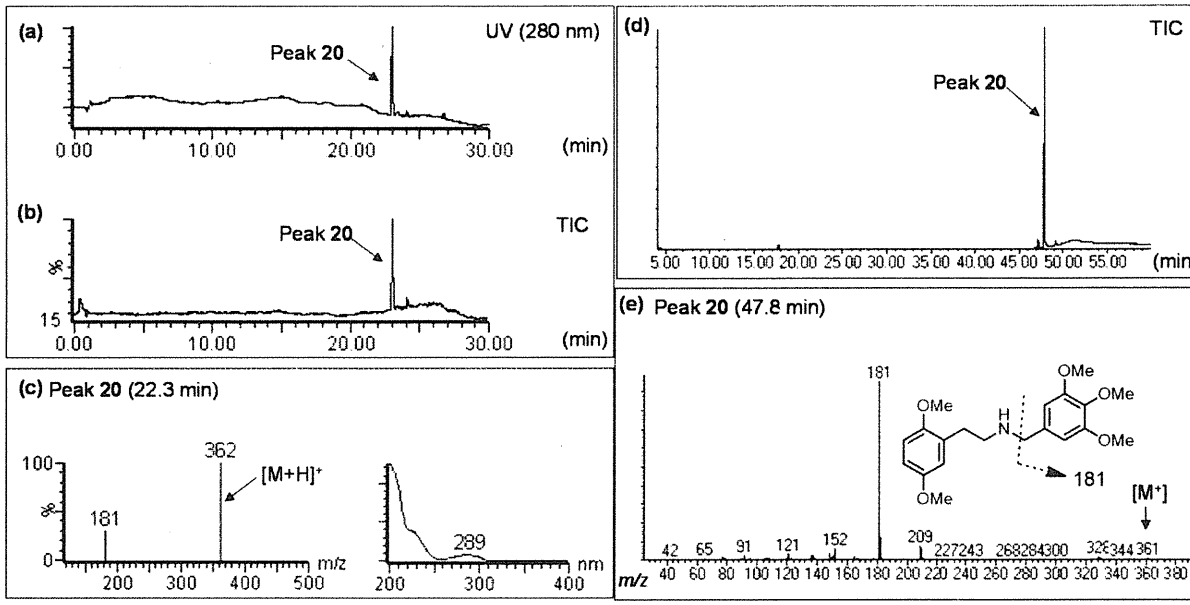


Fig. 16. LC-MS and GC-MS analyses of product M. LC-UV-PDA chromatogram (**a**) and TIC (**b**). ESI mass and UV spectra of peak **20** (**c**). TIC (**d**) and EI mass spectrum of peak **20** (**e**) obtained by the GC-MS analysis.

Table 1. NMR data for NNEI (**1**), 5-Chloro-NNEI (**3**) and NNEI indazole analog (**4**)

	NNEI (**1**)[a]	5-Chloro-NNEI (**3**)[b]		NNEI indazole analog (**4**)[a]	
No.	^{13}C	^{13}C	^{1}H	^{13}C	^{1}H
1	164.0	163.9	–	160.9	–
2'	132.3	132.1	7.83, 1H, brs	–	–
3'	110.9	111.1	–	137..3	–
3'a	125.5	125.6	–	123.0	–
4'	122.7	122.8	7.34, 1H, m, overlapped	122.9	8.92, 1H, d, *J*=8.3 Hz
5'	121.9	122.0	7.32, 1H, m, overlapped	122.9	7.78, 1H, ddd, *J*=7.3, 6.9 Hz
6'	120.1	120.3	8.13, 1H, m, overlapped	126.9	7.91, 1H, td, *J*=7.3, 0.9 Hz
7'	110.6	110.5	7.43, 1H, m	109.4	7.93, 1H, brd, *J*=8.3 Hz
7'a	136.7	136.7	–	141.1	–
1"	47.0	46.8	4.20, 2H, t, *J*=7.2 Hz	49.6	4.93, 2H, t, *J*=7.3 Hz
2"	29.6	29.3	1.92, 2H, q, *J*=7.2 Hz	29.5	2.48, 2H, q, *J*=7.3 Hz
3"	29.0	24.2	1.50, 2H, m	29.0	1.86, 2H, m, overlapped
4"	22.3	32.0	1.80, 2H, q, *J*=6.9 Hz	22.3	1.83, 2H, m, overlapped
5"	13.9	44.6	3.51, 2H, t, *J*=6.9 Hz	14.0	1.37, 3H, t, *J*=7.3 Hz
1"'	132.9	132.9	–	132.4	–
2"'	121.0	121.0	8.08, 1H, d, *J*=7.2Hz	119.4	8.79, 1H, d, *J*=7.3 Hz
3"'	125.9	125.9	7.52, 1H, m, overlapped	126.0	8.00, 1H, t, *J*=7.8 Hz
4"'	125.6	125.6	7.72, 1H, d, *J*=8.3Hz	125.0	8.16, 1H, d, *J*=8.3 Hz
4"'a	134.2	134.2	–	134.2	–
5"'	128.8	128.8	7.89, 1H, dd, *J*=7.6, 1.7 Hz	128.8	8.35, 1H, d, *J*=7.8 Hz
6"'	126.0	126.0	7.50, 1H, td, *J*=6.9, 1.4 Hz, overlapped	125.9	7.98, 1H, ddd, *J*=7.8, 7.3. 0.9 Hz
7"'	126.3	126.4	7.53, 1H, td, *J*=6.9, 1.4 Hz, overlapped	126.2	8.03, 1H, ddd, *J*=8.9, 8.3, 1.4 Hz
8"'	120.8	120.9	7.98, 1H, d, *J*=8.3Hz	120.5	8.52, 1H, d, *J*=8.3 Hz
8"'a	127.4	127.4	–	126.7	–
NH	–	–	8.12, 1H, brs, overlapped	–	9.90, 1H, s

[a] Recorded in $CDCl_3$ at 800MHz (^{1}H) and 200MHz (^{13}C), respectively; data in δ ppm (*J* in Hz).

[b] Recorded in $CDCl_3$ at 600MHz (^{1}H) and 150MHz (^{13}C), respectively; data in δ ppm (*J* in Hz).

Table 2. ^{13}C-NMR Data of compounds **6**, **7**, **9** – **11** and α-PVP [a]

No.	α-PVP [b]	α-PHPP (**6**) [b]	α-POP (**7**) [b]	4-Fluoro-α-PVP (**9**) [b]	α-EAPP (**10**) [c]	*N*-Ethyl-4-methyl-pentedrone (**11**) [c]
1	198.9	198.7	198.7	198.9	196.4	195.8
2	66.8	66.8	66.8	69.3	60.5	60.3
3	32.1	30.1	30.1	31.5	31.8	31.9
4	19.7	25.9	26.2	19.9	17.2	17.2
5	14.2	31.9	29.5	14.3	13.6	13.7
6	–	22.5	31.6	–	–	–
7	–	14.0	22.7	–	–	–
8	–	–	14.1	–	–	–
1'	137.0	136.9	137.0	133.8, d, *J*=2.9 Hz [d]	133.9	131.5
2'/6'	129.2	129.2	129.2	132.1, d, *J*=8.7 Hz [d]	128.7	128.9
3'/5'	129.3	129.3	129.3	115.8, d, *J*=21.7 Hz [d]	129.2	129.8
4'	134.1	134.2	134.2	165.8, d, *J*=252.9 Hz [d]	134.8	145.7
2"/5"	51.2	51.3	51.3	50.6	–	–
3"/4"	24.0	24.0	24.0	23.8	–	–
N-$\underline{C}H_2CH_3$	–	–	–	–	41.2	41.2
N-$CH_2\underline{C}H_3$	–	–	–	–	11.2	11.2
4'-Me	–	–	–	–	–	21.3

[a] Recorded at 600 MHz (^{1}H) and 150 MHz (^{13}C), respectively; data in δ ppm (*J* in Hz). [b] Recorded in pyridine-d_5. [c] Recorded in DMSO-d_6. [d] Observed as double signals by coupling with fluorine.

Table 3. ^{1}H-NMR Data of compounds **6**, **7**, **9** and **11** [a]

No.	α-PHPP (**6**) [b]	α-POP (**7**) [b]	4-Fluoro-α-PVP (**9**) [b]	N-Ethyl-4-methylpente-drone (**11**) [c]
1	–	–	–	–
2	5.02, 1H, brs	5.03, 1H, brs	4.88, 1H, brs	5.20, 1H, brs
3	2.09, 2H, m	2.11, 2H, m	2.05, 2H, m	1.85, 2H, m
4	1.35, 2H, m	1.37, 2H, m	1.36, 2H, m	1.27, 1H, m, overlapped 1.05, 1H, m
5	1.09, 2H, m, overlapped	1.12, 2H, m, overlapped	0.77, 3H, t, *J*=7.4 Hz	0.76, 3H, t, *J*=7.2 Hz
6	1.07, 2H, m, overlapped	1.02, 2H, m, overlapped	–	–
7	0.69, 3H, t, *J*=7.2 Hz	1.08, 2H, m, overlapped	–	–
8	–	0.72, 3H, t, *J*=7.6 Hz	–	–
1'	–	–	–	–
2'/6'	8.32, 2H, t, *J*=7.6 Hz	8.33, 2H, dd, *J*=8.6, 1.4 Hz	8.35, 2H, d, *J*=8.7 Hz	7.97, 2H, d, *J*=7.9 Hz
3'/5'	7.49, 2H, t, *J*=7.6 Hz	7.50, 2H, t, *J*=8.6 Hz	7.06, 2H, d, *J*=8.7 Hz	7.41, 2H, d, *J*=7.9 Hz
4'	7.57, 1H, t, *J*=7.6 Hz	7.58, 1H, tt, *J*=8.6, 1.4 Hz	–	–
2"/5"	3.27, 3.08, each 2H, brs	3.28, 3.10, each 2H, brs	3.23, 3.03, each 2H, brs	–
3"/4"	1.79, 4H, m	1.80, 4H, m	1.77, 4H, m	–
N-$\underline{C}H_2CH_3$	–	–	–	2.99, 2.89, each 1H, m
N-$CH_2\underline{C}H_3$	–	–	–	1.22, 3H, t, *J*=7.2 Hz
4'-Me	–	–	–	2.40, 3H, s

[a] Recorded at 600 MHz (^{1}H) and 150 MHz (^{13}C), respectively; data in δ ppm (*J* in Hz). [b] Recorded in pyridine-d_5. [c] Recorded in DMSO-d_6.

Table 4. NMR Data of 3,4-Dichloromethylphenidate (**14**)[a]

No.	^{13}C	^{1}H
1	170.5	–
2	52.0	4.16, 1H, d, *J*=8.6 Hz
1'	134.7	–
2'	130.9	7.61, 1H, brs
3'	131.6	–
4'	131.2	–
5'	131.1	7.68, 1H, d, *J*=8.3 Hz
6'	129.3	7.30, 1H, d, *J*=8.3 Hz
1"	–	NH 8.90, 1H, brs
2"	56.4	3.83, 1H, brs
3"	25.7	1.41, 1H, m, overlapped
		1.26, 1H, q, *J*=12.7 Hz
4"	21.2	1.67, 1H, t, *J*=12.7 Hz, overlapped
		1.41, 1H, m, overlapped
5"	21.6	1.67, 1H, t, *J*=12.7 Hz, overlapped
		1.54, 1H, q, *J*=12.7 Hz
6"	44.6	3.26, 1H, brd, *J*=12.7 Hz
		2.93, 1H, t, *J*=12.7 Hz
1-OMe	53.0	3.67, 3H, s

[a] Recorded in DMSO-d_6 at 600 MHz (^{1}H) and 150 MHz (^{13}C), respectively; data in δ ppm (*J* in Hz).

Table 5. NMR data for compound **16** and known related compounds

No.	Compound **16** [a,b]		2-Acetyl-1-methyl-1*H*-benzimidazole [c]	JWH-018 indazole analog [a]
	^{13}C	^{1}H	^{13}C	^{13}C
1	188.9	–	193.1	191.6
2'	147.3	–	146.5	–
3'	–	–	–	142.6
3'a	141.8	–	141.5	124.3
4'	122.3	7.87, 1H, d, *J*=8.3 Hz	121.2	123.1
5'	123.8	7.35, 1H, ddd, *J*=8.3, 7.2, 1.0 Hz	124.2	123.7
6'	125.9	7.46, 1H, ddd, *J*=8.3, 7.2, 1.0 Hz	126.3	126.9
7'	110.6	7.51, 1H, m, overlapped	111.3	109.5
7'a	136.1	–	137.3	140.6
1"	45.4	4.70, 2H, t, *J*=7.6 Hz	31.8 (NMe)	49.8
2"	30.1	2.05, 2H, q, *J*=7.9 Hz	27.1 (COMe)	29.4
3"	22.8, d, *J*=4.3 Hz [c]	1.59, 2H, m	–	28.8
4"	30.0, d, *J*=20.2Hz [c]	1.80 and 1.76, each 1H, m, overlapped	–	22.2
5"	83.7, d, *J*=164.7 Hz [c]	4.48 and 4.41, each 1H, t, *J*=5.8 Hz	–	13.9
1"'	134.4	–	–	136.3
2"'	131.9	8.03, 1H, dd, *J*=7.2, 1.0 Hz	–	129.3
3"'	124.3	7.56, 1H, m, overlapped	–	124.3
4"'	133.3	8.05, 1H, d, *J*=8.3 Hz	–	131.4
4"'a	134.0	–	–	133.8
5"'	128.6	7.91, 1H, d, *J*=7.9 Hz	–	128.3
6"'	126.5	7.53, 1H, m, overlapped	–	126.1
7"'	127.9	7.57, 1H, m, overlapped	–	127.1
8"'	125.3	8.46, 1H, d, *J*=8.3 Hz	–	125.8
8"'a	131.2	–	–	131.1

[a] Recorded in $CDCl_3$ at 600MHz (^{1}H) and 150MHz (^{13}C), respectively; data in δ ppm (*J* in Hz)

[b] Observed as double signals by coupling with fluorine

[c] [Ref] Lopyrev VA, et al., Org. Magn. Reson. (1982) 20:212–216., recorded in CD_3OD