Isoxanthohumol (1): white amorphous powder, $[\alpha]_D$ +0.0° (*c* 0.2, MeOH); UV λ_{max} (MeOH) (log ε) 286 (4.34), 397 (3.56); IR (KBr) ν_{max}: 3393, 1597, 1519, 1450, 1415, 1349, 1274, 1148, 1092, 834 cm^{-1}; ^1H NMR (CD_3OD, 500 MHz) δ 7.30 (2H, d, *J* = 8.5 Hz, H-2′, 6′), 6.82 (2H, d, *J* = 8.5 Hz, H-3′, 5′), 6.12 (1H, s, 1H), 5.26 (1H, dd, *J* = 12.8, 2.8 Hz, H-2), 5.13 (1H, brt, *J* = 7.2 Hz, H-2′′), 3.79 (3H, s, 5-OC*H*$_3$), 3.20 (2H, m, H-1′′), 2.96 (1H, dd, *J* = 16.8, 13.0 Hz, H-3a), 2.66 (1H, dd, *J* = 16.8, 3.0 Hz, H-3b), 1.61 (3H, s, H-5′′), 1.55 (3H, s, H-4′′); ^{13}C NMR (CD_3OD, 125 MHz) δ 193.2 (C-4), 164.5 (C-8a) 164.0 (C-7), 162.0 (C-5), 158.9 (C-4′), 131.9 (C-3′′), 131.7 (C-1′), 129.0 (C-2′,6′), 124.0 (C-2′′), 116.0 (C-3′,5′), 110.1 (C-8), 105.9 (C-4a), 93.6 (C-6), 80.1 (C-2), 56.1 (5-O*C*H$_3$), 46.3 (C-3), 26.1 (C-5′′), 22.8 (C-1′′), 18.1 (C-4′′); EIMS 70eV *m/z* 354 $[M]^+$, 339, 311, 299, 234, 219, 191, 179, 120 (calcd. for $C_{21}H_{22}O_5$).

Figure S1. ^1H NMR spectrum of **1**

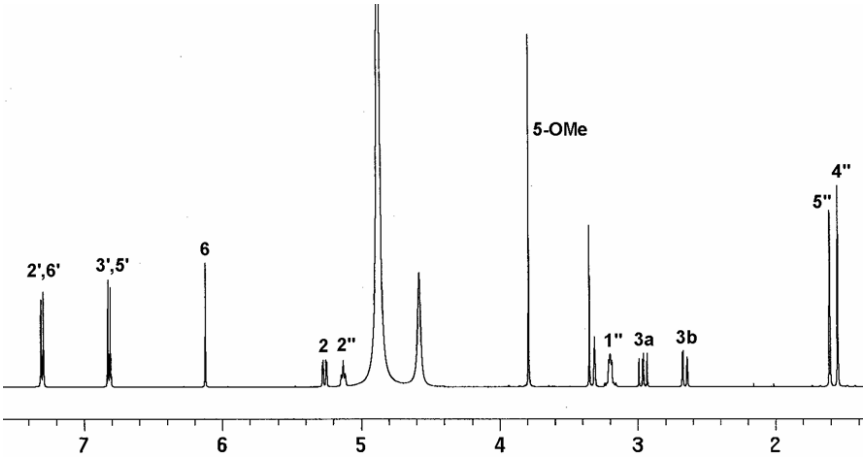
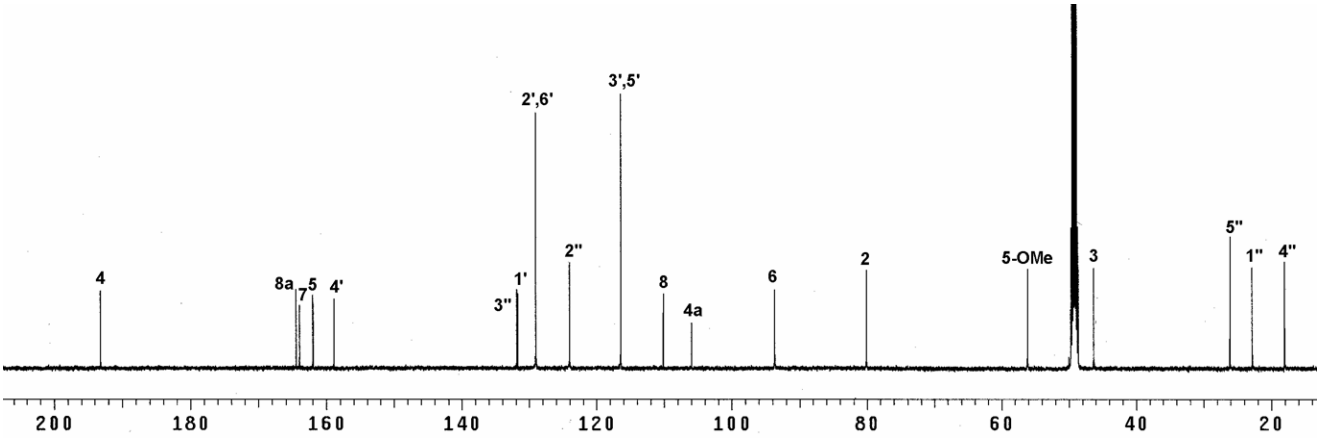
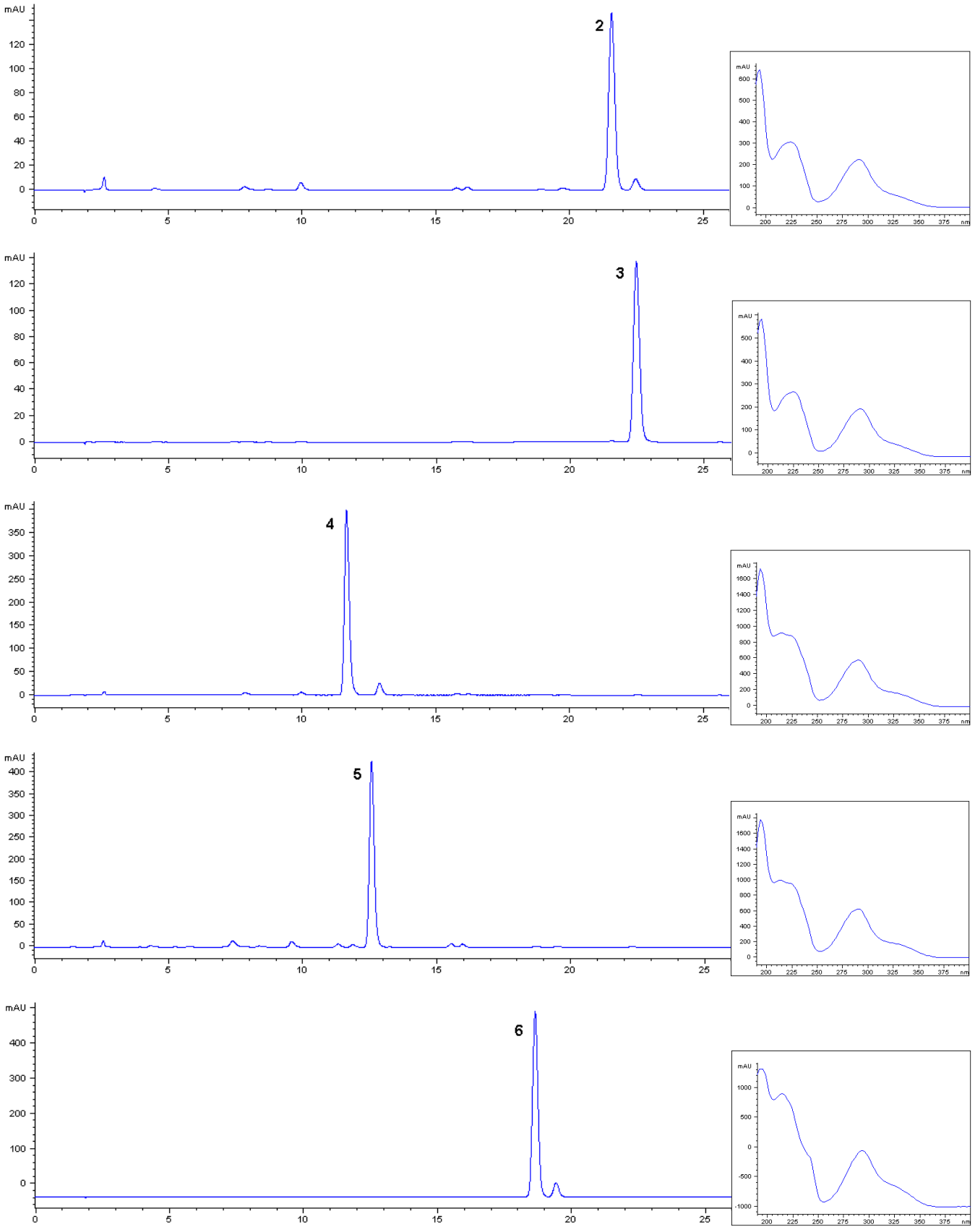
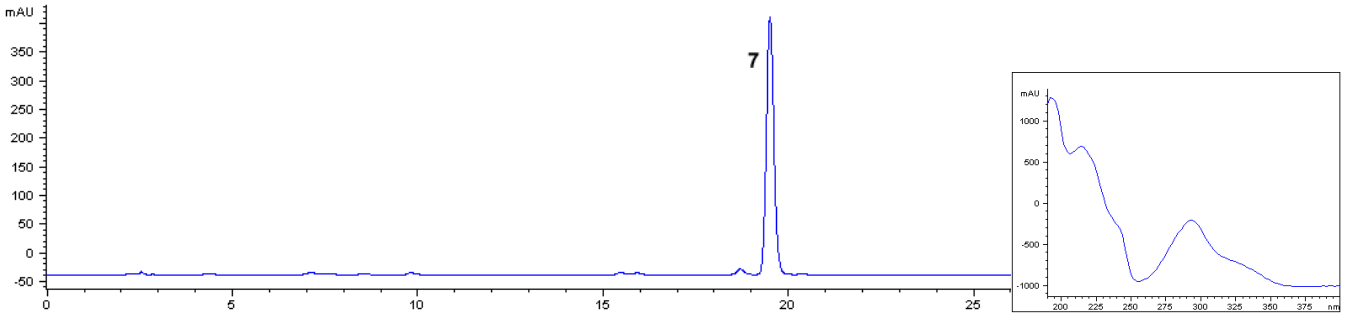


Figure S2. ^{13}C NMR spectrum of **1**



Scheme S1. HPLC profiles of oxygenated metabolites (**2-7**) of isoxanthohumol (**1**)





HPLC was performed on a Hewlett Packard 1100 series composed of a degasser, a binary mixing pump, a column oven and a DAD detector using Waters SunFire™ (4.6 × 150 mm, 5 µm) with acetonitrile (solvent A) and water containing 0.1% formic acid (solvent B) at 1 mL/min under the wavelength 280 nm.

Figure S3. ^{1}H NMR spectrum of the new compound **2**

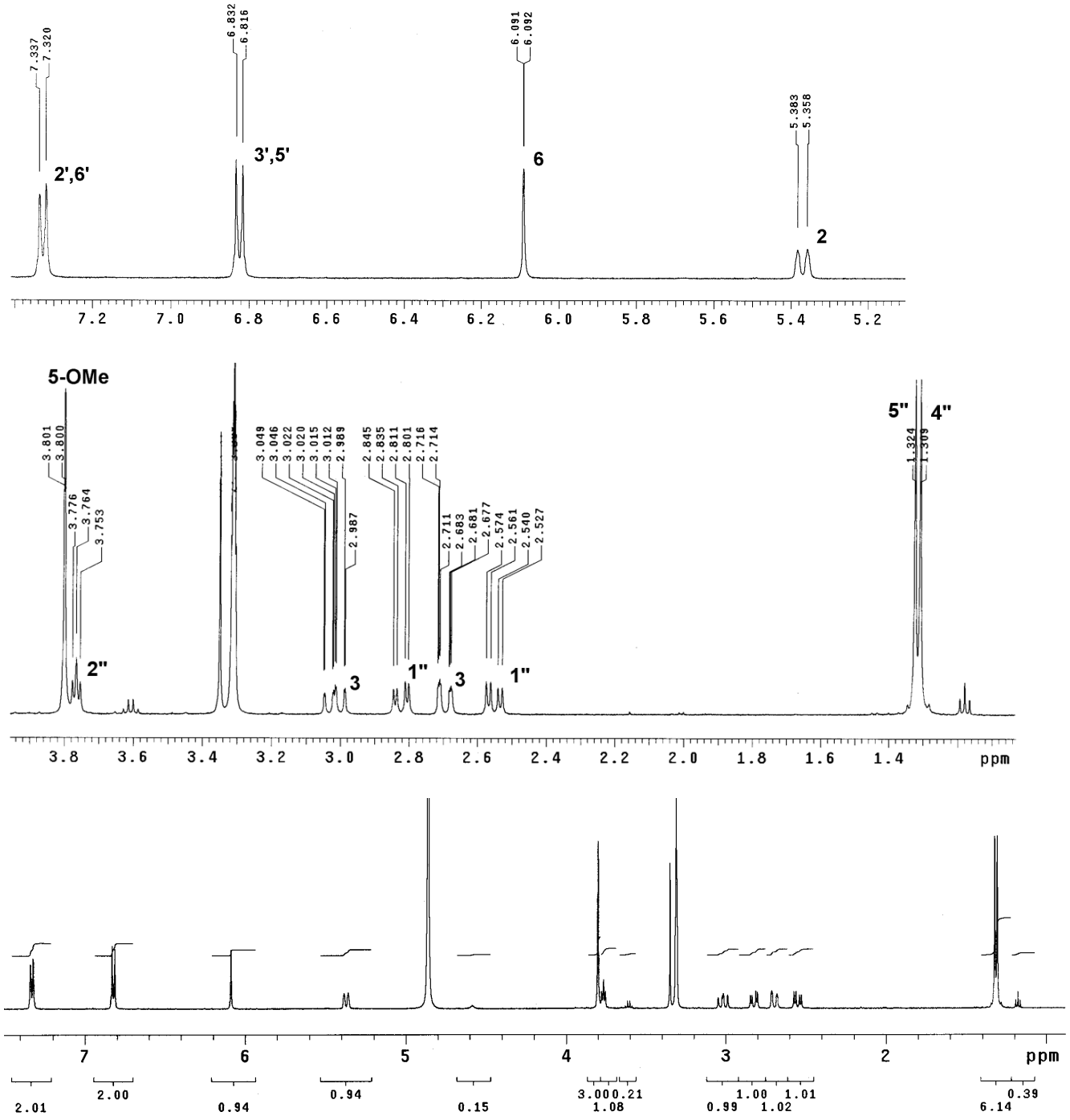


Figure S4. ^{13}C NMR spectrum of **2**

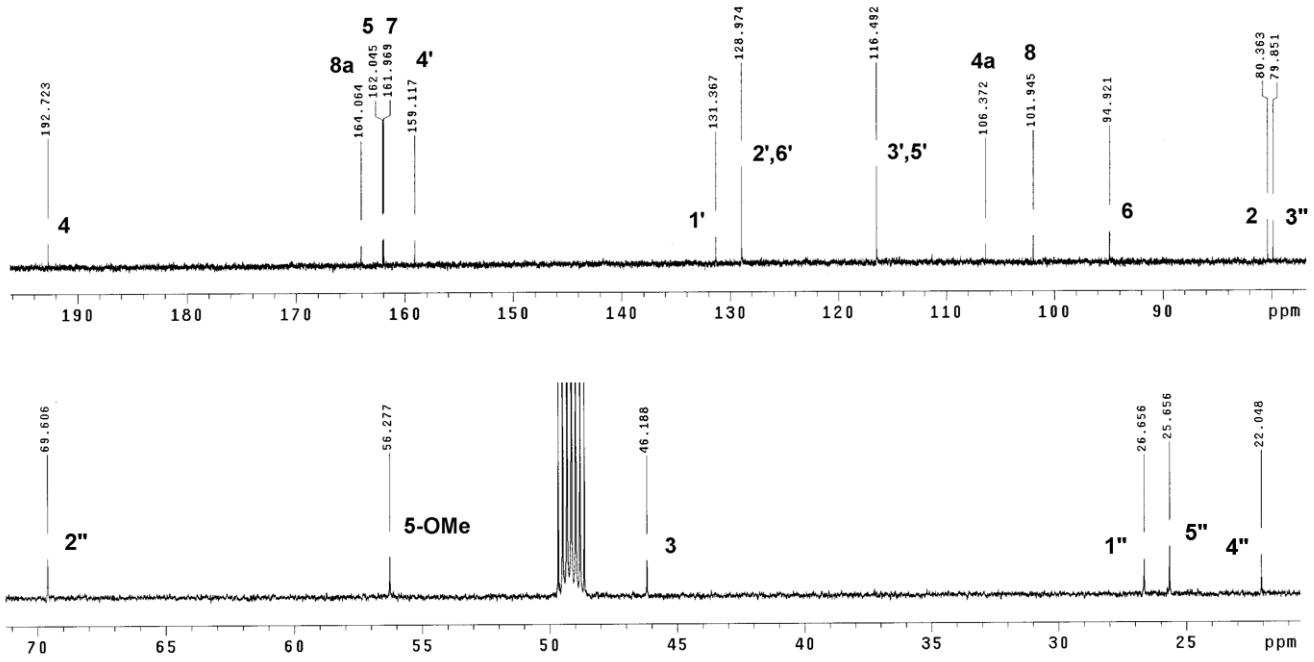


Figure S5. ^{1}H NMR spectrum of the new compound **3**

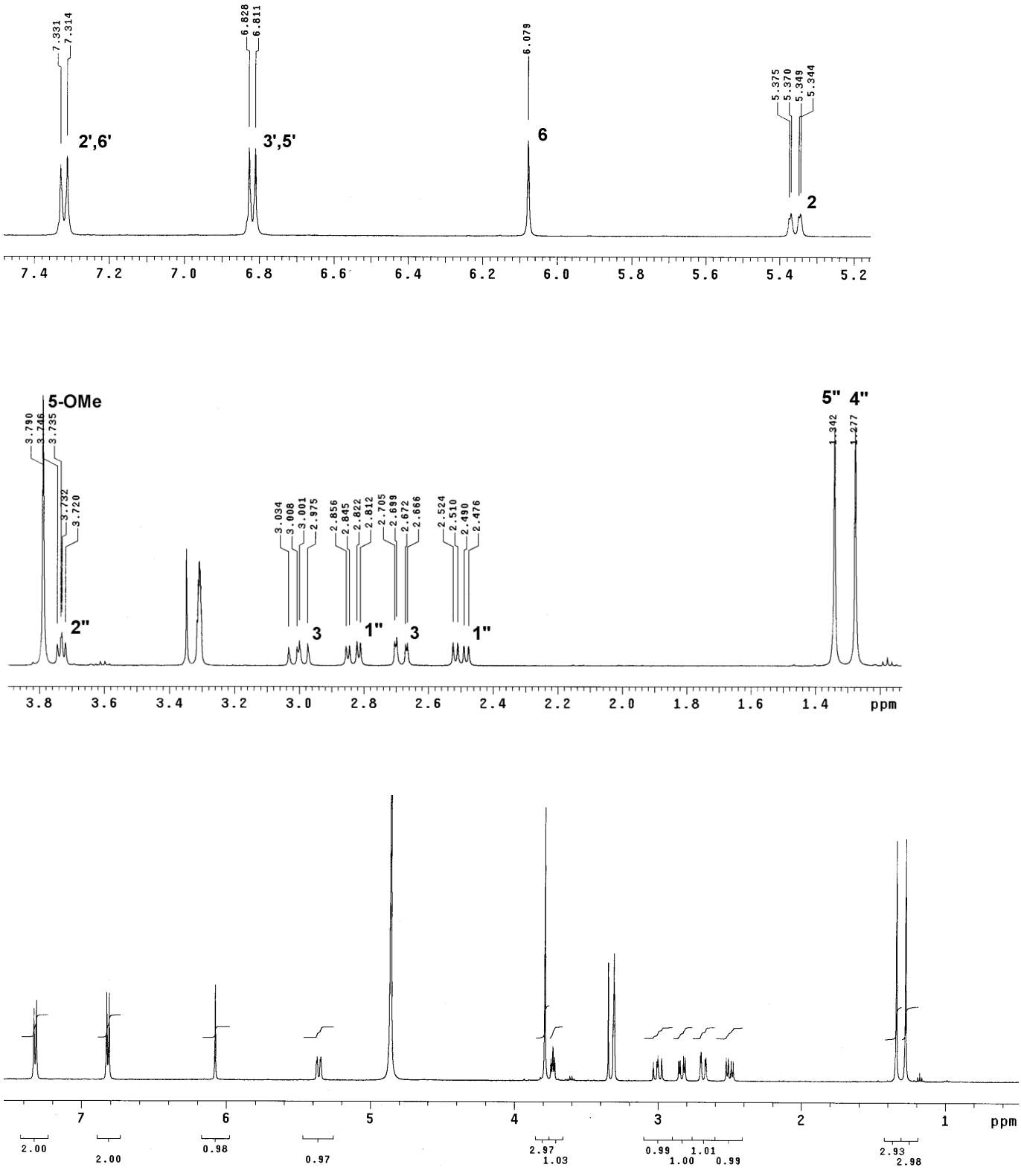


Figure S6. ^{13}C NMR spectrum of the new compound **3**

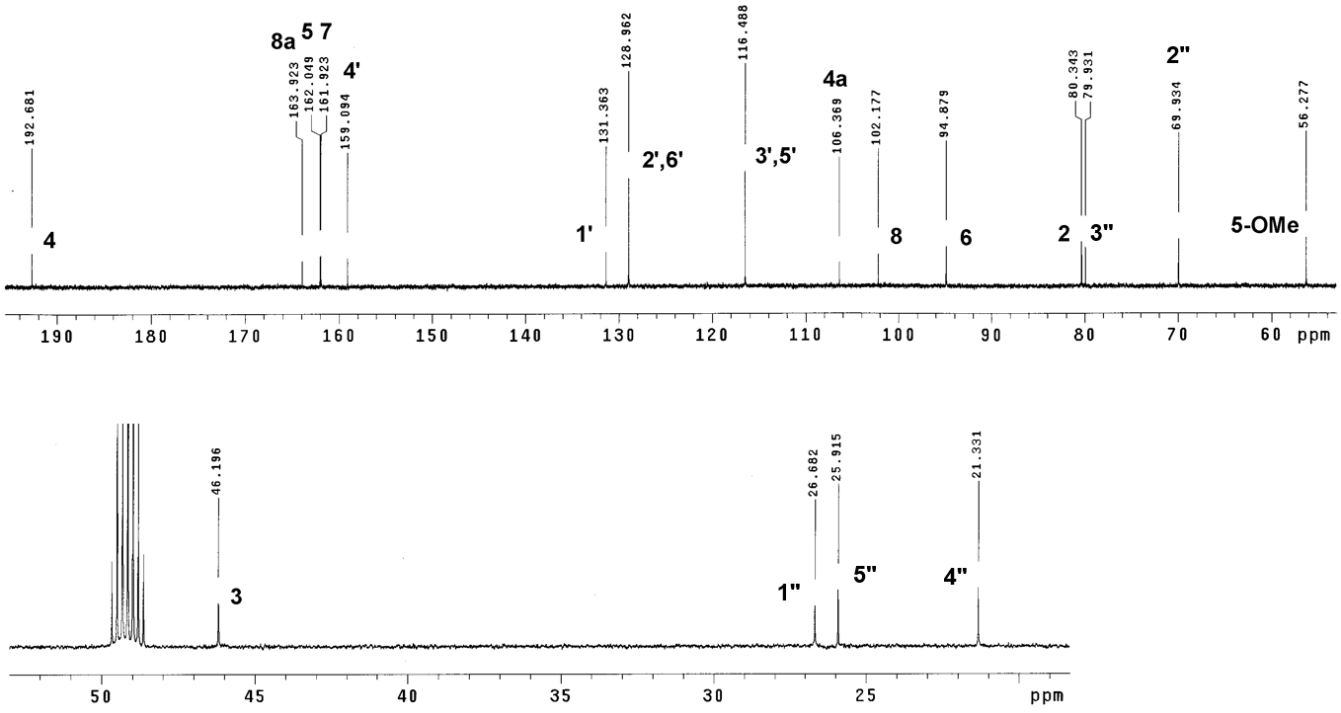


Figure S7. HSQC NMR spectrum of a mixture of **2** and **3**

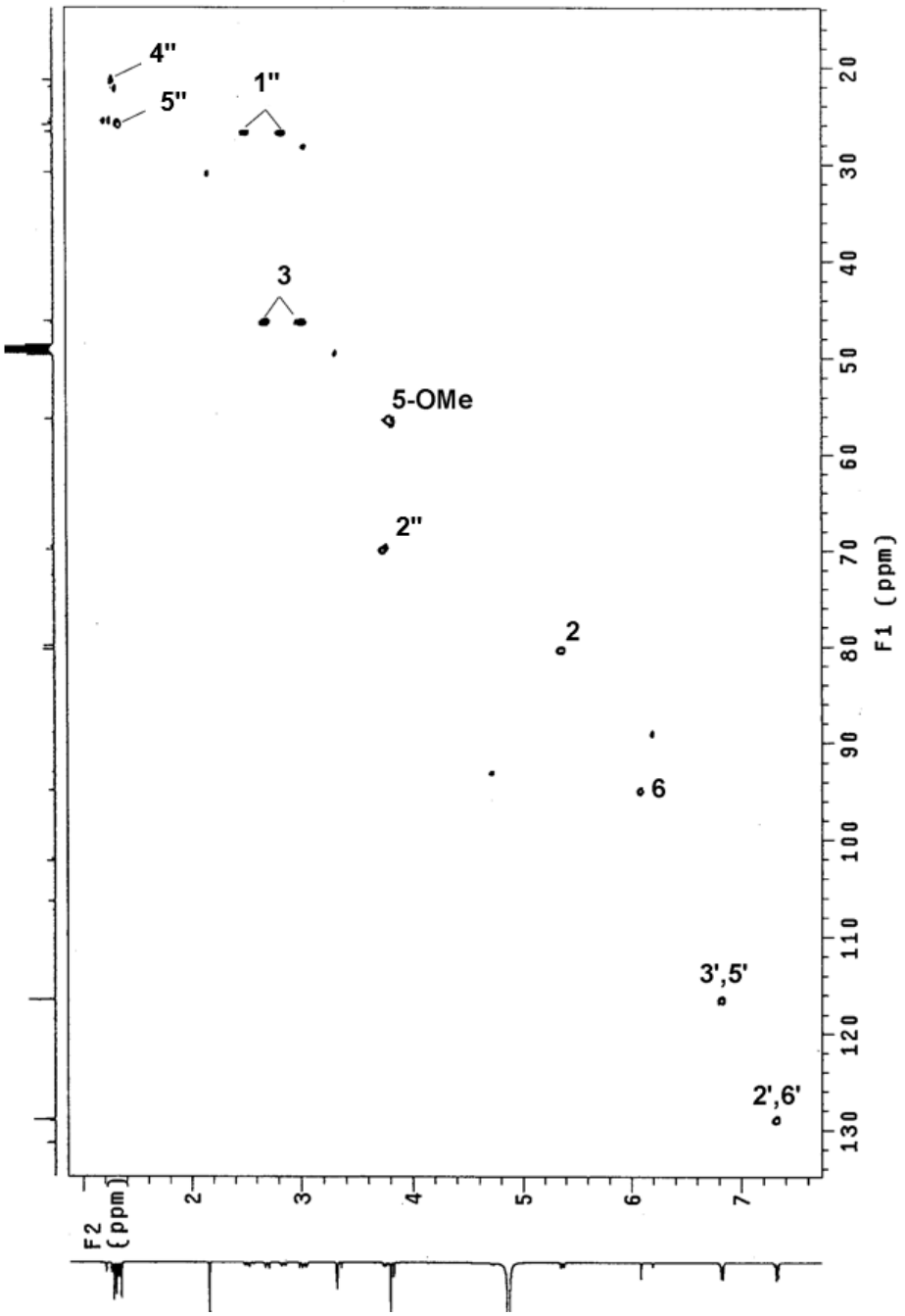


Figure S8. HMBC NMR Spectrum of a mixture of **2** and **3**

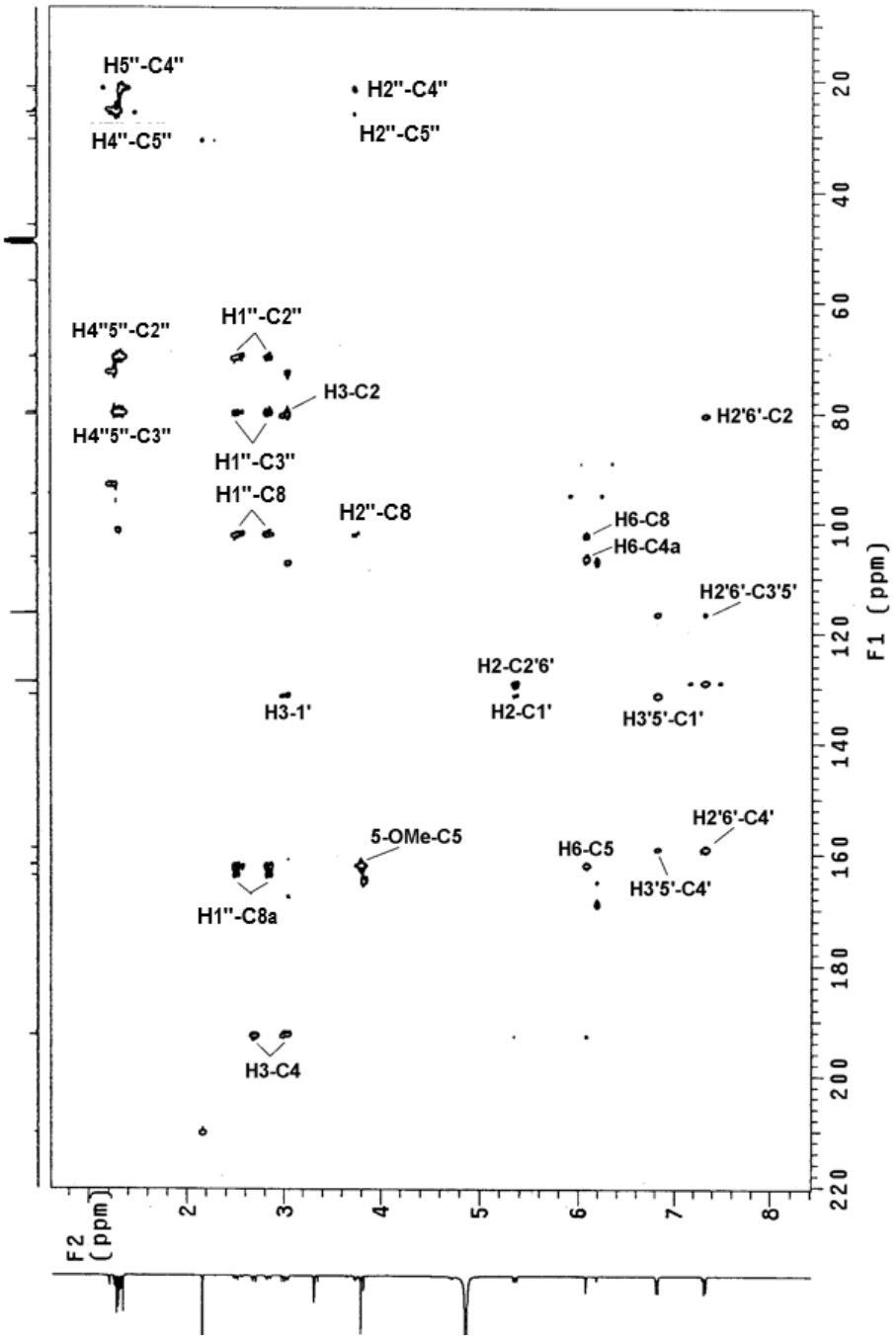


Figure S9. ^{1}H NMR spectrum of the new compound **4**

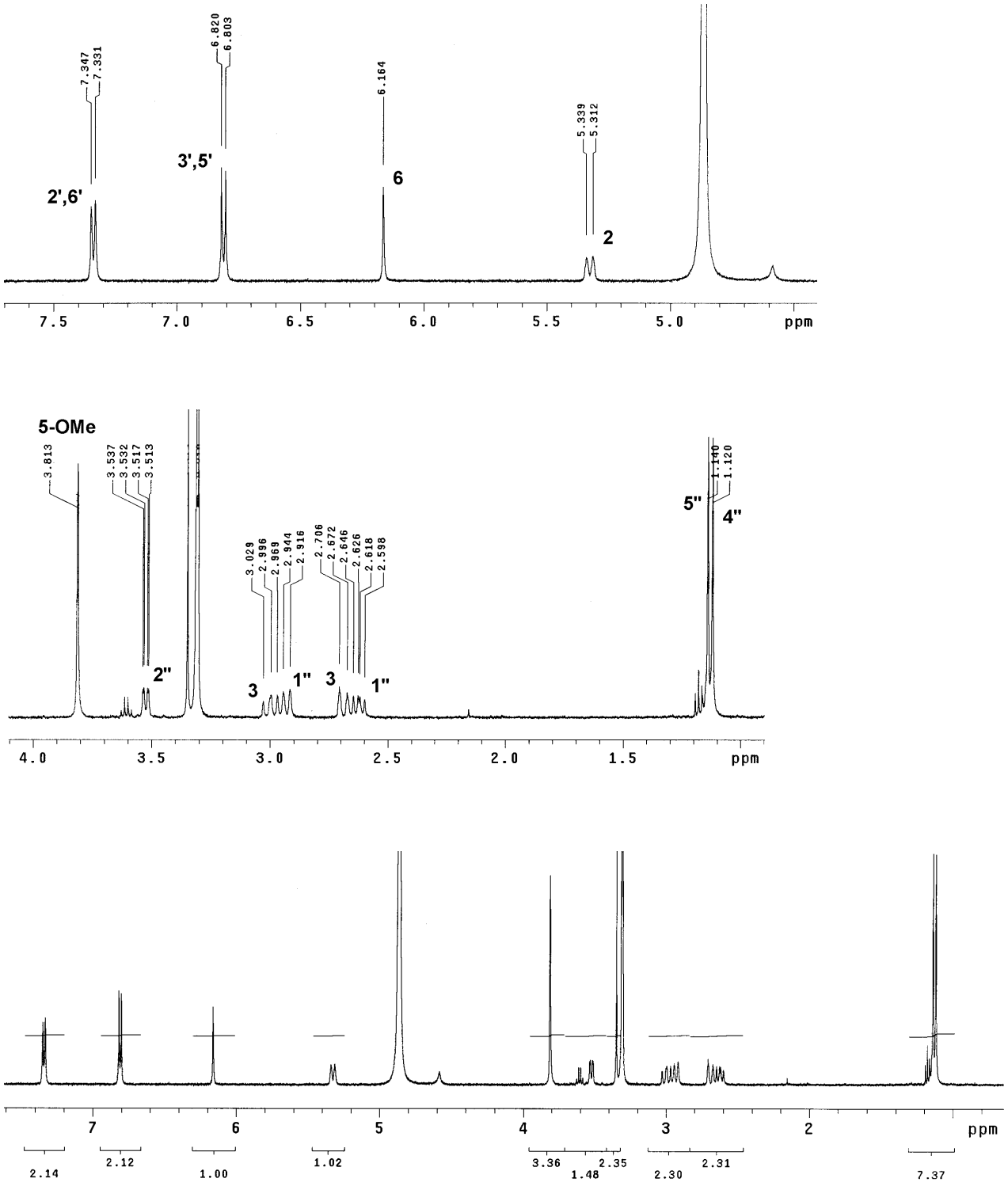


Figure S10. ^{13}C NMR spectrum of the new compound **4**

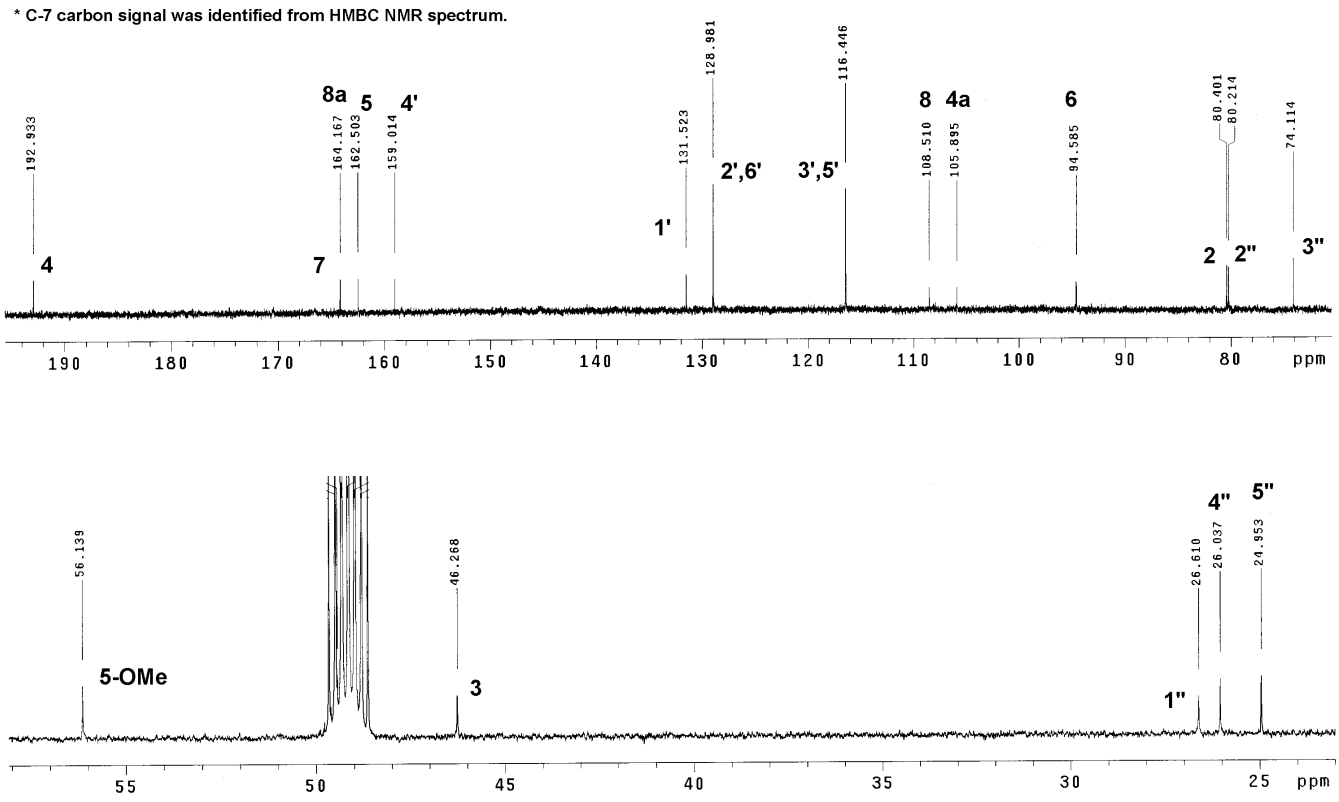


Figure S11. ^{1}H NMR spectrum of the new compound **5**

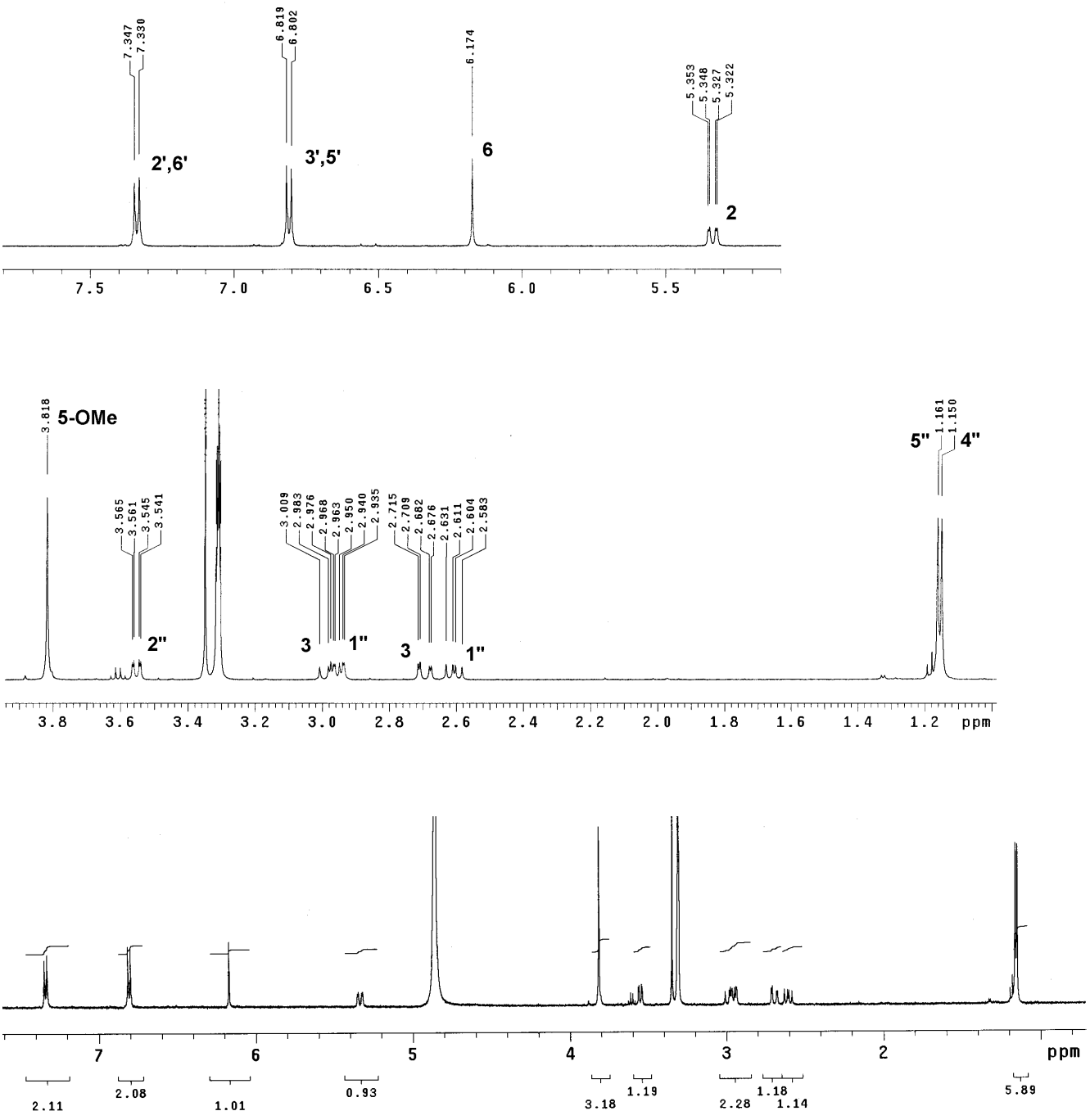


Figure S12. ^{13}C NMR spectrum of the new compound **5**

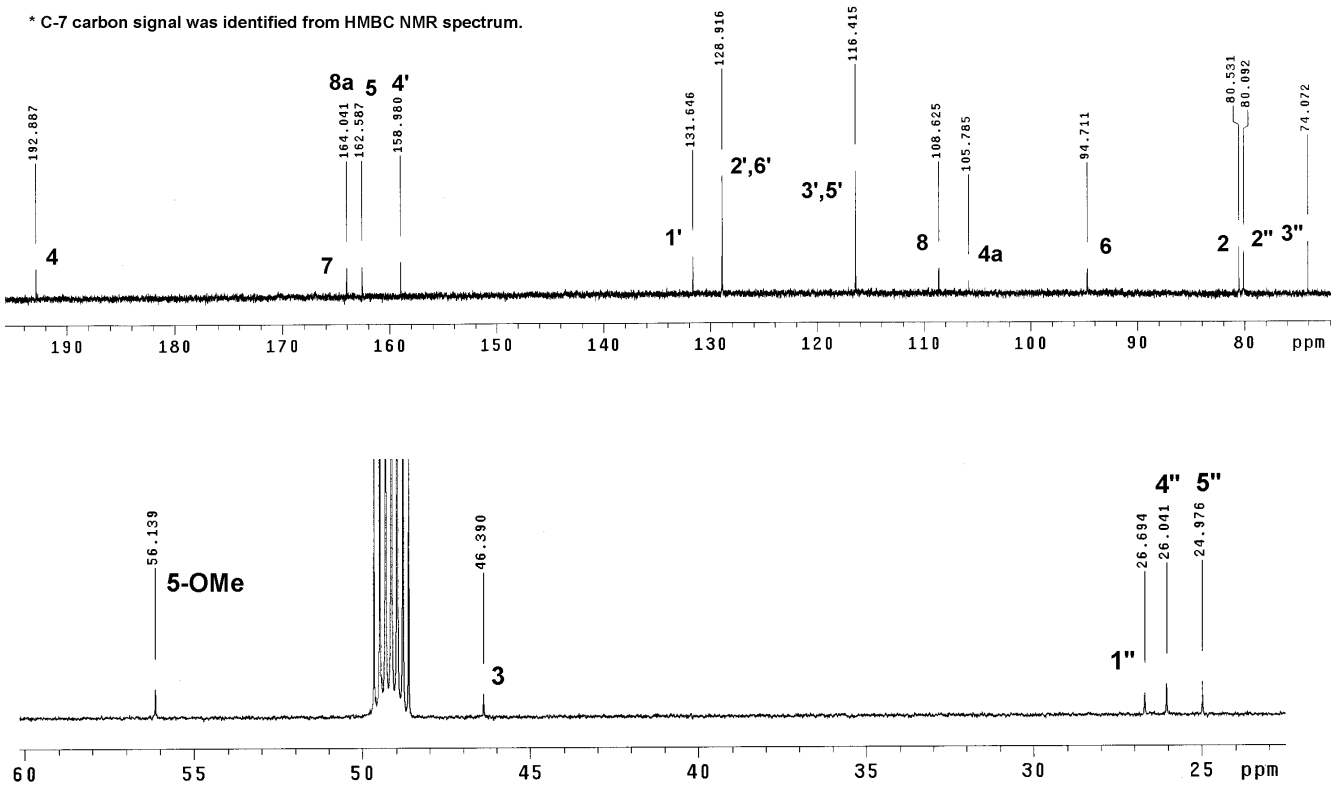


Figure S13. HSQC NMR spectrum of a mixture of **4** and **5**

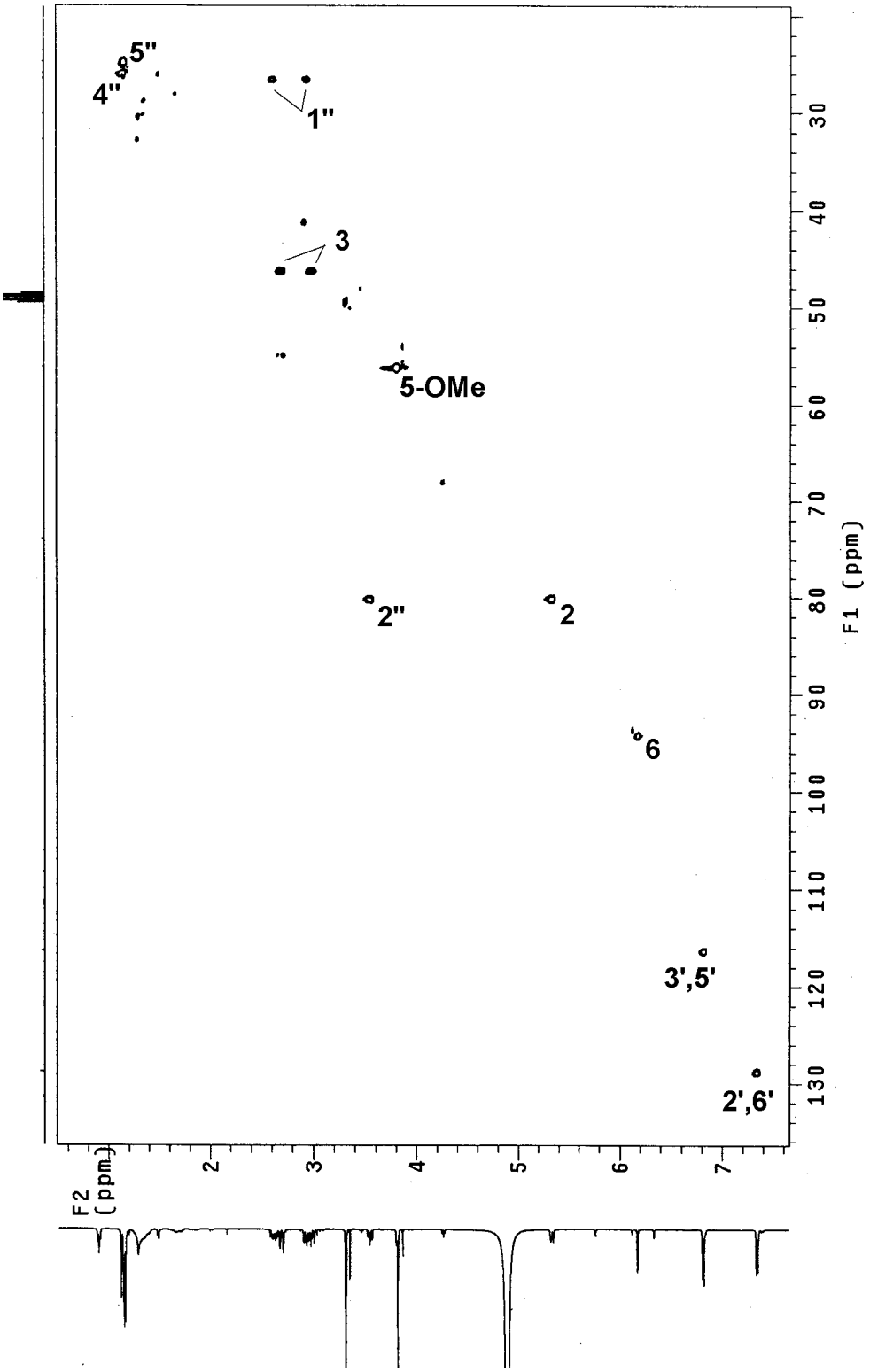


Figure S14. HMBC NMR spectrum of a mixture **4** and **5**

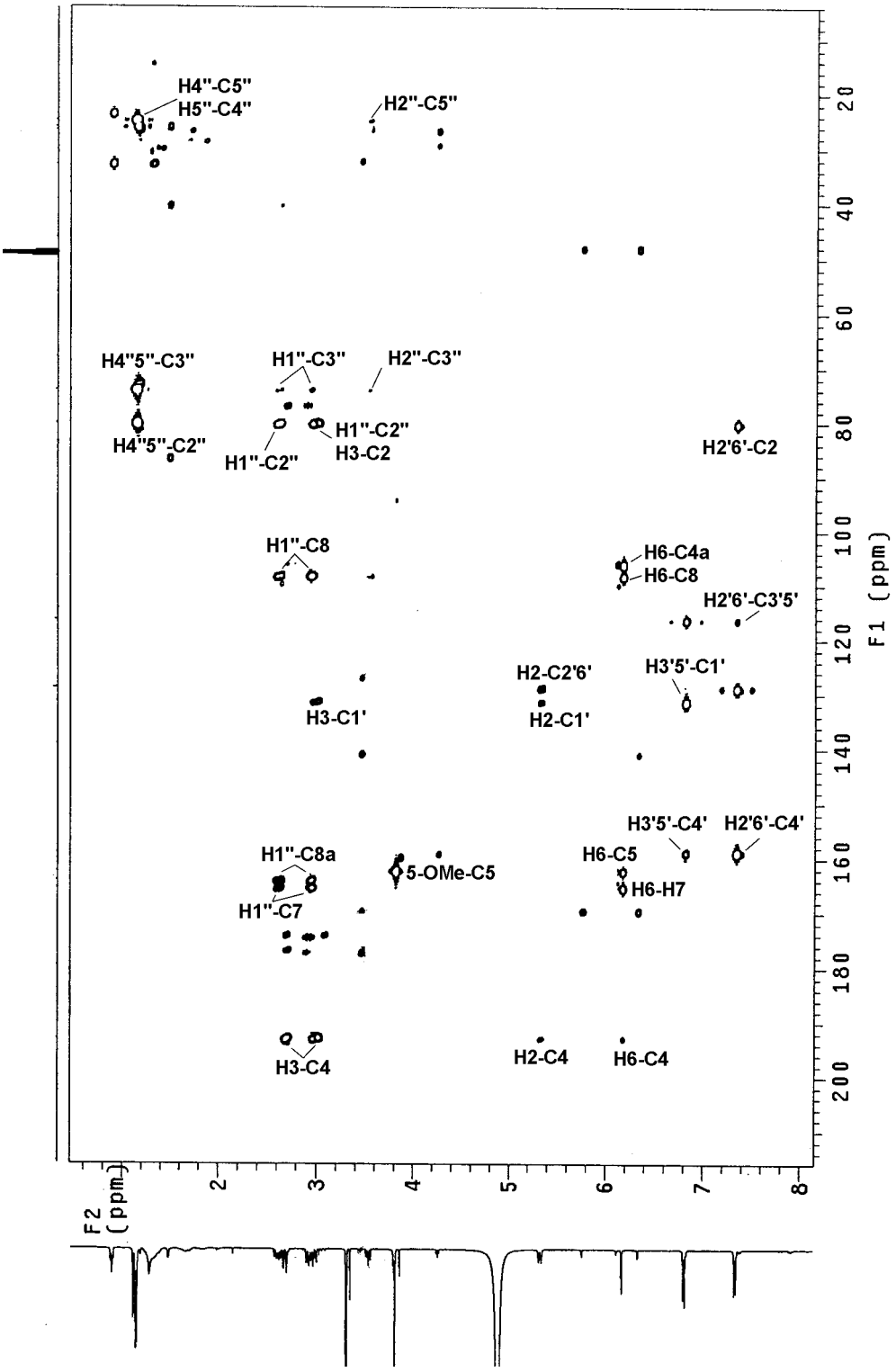


Figure S15. ^{1}H NMR spectrum of **6**

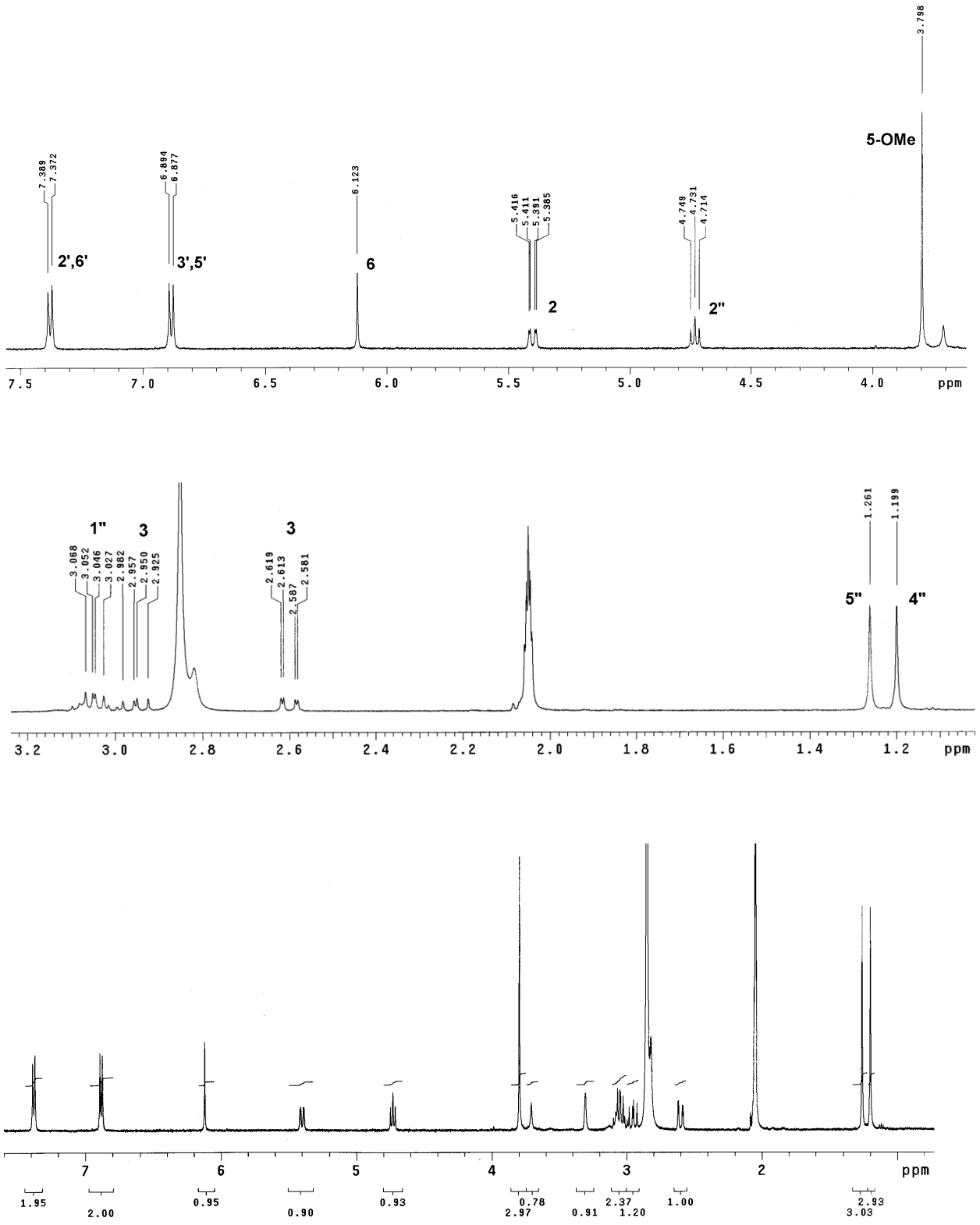


Figure S16. ^{13}C NMR spectrum of **6**

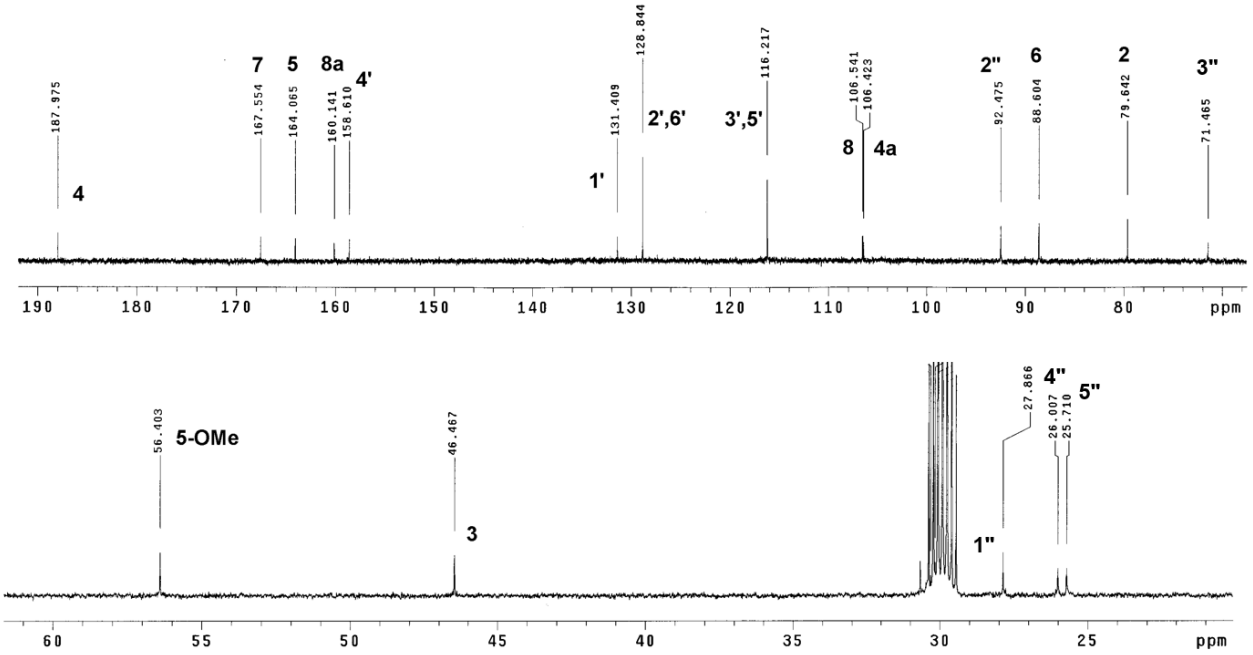


Figure S17. ^{1}H NMR spectrum of **7**

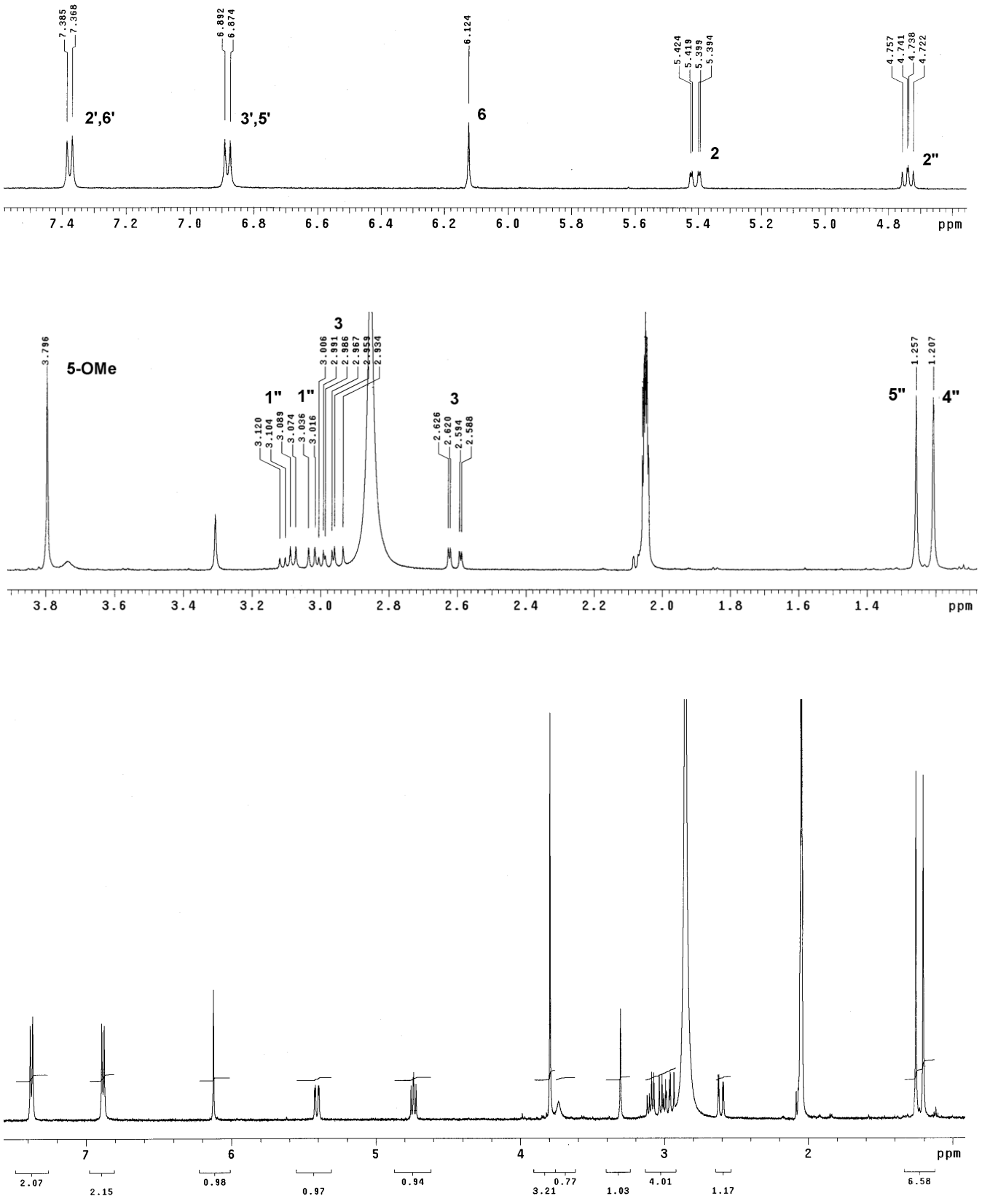


Figure S18. ^{13}C NMR spectrum of **7**

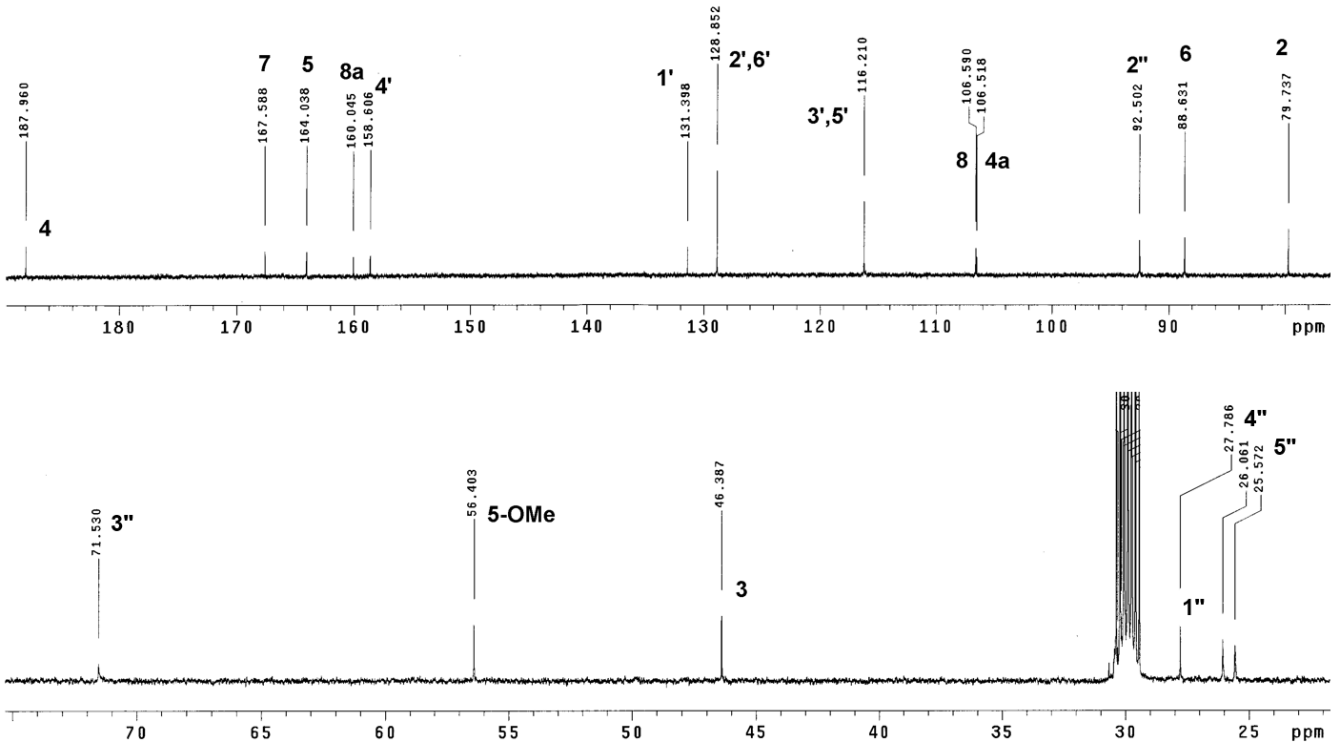
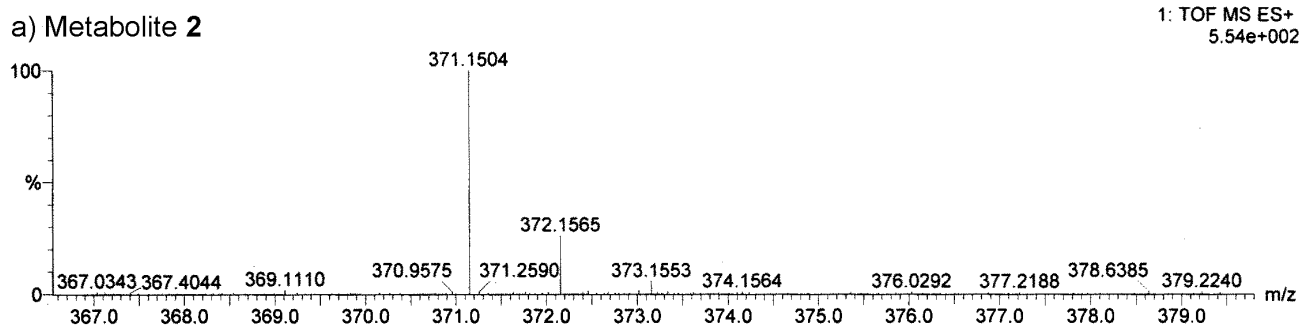


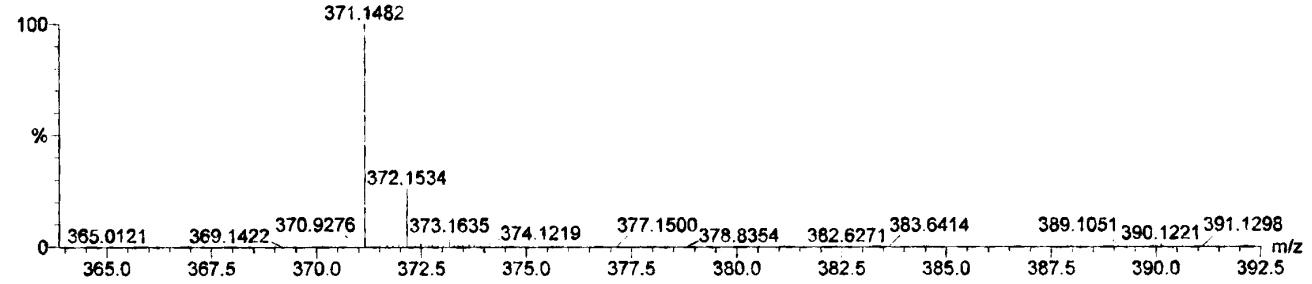
Figure S19. High resolution ESIMS data of metabolites **2**–**7**

a) Metabolite **2**



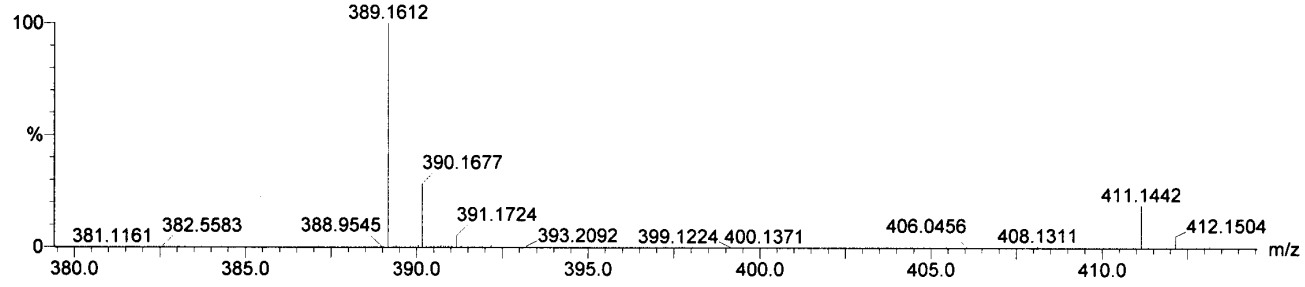
Minimum:				-1.5			
Maximum:		3.0	10.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
371.1504	371.1495	0.9	2.4	10.5	92.8	0.0	C21 H23 O6

b) Metabolite **3**



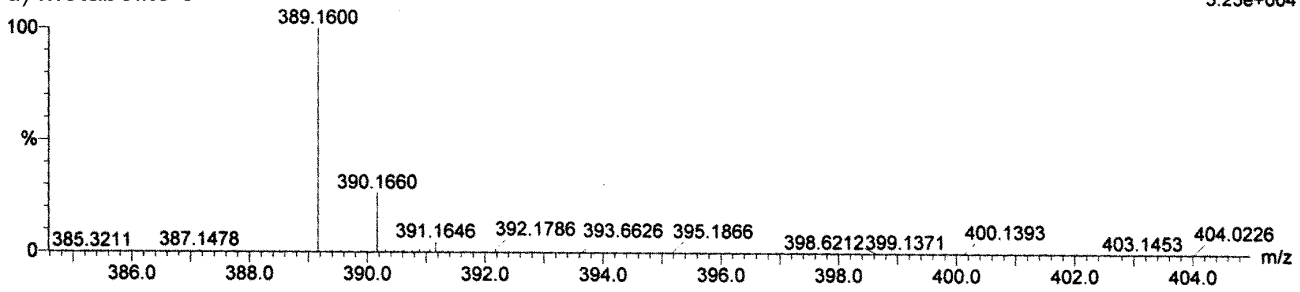
Minimum:				-1.5			
Maximum:		3.0	10.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
371.1482	371.1495	-1.3	-3.5	10.5	195.2	0.0	C21 H23 O6

c) Metabolite **4**



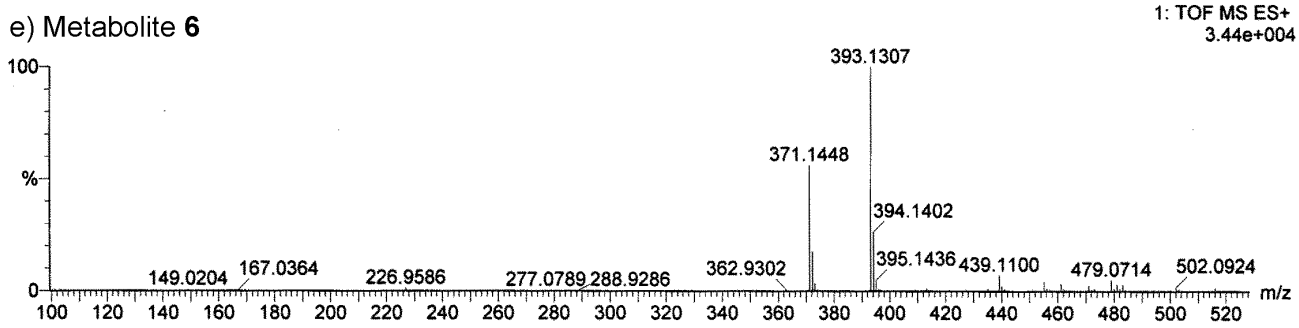
Minimum:				-1.5			
Maximum:		3.0	10.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
389.1612	389.1600	1.2	3.1	9.5	341.7	0.0	C21 H25 O7

d) Metabolite **5**



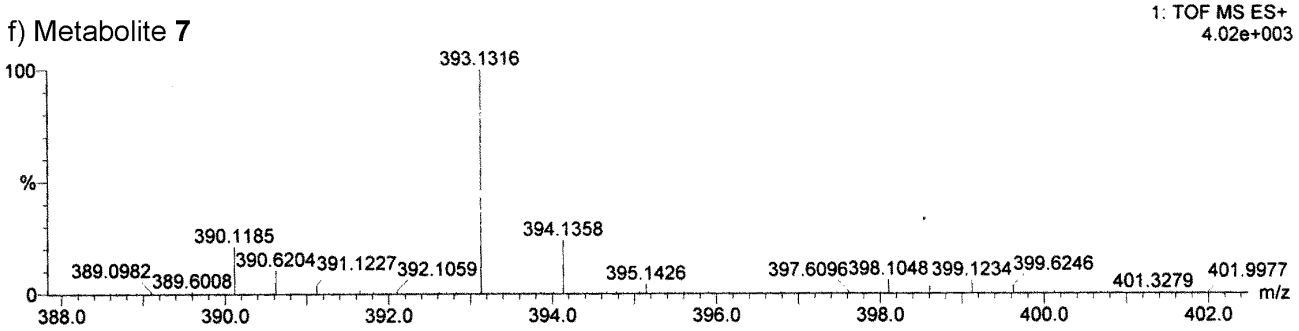
Minimum:				-1.5			
Maximum:		3.0	10.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
389.1600	389.1600	0.0	0.0	9.5	247.2	0.0	C21 H25 O7

e) Metabolite **6**



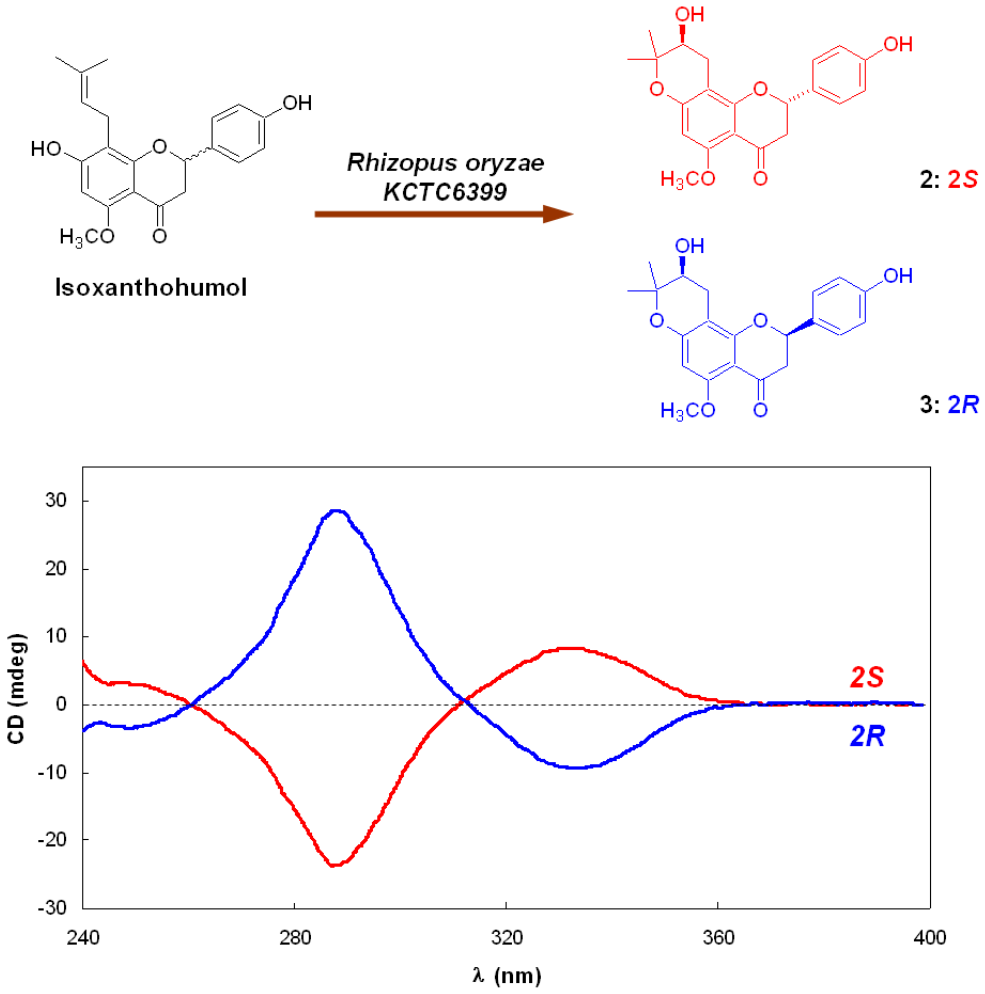
Minimum:				-1.5			
Maximum:		5.0	10.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
393.1307	393.1314	-0.7	-1.8	10.5	344.2	0.0	C21 H22 O6 Na

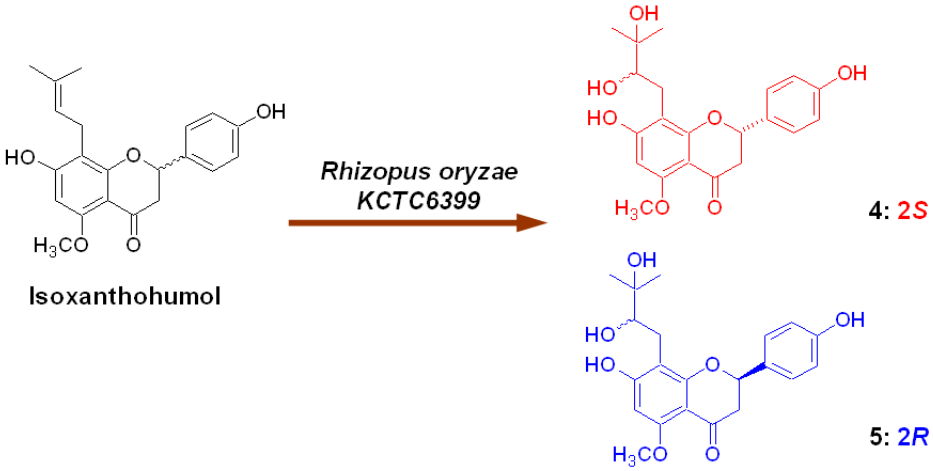
f) Metabolite **7**

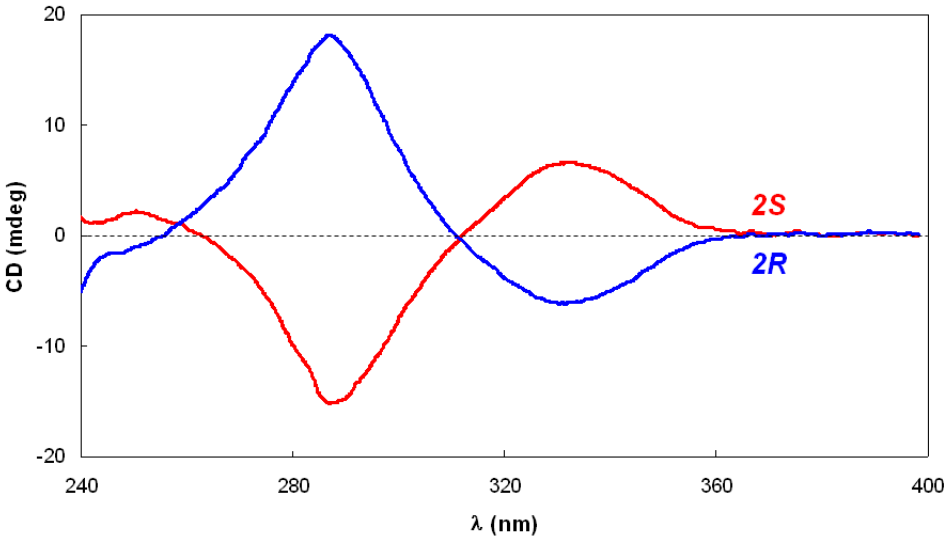


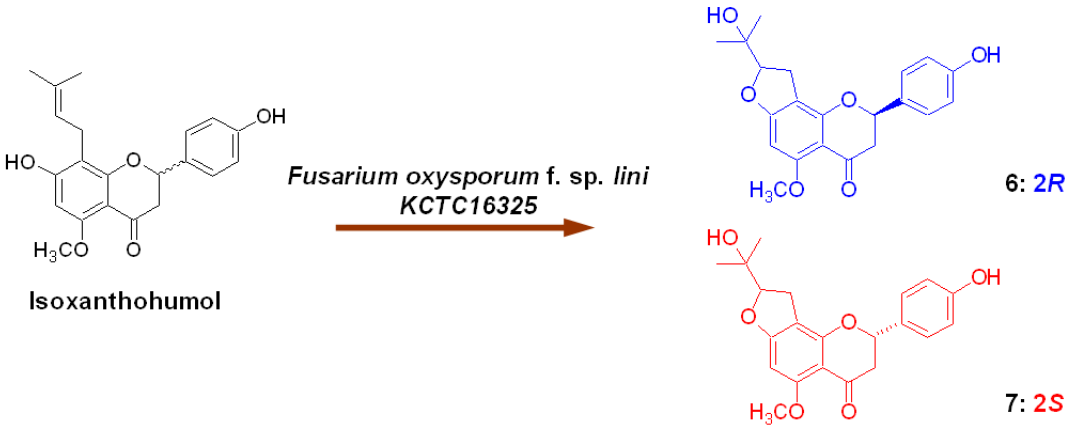
Minimum:				-1.5			
Maximum:		10.0	10.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
393.1316	393.1314	0.2	0.5	10.5	195.6	0.0	C21 H22 O6 Na

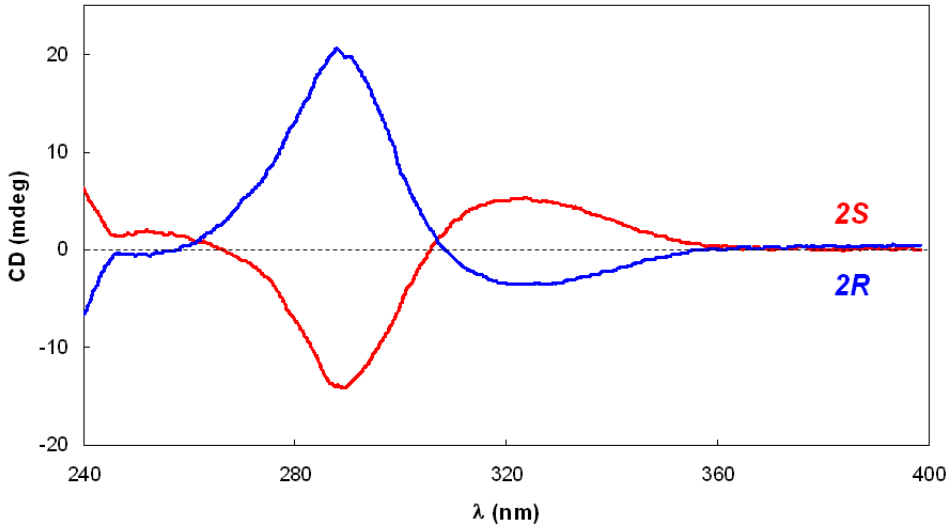
Figure S20. Circular dichroism (CD) profiles of metabolites **2**–**7**




Isoxanthohumol
Rhizopus oryzae
KCTC6399
4: 2S
5: 2R


CD (mdeg)
λ (nm)
2S
2R


HO
OH
O
H3CO
O
Isoxanthohumol
Fusarium oxysporum f. sp. lini
KCTC16325
HO
OH
O
O
H3CO
O
6: 2R
HO
OH
O
O
H3CO
O
7: 2S


20
10
0
-10
-20
CD (mdeg)
240
280
320
360
400
λ (nm)
2S
2R