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Supporting Information

Implementing one-shot multiple-FID acquisition into homonuclear and heteronuclear NMR experiments

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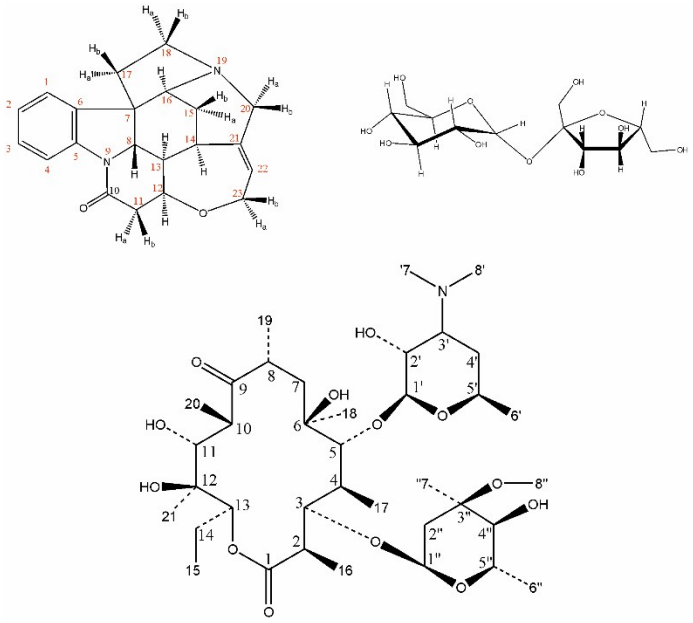
Experimental Section

All experimental NMR spectra were recorded on a Bruker AVANCE spectrometer equipped with a 5mm TCI $^{1}H/^{13}C/^{15}N$ cryoprobe operating at 500.13 MHz for ^{1}H at 298K. Our starting point to record the reported MFA-COSY and MFA-HMBC experiments was those of the conventional gradient-selected magnitude-mode COSY (BRUKER pulse program: cosygpqf), HMQC (BRUKER pulse program: hmqcgpqf) and HMBC (BRUKER pulse program: hmbcgpqf) experiments, respectively. The samples used in this work were: 20 mg of sucrose dissolved in 0.6 ml of D_2O, 25 mg of erythromycin A dissolved in $CDCl_3$, and 20 mg of strychnine dissolved in $CDCl_3$.



Basic conditions for the MFA-COSY/RELAY-3 experiment (Figure 1A): A pre-scan delay of 1s and 2 scans for each one of the 128 t_1 increment was used (1024 points of time domain in the acquisition F2 dimension). A basic two-step phase cycling was applied: Φ_1=x, -x; $\Phi_{rec.}$= x, -x. The acquisition time Δ' was of 93 ms, the overall duration of the gradient (1 ms) and its recovery delay (δ) was 1.2 ms and the gradient ratio G1:G2:G3:G4 used was 50:30:40:17. The equivalent MFA-COSY/RELAY and MFA-COSY/RELAY-2 (Figure S2A) were acquired exactly under the same conditions. MFA-COSY/TOCSY experiment (Figure 2A) was also recorded under the same conditions, using a z-filtered DIPSI pulse trains of 60 ms and a gradient ratio G1:G2:G3 of 10:33:20. The heteronuclear MFA-HMBC/HMBC-TOCSY (Figure 3A) and MFA-HMBC/HMBC-COSY (Figure S4A) experiments were recorded under the same conditions described previously, using a Δ delay adjusted to 62.5 ms (8 Hz

optimization). The gradient ratio G1:G2:G3 in MFA-HMBC/HMBC-TOCSY was 30:50:17 and in MFA-HMBC/HMBC-COSY of 30:50:40. Experimental times are shown in Table S1.

Basic conditions for the MFA-MBOB-COSY experiment (Figure S5): A pre-scan delay of 1s and 8 scans for each t_1 increment was used (TD2=1K, TD1=128), with an overall experimental time of 2 h. The Δ and Δ' delay were adjusted to 62.5 ms (8 Hz) and 85ms, respectively. Gradient ratio used was 50:30:40:15. *J*min and *J*max for ^1J filtering were adjusted to 120 Hz and 170 Hz respectively.

For all homonuclear and heteronuclear NMR experiments: Because each FID is allocated in different memory blocks, they were individually processed in the usual way using a zero-filling in both F1 and F2 dimensions, up 2048 and 1024 data matrix respectively, and applying a non-shifted sine-bell window function in both dimensions prior to Fourier transformation.

Pattern Experiment	Experimental time	MFA Experiment	Experimental Time	Comparative Incremental (in %)
COSY	4m 54s	MFA-COSY/RELAY	5m 11s	6%
		MFA-COSY/RELAY-2	5m 34s	14%
		MFA-COSY/RELAY-3	5m 57s	21%
		MFA-COSY/TOCSY	5m 31s	13%
HMQC	4m 50s	MFA-HMQC/HMQC-COSY	5m 14s	8%
		MFA-HMQC/HMQC-RELAY-3	6m 3s	25%
		MFA-HMQC/HMQC-TOCSY	5m 31s	14%
HMBC	5m 11s	MFA-HMBC/HMBC-COSY	5m 37s	8%
		MFA-HMBC/HMBC-TOCSY	5m 53s	14%

Table S1. Comparison of experimental measurement times between different pattern and MFA experiments. Experimental parameters: pre-scan delay of 1 s; 2 scans per t_1 increment; 128 t_1 increments of 1024 points each one; sw(^{1}H)= 10 ppm, sw(^{13}C)=160 ppm; FID acquisition time of 90 ms; TOCSY mixing time of 60 ms.

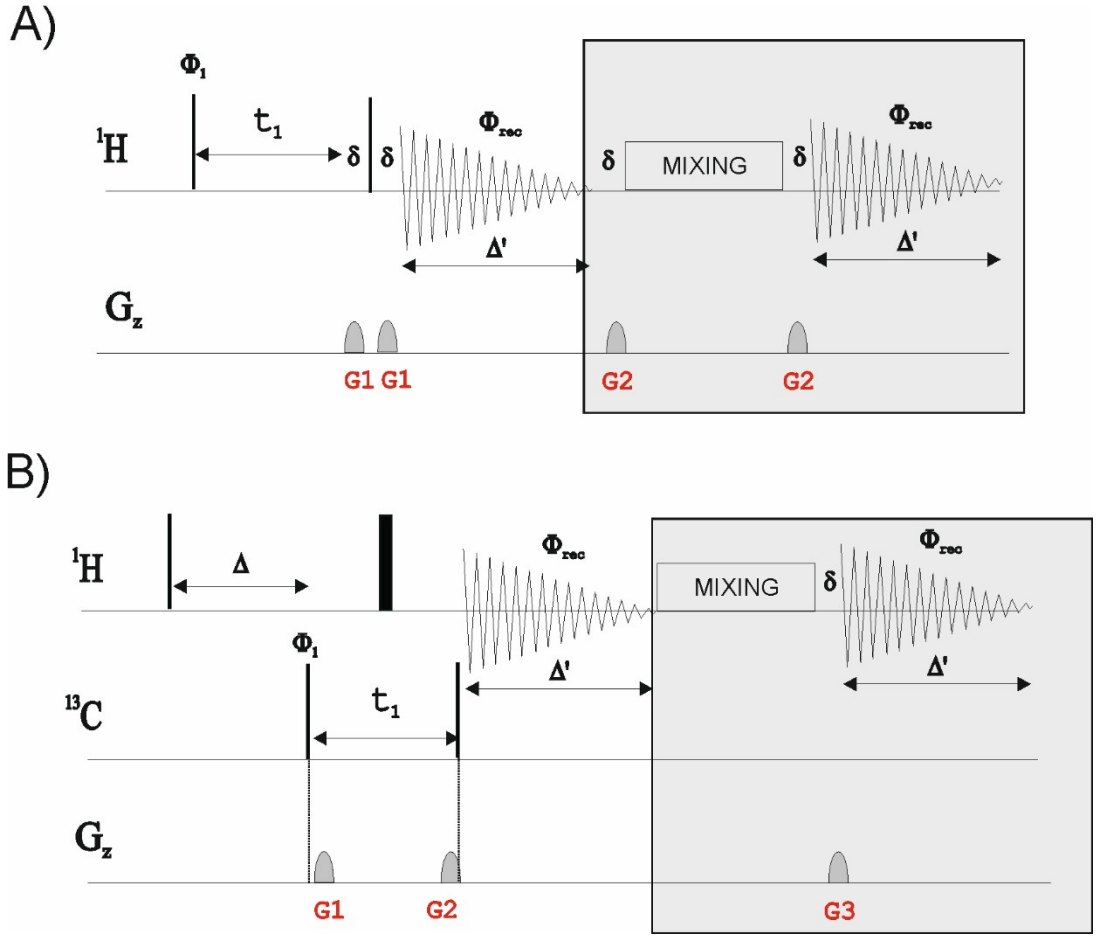


Figure S1: General scheme showing the incorporation of the MFA strategy in A) homonuclear (the example shows the gradient-enhanced COSY as a pattern experiment) and B) heteronuclear (the example shows the gradient-enhanced HMBC as a pattern experiment) NMR experiments. Grey boxes stand for additional COSY-based or TOCSY-based transfers appended after the conventional FID acquisition with the aim of collecting multiple NMR data into the same scan.

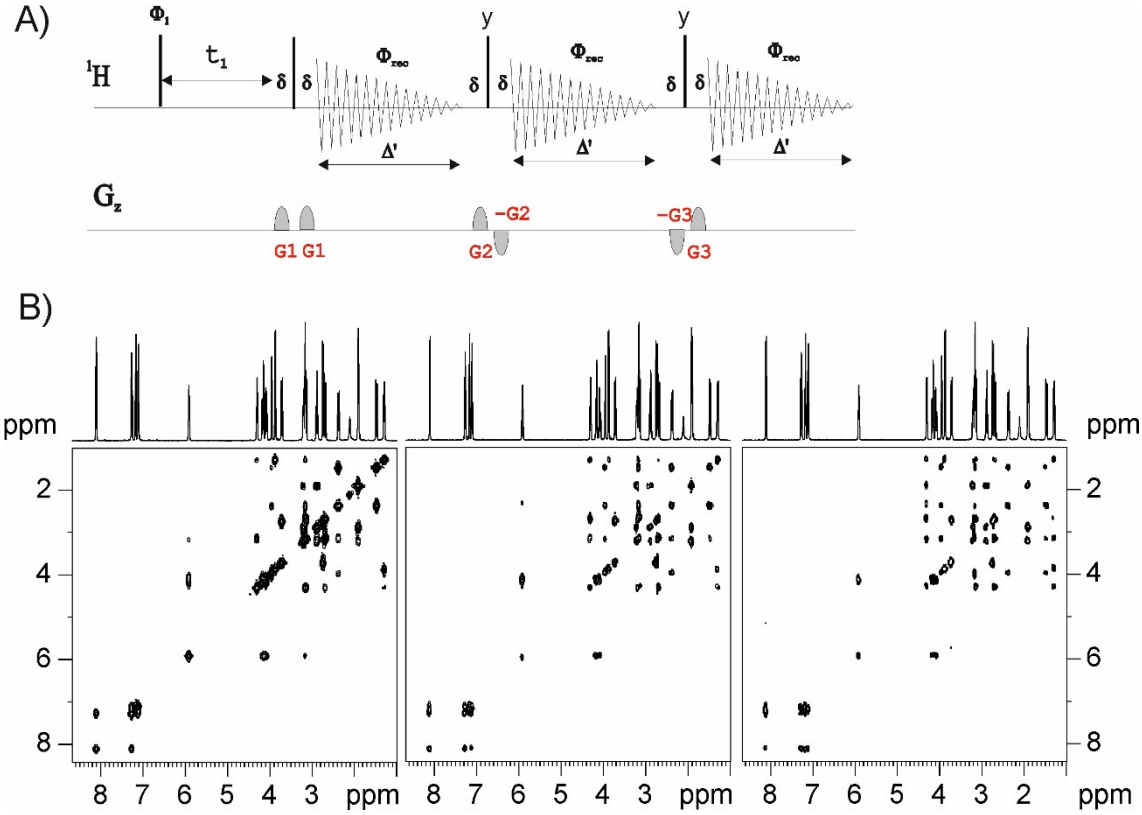


Figure S2: A) Pulse scheme of the MFA-COSY-RELAY-2 experiment. B) Separated 2D COSY, RELAY, and RELAY-2 NMR spectra of strychnine simultaneously obtained from the pulse scheme of Fig. A. See experimental section for details.

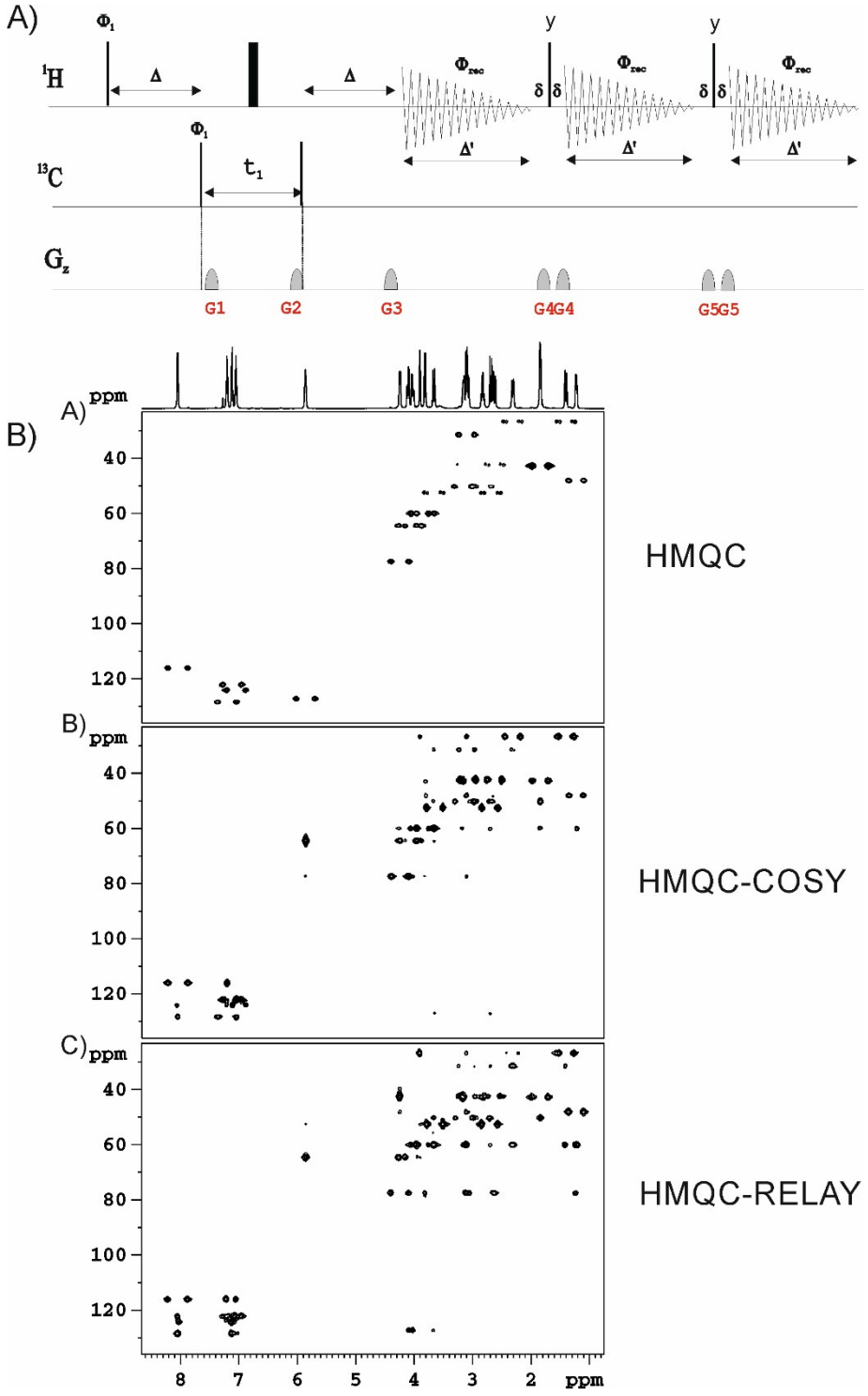


Figure S3: A) Pulse scheme of the MFA-HMQC/HMQC-COSY experiment. B) Separated 2D HMQC, 2D HMQC-COSY and 2D HMQC-RELAY NMR spectra of strychnine simultaneously obtained from the pulse scheme of Fig. S3A.

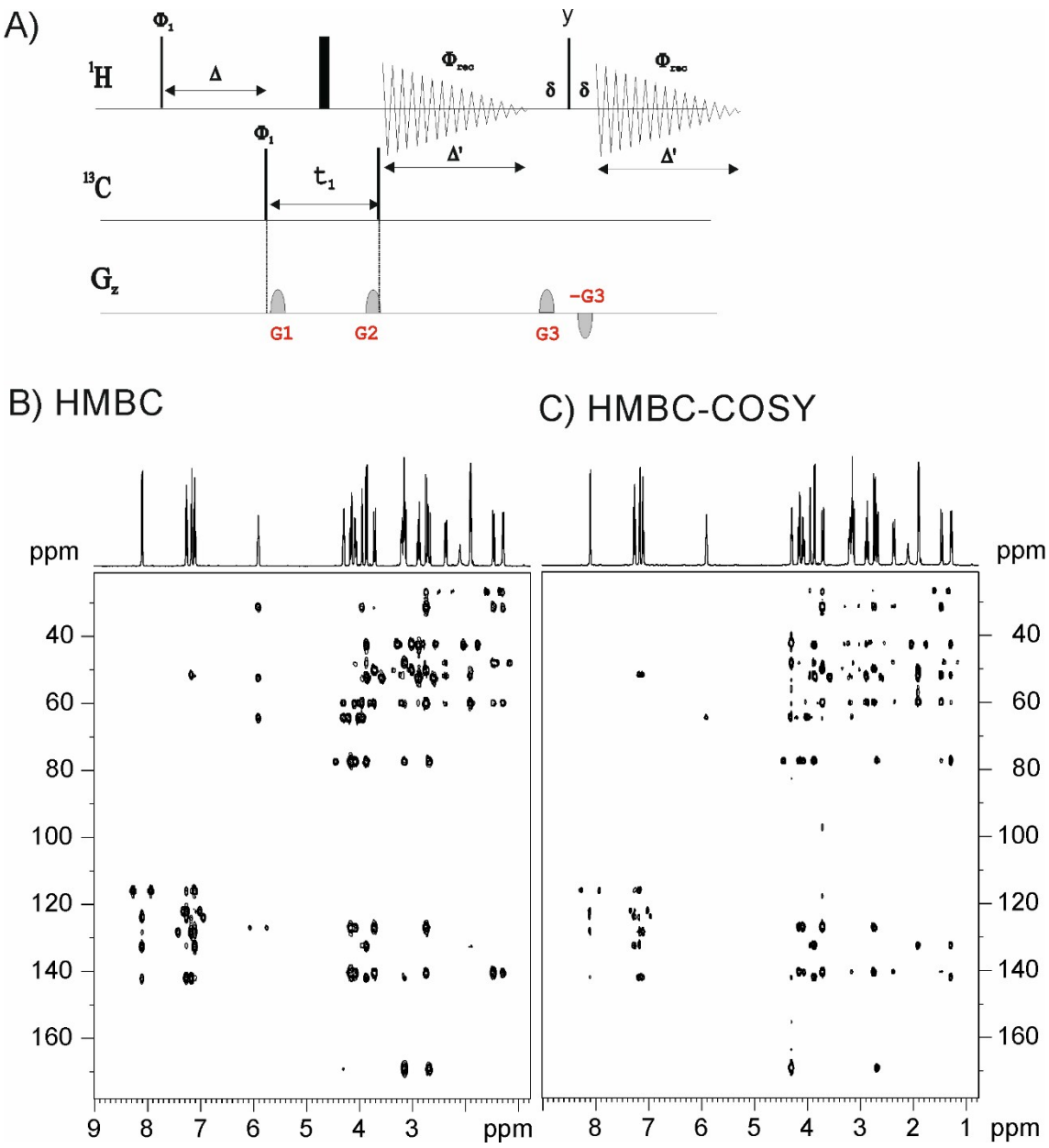


Figure S4: A) Pulse scheme of the MFA-HMBC/HMBC-COSY experiment. B) Separated 2D HMBC and HMBC-COSY NMR spectra of strychnine simultaneously obtained from the pulse scheme of Fig. S4A.

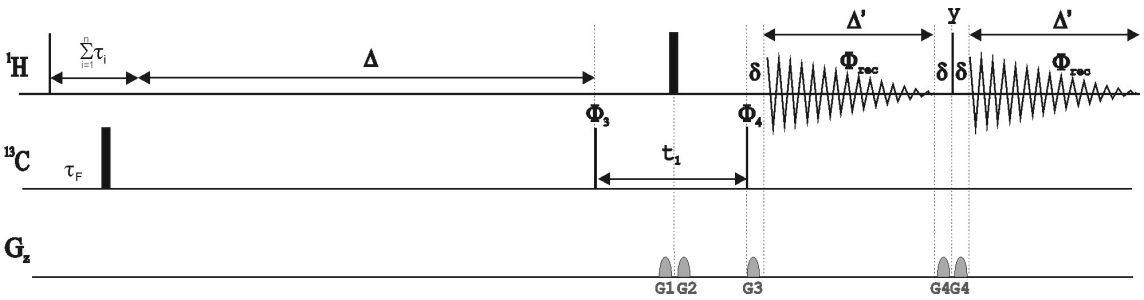


Figure S5: Pulse sequence of the MA-MBOB-COSY experiment. τ_i is the overall duration of low-pass J filter. The durations into the second-order low-pass J filter element were τ_F = (0, τ_1, τ_2, τ_1+ τ_2), τ_1 = $(2*(^1J_{min} + 0.146(^1J_{max} - {}^1J_{min})))^{-1}$ $\alpha\nu\delta$ τ_1 = $(2*(^1J_{min} - 0.146(^1J_{max} - {}^1J_{min})))^{-1}$. The interpulse Δ delay in the MBOB experiment was optimized at 8 Hz (=$1/(2*{}^nJ_{CH})$) and Δ' stands for the acquisition time. The duration of each gradient is specified as δ and the gradient ratio was set to G1:G2:G3:G4 is 50:30:40:15. Phase cycling is Φ_1=x, -x, x, -x; Φ_2=x, x, -x, -x. $\Phi_{rec.}$= x, -x, -x, x.

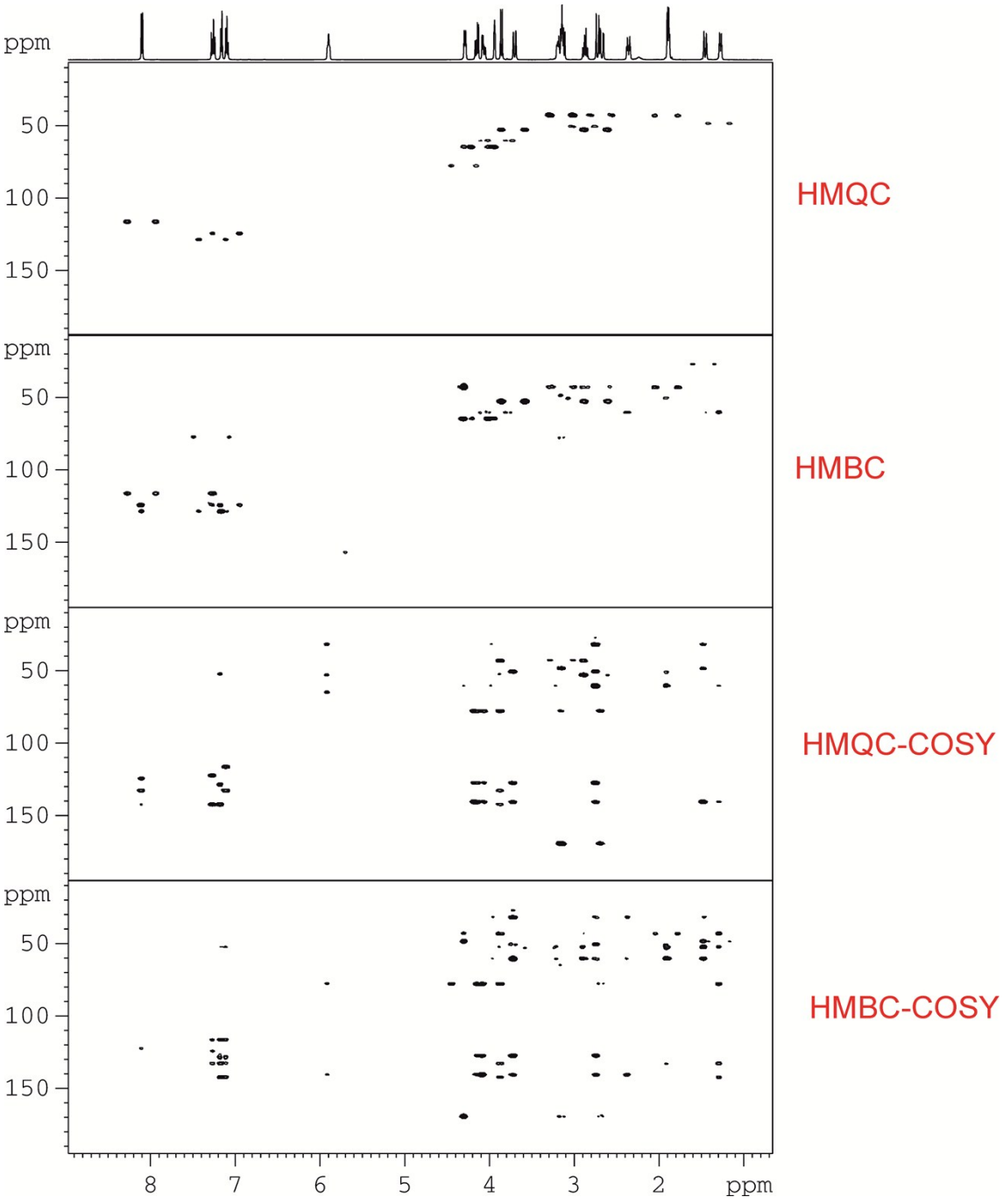


Figure S6: A) Separated 2D HMQC, 2D HMQC-COSY, 2D HMBC and 2D HMBC-COSY spectra of strychnine obtained simultaneously by the herein proposed MA-MBOB-COSY pulse sequence of Fig. S5. B) Expanded areas showing one-bond (HMQC), two-bond (HMQC-COSY), two- and three-bond (HMBC), and two, three- and four-bond correlations (HMBC-COSY).

Pulse Programs (for Topspin v1.3)

```
; mfa-cosyrelay
;topspin v1.3
#include <Avance.incl>
#include <Grad.incl>
"d0=3u"
"d13=4u"
1 ze
2 d1
3 50u
  p1 ph1
  d0
  d13 UNBLKGRAD
  p16:gp1
  d16
  p1 ph2
  d13
  p16:gp1
  d16
  goscnp ph31
  d13 wr #1
  p16:gp2
  d16
  p1 ph11
  d13
  p16:gp2*-1
  d16
  goscnp ph31
  d13 wr #2
  p16:gp3*-1
  d16
  p1 ph11
  d13
  p16:gp3
  d16
  goscnp ph31
  d13 wr #3
  p16:gp4
  d16
  p1 ph11
  d13
  p16:gp4*-1
  d16 BLKGRAD
  gosc ph31
  d1 wr #4
  lo to 3 times 2
  30u if #1
  30u if #2
  30u if #3
  30u if #4
  30u id0
  lo to 3 times td1
```

```
exit

ph1=0 2
ph2=0
ph11=1
ph31=0 2


;pl1 : f1 channel - power level for pulse (default)
;p0 : f1 channel -  20 to 90 degree high power pulse
;p1 : f1 channel -  90 degree high power pulse
;p16: homospoil/gradient pulse
;d0 : incremented delay (2D)                          [3 usec]
;d1 : relaxation delay; 1-5 * T1
;d13: short delay                                     [4 usec]
;d16: delay for homospoil/gradient recovery
;in0: 1/(1 * SW) = 2 * DW
;nd0: 1
;NS: 1 * n
;DS: 16
;td1: number of experiments
;FnMODE: QF
;for z-only gradients:
;gpz1: 50%
;gpz2: 30%
;gpz3: 40%
;gpz4: 17%
;use gradient files:
;gpnam1: SINE.100
;gpnam2: SINE.100
;gpnam3: SINE.100
;gpnam4: SINE.100
```

```
;mf_cosy-tocsy
;topspin v1.3
#include <Avance.incl>
#include <Grad.incl>
#include <Delay.incl>
"p7=p6*2"
"d13=4u"
"d0=in0/2-p1*2/3.1416-4u"
"FACTOR1=(d9/(p6*115.112))/2+0.5"
"l1=FACTOR1*2"
1 ze
2 d1
3 50u
  p1 ph1
  d0
  50u UNBLKGRAD
  p16:gp1
  d16
  p1 ph2
  50u
  p16:gp1
  d16 BLKGRAD
  goscnp ph31
  50u wr #1
  50u UNBLKGRAD
  p1 ph2
  50u
  p16:gp3
  d16
  4u pl10:f1
4 p6*3.556 ph23
  p6*4.556 ph25
  p6*3.222 ph23
  p6*3.167 ph25
  p6*0.333 ph23
  p6*2.722 ph25
  p6*4.167 ph23
  p6*2.944 ph25
  p6*4.111 ph23
  p6*3.556 ph25
  p6*4.556 ph23
  p6*3.222 ph25
  p6*3.167 ph23
  p6*0.333 ph25
  p6*2.722 ph23
  p6*4.167 ph25
  p6*2.944 ph23
  p6*4.111 ph25
  p6*3.556 ph25
  p6*4.556 ph23
  p6*3.222 ph25
  p6*3.167 ph23
  p6*0.333 ph25
  p6*2.722 ph23
  p6*4.167 ph25
  p6*2.944 ph23
```

```
  p6*4.111 ph25
  p6*3.556 ph23
  p6*4.556 ph25
  p6*3.222 ph23
  p6*3.167 ph25
  p6*0.333 ph23
  p6*2.722 ph25
  p6*4.167 ph23
  p6*2.944 ph25
  p6*4.111 ph23
  lo to 4 times l1
  d12 pl1:f1
  p1 ph2
  50u
  p16:gp2
  d16 BLKGRAD
  goscnp ph31
  d1 wr #2
  lo to 3 times 2
  30u if #1
  30u if #2
  30u id0
  lo to 3 times td1
exit

ph1=0 2
ph2=0
ph23=3
ph25=1
ph31=0 2

;pl1 : f1 channel - power level for pulse (default)
;pl10: f1 channel - power level for TOCSY-spinlock
;p1 : f1 channel -  90 degree high power pulse
;p5 : f1 channel -  60 degree low power pulse
;p6 : f1 channel -  90 degree low power pulse
;p7 : f1 channel - 180 degree low power pulse
;p17: f1 channel - trim pulse                          [2.5 msec]
;d0 : incremented delay (2D)
;d1 : relaxation delay; 1-5 * T1
;d9 : TOCSY mixing time
;d12: delay for power switching                        [20 usec]
;in0: 1/(1 * SW) = 2 * DW
;nd0: 1
;NS: 2 * n
;DS: 8
;td1: number of experiments
;FnMODE: QF
;for z-only gradients:
;gpz1: 10%
;gpz2: 20%
;gpz3: 33%
;use gradient files:
;gpnam1: SINE.100
;gpnam2: SINE.100
;gpnam3: SINE.100
```

```
;mf_hmbctocsy
;topspin v1.3
#include <Avance.incl>
#include <Grad.incl>
#include <Delay.incl>
"p5=p6*.667"
"p7=p6*2"
"p2=p1*2"
"d0=3u"
"d13=3u"
"d6=1s/(cnst13*2)"
"DELTA1=50u+p16+d16+4u"
"SCALEF=p7*2/p5+0.5"
"FACTOR1=((d9-p17*2)/(p6*64+p5))/SCALEF+0.5"
"l1=FACTOR1*SCALEF"

1 ze
2 d1
3 d12 pl1:f1
  p1 ph1
  d6
  p3:f2 ph4
  d0
  50u UNBLKGRAD
  p16:gp1
  d16
  p2 ph2
  50u
  p16:gp2
  d16
  d0
  p3:f2 ph5
  goscnp ph31
  50u wr #1
  p16:gp3
  d16
  4u pl10:f1
  (p17 ph26)
                                    ;begin MLEV17
4 (p6 ph22 p7 ph23 p6 ph22)
  (p6 ph24 p7 ph25 p6 ph24)
  (p6 ph24 p7 ph25 p6 ph24)
  (p6 ph22 p7 ph23 p6 ph22)
  (p6 ph24 p7 ph25 p6 ph24)
  (p6 ph24 p7 ph25 p6 ph24)
  (p6 ph22 p7 ph23 p6 ph22)
  (p6 ph22 p7 ph23 p6 ph22)
  (p6 ph24 p7 ph25 p6 ph24)
  (p6 ph22 p7 ph23 p6 ph22)
  (p6 ph22 p7 ph23 p6 ph22)
  (p6 ph24 p7 ph25 p6 ph24)
  (p6 ph22 p7 ph23 p6 ph22)
  (p6 ph22 p7 ph23 p6 ph22)
  (p6 ph24 p7 ph25 p6 ph24)
  (p6 ph24 p7 ph25 p6 ph24)
  (p5 ph23)
```

```
  lo to 4 times l1
                                    ;end MLEV17
  (p17 ph26)
  50u
  p16:gp3*-1
  d16 BLKGRAD
  gosc  ph31
  d1 wr #2
  lo to 3 times 2
  10m if #1
  10m if #2
  10m id0
  lo to 3 times td1
exit

ph1=0
ph11=1
ph2=0
ph3=0
ph4=0 2
ph5=0 0 2 2
ph22=3
ph23=0
ph24=1
ph25=2
ph26=0
ph31=0 2 2 0

;pl1 : f1 channel - power level for pulse (default)
;pl2 : f2 channel - power level for pulse (default)
;p1 : f1 channel -  90 degree high power pulse
;p2 : f1 channel - 180 degree high power pulse
;p3 : f2 channel -  90 degree high power pulse
;p16: homospoil/gradient pulse
;d0 : incremented delay (2D)                  [3 usec]
;d1 : relaxation delay; 1-5 * T1
;d2 : 1/(2J)XH
;d6 : delay for evolution of long range couplings
;d16: delay for homospoil/gradient recovery
;cnst2: = J(XH)
;cnst13: = J(XH) long range
;in0: 1/(2 * SW(X)) = DW(X)
;nd0: 2
;NS: 2 * n
;DS: 16
;td1: number of experiments
;FnMODE: QF
;for z-only gradients:
;gpz1: 30%
;gpz2: 50%
;gpz3: 17% for C-13
;use gradient files:
;gpnam1: SINE.100
;gpnam2: SINE.100
;gpnam3: SINE.100
```

```
;teo_mf_hmbccosy

#include <Avance.incl>
#include <Grad.incl>
#include <Delay.incl>

"p2=p1*2"
"d0=3u"
"d13=3u"
"d6=1s/(cnst13*2)"
"DELTA1=50u+p16+d16+4u"

1 ze
2 d1
3 p1 ph1
  d6
  p3:f2 ph4
  d0
  50u UNBLKGRAD
  p16:gp1
  d16
  p2 ph2
  50u
  p16:gp2
  d16
  d0
  p3:f2 ph5
  goscnp ph31
  50u wr #1
  p16:gp3
  d16
  p1 ph11
  50u
  p16:gp3*-1
  d16 BLKGRAD
  gosc  ph31
  d1 wr #2
  lo to 3 times 2
  10m if #1
  10m if #2
  10m id0
  lo to 3 times td1
exit


ph1=0
ph11=1
ph2=0
ph3=0
ph4=0 2
ph5=0 0 2 2
ph31=0 2 2 0



;pl1 : f1 channel - power level for pulse (default)
```

```
;pl2 : f2 channel - power level for pulse (default)
;p1 : f1 channel -  90 degree high power pulse
;p2 : f1 channel - 180 degree high power pulse
;p3 : f2 channel -  90 degree high power pulse
;p16: homospoil/gradient pulse
;d0 : incremented delay (2D)                  [3 usec]
;d1 : relaxation delay; 1-5 * T1
;d2 : 1/(2J)XH
;d6 : delay for evolution of long range couplings
;d16: delay for homospoil/gradient recovery
;cnst2: = J(XH)
;cnst13: = J(XH) long range
;in0: 1/(2 * SW(X)) = DW(X)
;nd0: 2
;NS: 2 * n
;DS: 16
;td1: number of experiments
;FnMODE: QF
```

```
;mf-mbob-cosy

#include <Avance.incl>
#include <Grad.incl>
#include <Delay.incl>

"p4=p3*2"
"p2=p1*2"
"d0=3u"
"d13=3u"
"d2=0s"
"d3=0.5s*(1/(cnst8+0.146*(cnst9-cnst8)))"    ;cnst9: jmax
"d4=0.5s*(1/(cnst9-0.146*(cnst9-cnst8)))"    ;cnst8: jmin
"d5=d3+d4"

"d6=1s/(cnst13*2)"
"d7=d2+d3+d4+d5"

"DELTA2=d7-d2-p4"
"DELTA3=d7-d3-p4"
"DELTA4=d7-d4-p4"
"DELTA5=d7-d5-p4"

1 ze
2 d1 pl1:f1 pl2:f2
3 p1 ph1

  if "cnst26 == 0"
     {
     d2
     }
  if "cnst26 == 1"
     {
     d3
     }
  if "cnst26 == 2"
     {
     d4
     }
  if "cnst26 == 3"
     {
     d5
     }


  p4:f2 ph1


  if "cnst26 == 0"
     {
     DELTA2
     }
  if "cnst26 == 1"
     {
     DELTA3
```

```
    }
  if "cnst26 == 2"
    {
    DELTA4
    }
  if "cnst26 == 3"
    {
    DELTA5
    }

  d6
  p3:f2 ph3
  d0
  50u UNBLKGRAD
  p16:gp1
  d16
  p2 ph2
  50u
  p16:gp2
  d16
  d0
  p3:f2 ph4
  4u
  p16:gp3
  d16
  goscnp ph31
  10u wr #1
  p16:gp4
  d16
  p1 ph11
  10u
  p16:gp4
  d16 BLKGRAD
  gosc ph31
  d1 wr #2
  lo to 3 times ns
  10u if #1
  10u if #2
  10u id0
  lo to 2 times td1
exit

ph1=0
ph11=1
ph2=0
ph3=0 2
ph4=0 0 2 2
ph31=0 2 2 0

;pl1 : f1 channel - power level for pulse (default)
;pl2 : f2 channel - power level for pulse (default)
;p1 : f1 channel -  90 degree high power pulse
;p2 : f1 channel - 180 degree high power pulse
;p3 : f2 channel -  90 degree high power pulse
;p16: homospoil/gradient pulse
;d0 : incremented delay (2D)                  [3 usec]
```

```
;d1 : relaxation delay; 1-5 * T1
;d2 : 1/(2J)XH
;d6 : delay for evolution of long range couplings
;d16: delay for homospoil/gradient recovery
;cnst2: = J(XH)
;cnst13: = J(XH) long range
;in0: 1/(2 * SW(X)) = DW(X)
;nd0: 2
;NS: 2 * n
;DS: 16
;td1: number of experiments
;FnMODE: QF
```