

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

ORGANIC CHEMISTRY 5.46

Summary of important 2D pulse sequences

For through-bond (J) pulse sequences, remember J's can be zero preventing magnetization from getting passed further. For all through-space (dipolar) pulse sequences: False positives can arise from J-coupling and/or chemical exchange.

Pulse Sequence	Information Content	Caveats, Comments
non-phase-sensitive COSY (CORrelation SpectroscopY) including gradient-version gCOSY	Gives cross-peaks between strongly J-coupled spins (done mostly with ^1H)	A coupling of zero (dihedral gives null in Karplus diagram) results in no cross peaks. Cannot measure J's, requires symmetrization.
(phase-sensitive) COSY	“	Can be used to measure J_{ab} 's without analyzing a complete multiplet. Overlapping cross-peaks give partial cancellation due to dispersive (as opposed to absorptive) signals. Cross peaks near the diagonal can be obscured by strong diagonal intensity.
DQFCOSY (Double Quantum Filtered COSY)	“	Same as above, except diagonal intensity is suppressed (not for diastereotopic protons), thus allowing the observations of cross peaks near the diagonal.
TOCSY (Total Correlation SpectroscopY)	Gives J-coupled cross-peaks through isolated spin-systems (given long enough mixing time)	Mixing time can be varied between 20ms and ~300ms. 30ms will be sensitive to J's > ~1-2Hz, 50ms and longer allows passage of magnetization via intermediates. Cross peaks with solvent (or other groups) can be caused by chemical exchange.
^1H -X HSQC (Heteronuclear Single Quantum Correlation)	Generates signal between X-nuclei and their directly-attached protons	Proton-detected. Exploits the average $^1J_{\text{XH}}$ to generate a cross peak. More sensitive than directly-detected COSY (HETCOR or HETeronuclear CORrelation). Gives narrower signals but is more susceptible to pulse imperfections than HMQC (below).
^1H -X HMQC (Heteronuclear Multiple Quantum Correlation)	Generates signal between X-nuclei and their directly-attached protons	Proton-detected. Exploits the average $^1J_{\text{XH}}$ to generate a cross peak. More sensitive than directly-detected COSY (HETCOR or HETeronuclear CORrelation). Gives broader cross peaks than HSQC but more tolerant of pulse imperfections.
^1H -X HMBC (Heteronuclear Multiple-Bond Correlation)	Gives cross peaks between protons and X-nuclei 3-5 bonds distant ($J \sim 2\text{-}8\text{ Hz}$)	Proton-detected. Having the X decoupler off during acquisition of the FID allows HSQC peaks to be readily identified by the $^1J_{\text{XH}}$ splitting. Usually set to have maximum sensitivity to $^nJ_{\text{XH}} \sim 4.5\text{ Hz}$ (from 1-2 Hz up).
^1H NOESY (Nuclear Overhauser Effect SpectroscopY)	Gives cross-peaks from through-space dipolar relaxation.	Has a variable mixing time. Mixing takes place along z-axis. Also shows TOCSY cross peaks. NOESY cross peaks can be completely suppressed if NOE molecular tumbling is moderate ($MW \sim 1000$). Cross peaks between large molecules and solvent tend to be negative.
^1H ROESY (Rotational Overhauser Effect SpectroscopY)	Gives cross-peaks from through-space dipolar relaxation	Mixing takes place in the xy-plane during a spin-lock. RF heating can be a problem. Can also show TOCSY cross peaks (opposite sign). Molecular motion must be <i>much</i> slower than for NOESY to suppress cross peaks.
^{13}C - ^{13}C INADEQUATE (Incredible Natural Abundance Double QUAntum TransfEr)	Gives pairs of peaks at the same height for ^{13}C - ^{13}C pairs	Odds of having two ^{13}C nuclei next to each other is only $(0.011)^2$, thus making this experiment require lots of time.