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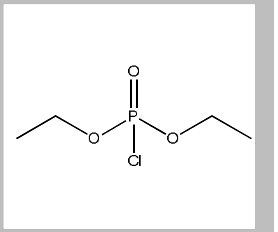

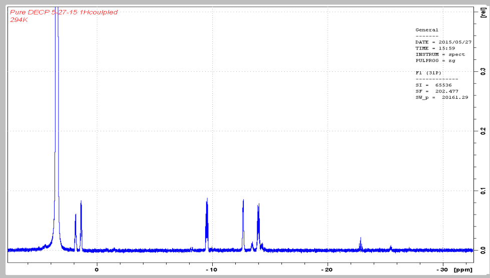

Investigating the Hydrolysis Reactions of CWA Simulants using NMR Spectroscopy on Multiple Nuclei

A systematic study that tracks ^{31}P containing species in a reaction of a Sarin surrogate

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July 23, 2015

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Sandia National Laboratories

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U.S. DEPARTMENT OF ENERGY

NNSA National Nuclear Security Administration

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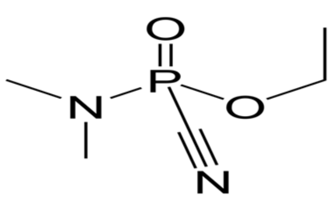
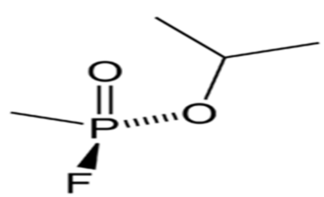
Background

- Nerve agents were developed by German Scientists in the 1940’s.
- Dr. Gerhard Schrader a German scientist first synthesized tabun (GA). Further research lead to the development of sarin (GB), soman (GD), and cyclosarin (GF).
- These Chemical Warfare Agents (CWAs) were mass produced by the Germans by 1945.
- The US designated these types of agents as “G-agents”.

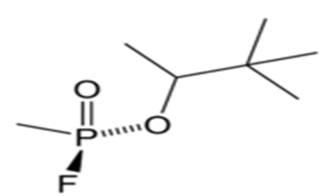
<u>Different types of “G-agents”:</u>



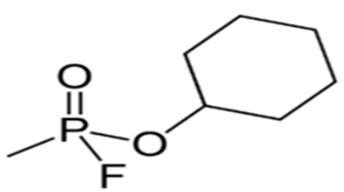
GA – Tabun (1936)



GB – Sarin (1939)



GD – Soman (1944)



GF – Cyclosarin (1949)

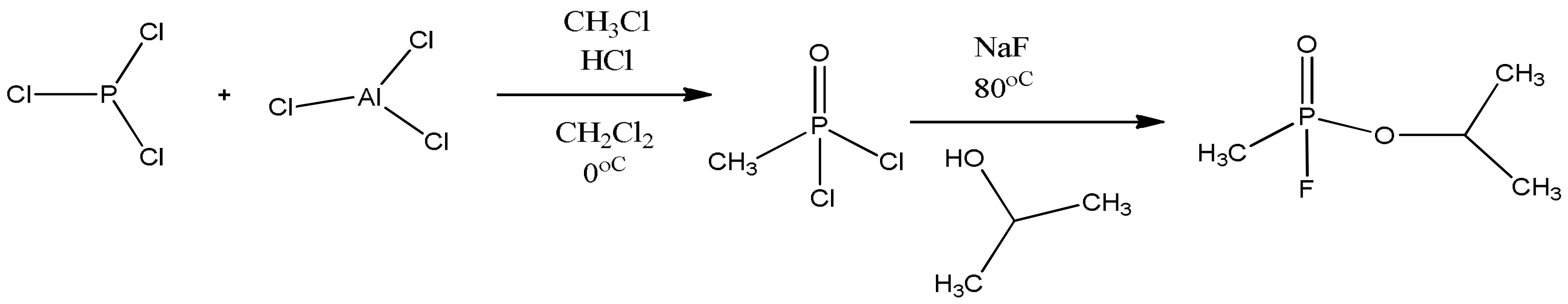
Sarin Background and Timeline

- Originally intended to be used as a pesticides.
- Most toxic of the four “G agents”.
- Sarin named in honor of researchers: **S**chrader, **A**mbros, **R**itter, and L**in**de.

- 1925-Geneva Protocol attempts to ban CWAs
- 1938-Discovery of Sarin
- 1950-USSR and US make Sarin for military use
- 1956-US stops Sarin production
- 1988-Halabja in norther Iraq bombed with CWAs estimated 5,000 deaths
- 1988-Sarin used four times against Iranian soldiers in Iraq-Iran war
- 1993-UN Chemical Weapons Convention signed by 162 countries banning stockpiling and production of CWAs
- 1994-Japanese religious sect Aum Shinrkyo released an impure form of sarin in Matsumoto, Nagano, killing eight people and harming over 200.
- 1995-Aum Shinrkyo released impure sarin in the Tokyo Metro, thirteen people died.
- 2004-Iraqi insurgents detonated a 155mm shell containing binary precursors for Sarin near a US convoy in Iraq
- 2013-Sarin used in attack in Ghouta, Syria. The US estimates 1,429 deaths.

Motivation and Sarin

- Chemical Warfare Agents (CWAs) are opportunities for terror attacks.
- Sarin is a deadly CWA with LD_{50}'s (lethal dose to kill 50% of the population) on the order of $5 - 20 \frac{\mu g}{kg}$ by absorbtion[1] for various cases, its vapors are deadly.
- Sarin cause irreversible inhibition to a class of enzymes known as cholinesterases.
- It is not very stable and vaporizes easily. Typically is only found pure for a few weeks to a few months at max.
- Most synthetic routes are few steps and available online free of charge and are only a two step synthesis[2].

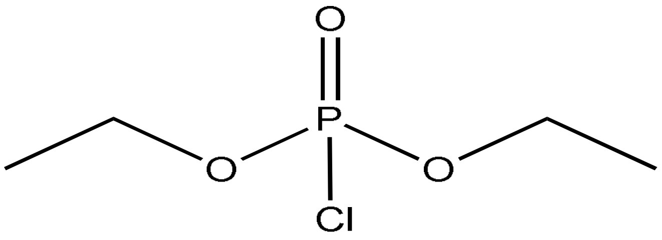


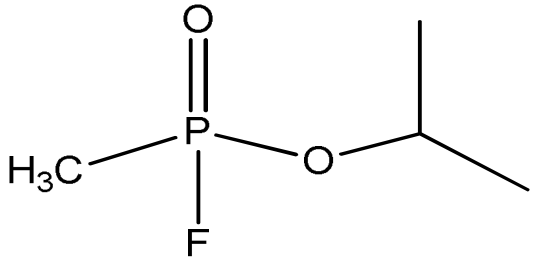
Cape Ray

- Housed 1,038.5 tons of CWAs and precursors that Syria declared.
- Ship contained two field hydrolysis units.
  - Must dilute the CWA to decontaminate with reactor.
- Mission took place in the Mediterranean Sea.
- Endeavor Started on July 3, 2014.
- August 11, 2014 marked 75% decontamination.
- August 18, 2014 the neutralization process was finished.

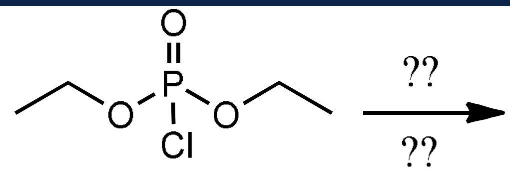
Precursors and DECP

- DECP-diethyl chlorophosphate is similar in structure to sarin, and other precursors but much more stable.
- This is a safer compound with similar reactivity due to the phosphorus-halogen bond, and phosphoester nature of the molecule.
- With this compound we can simulate situations that could be encountered in the field. Specifically, high concentration of CWAs and low concentration decontamination reagent.
  - Hydrolysis reactions of DECP are completely different depending on concentration.
  - At low concentration, there is primarily one product formed.
  - At high concentration, there are many products formed and an increase in the complexity of the reaction.



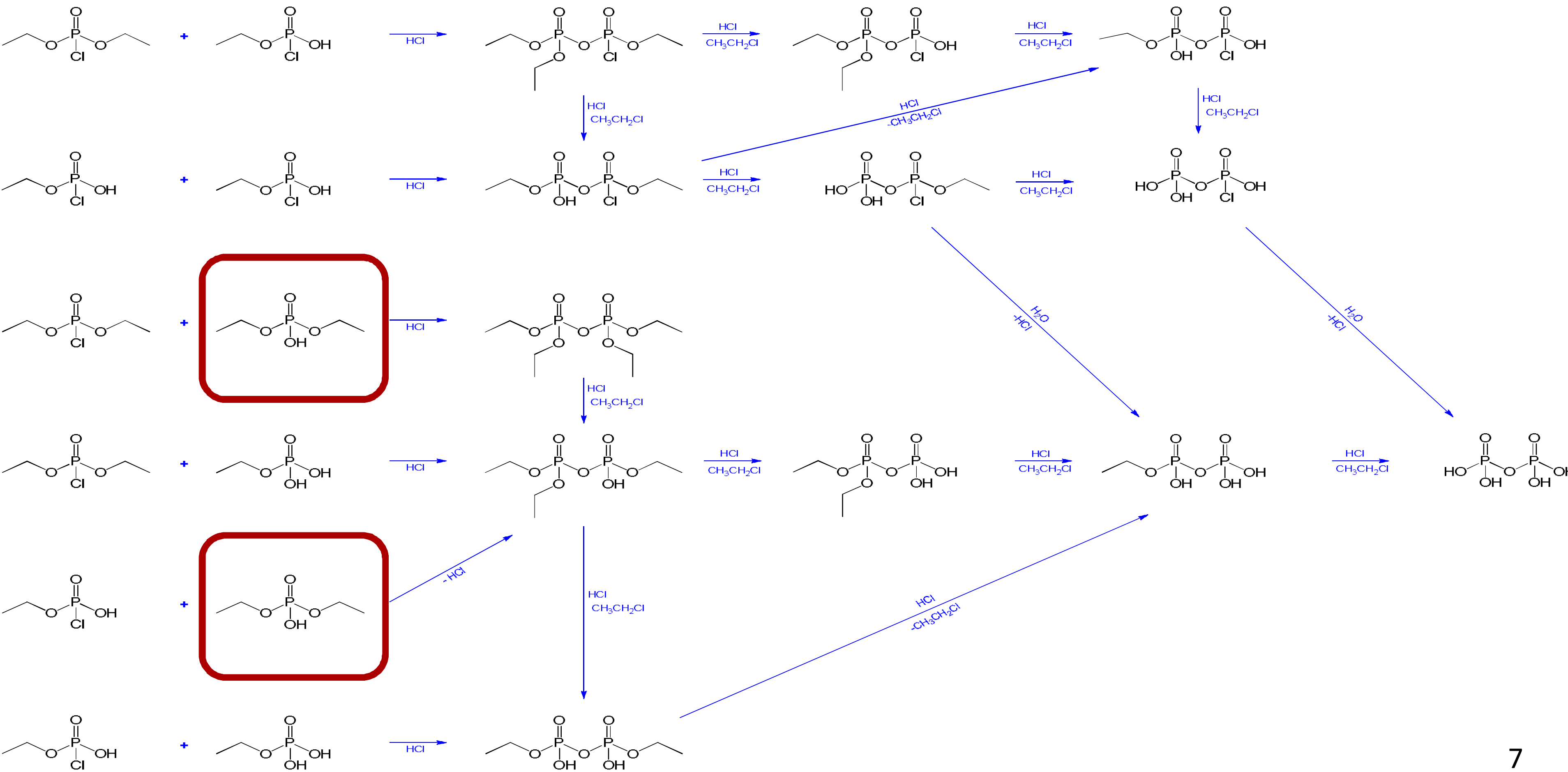


Complexity of the Reactions

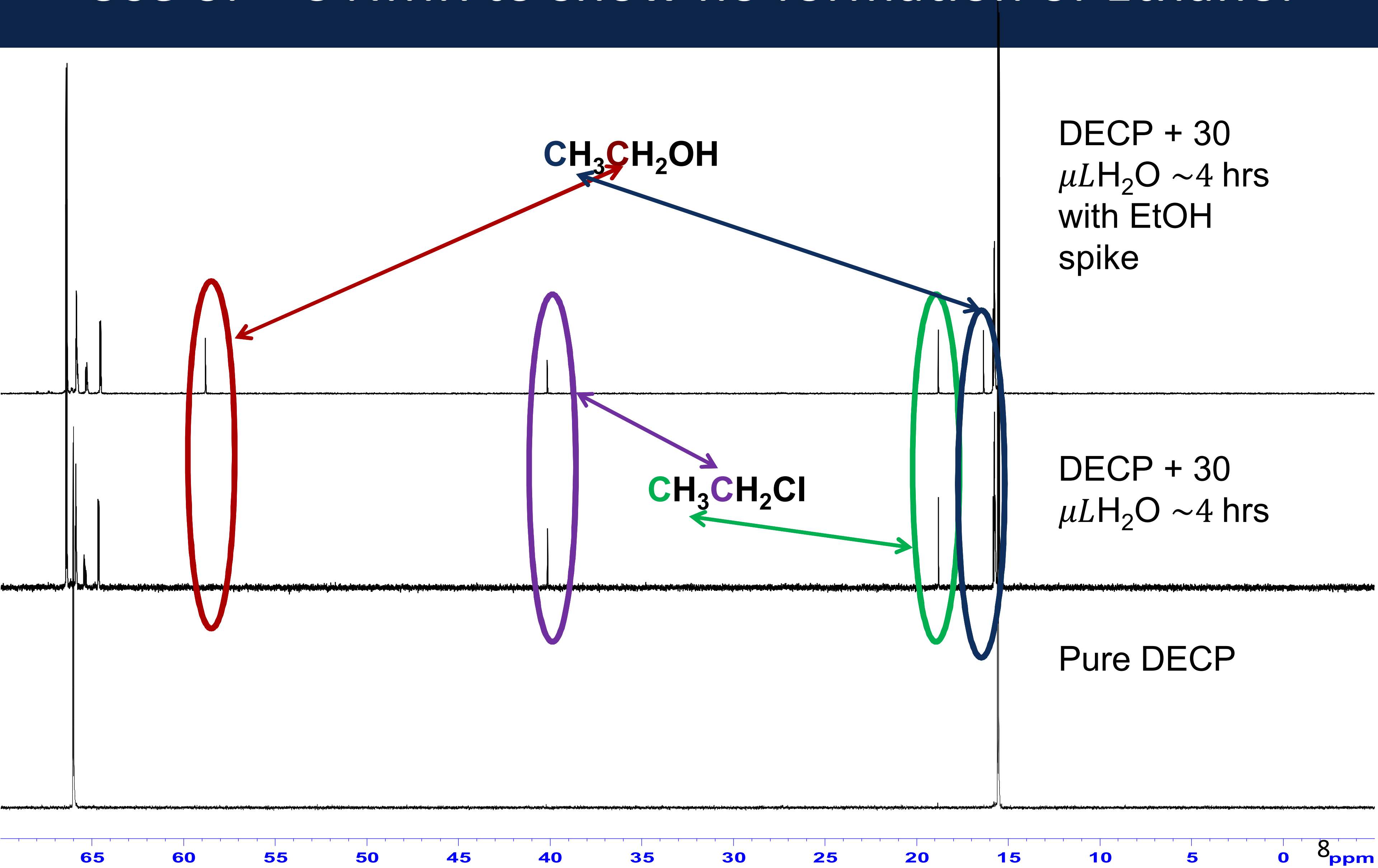


-Decontamination of DECP

-Polymerization of phosphoesters

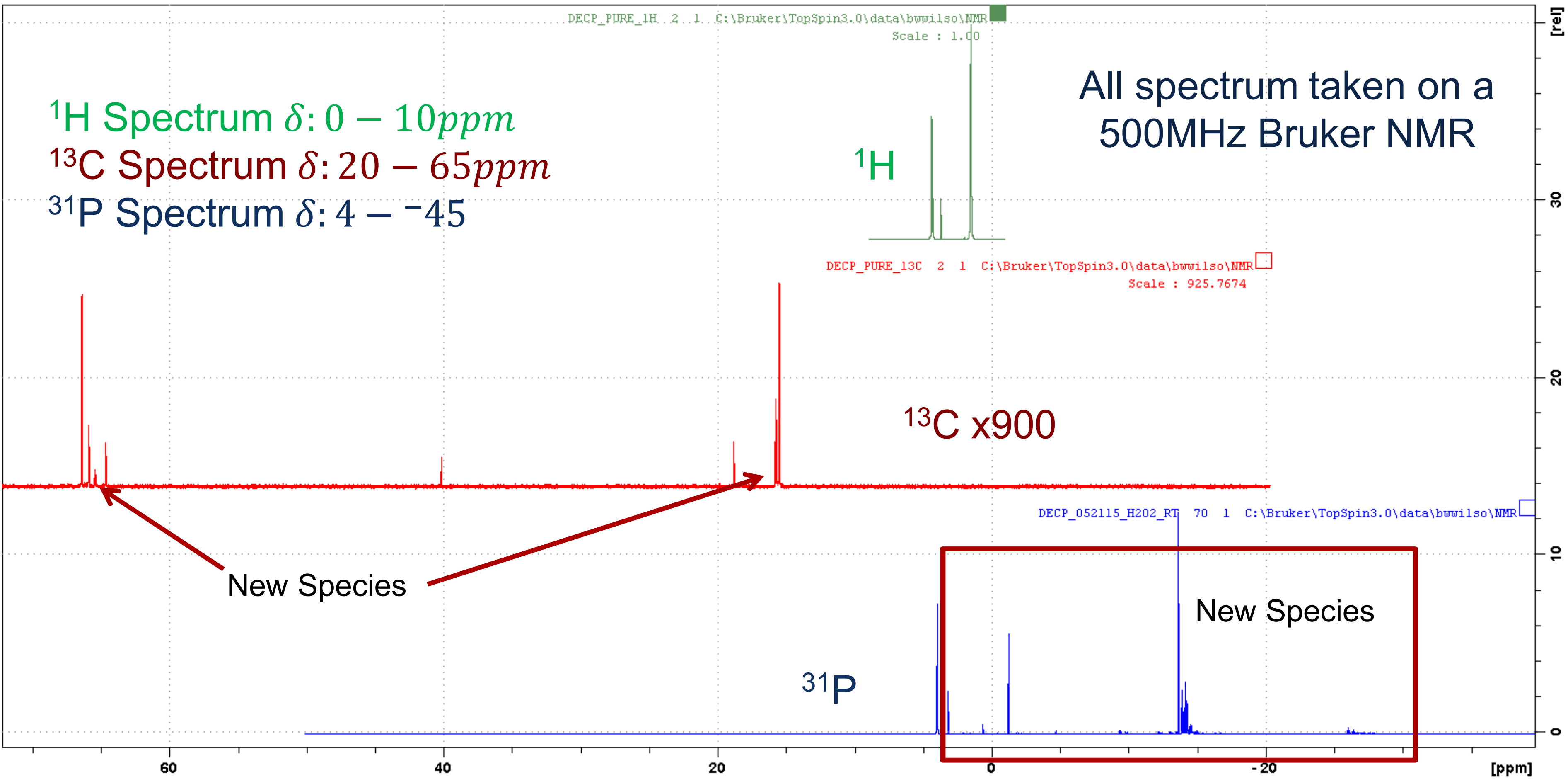


Use of ^{13}C NMR to show no formation of Ethanol

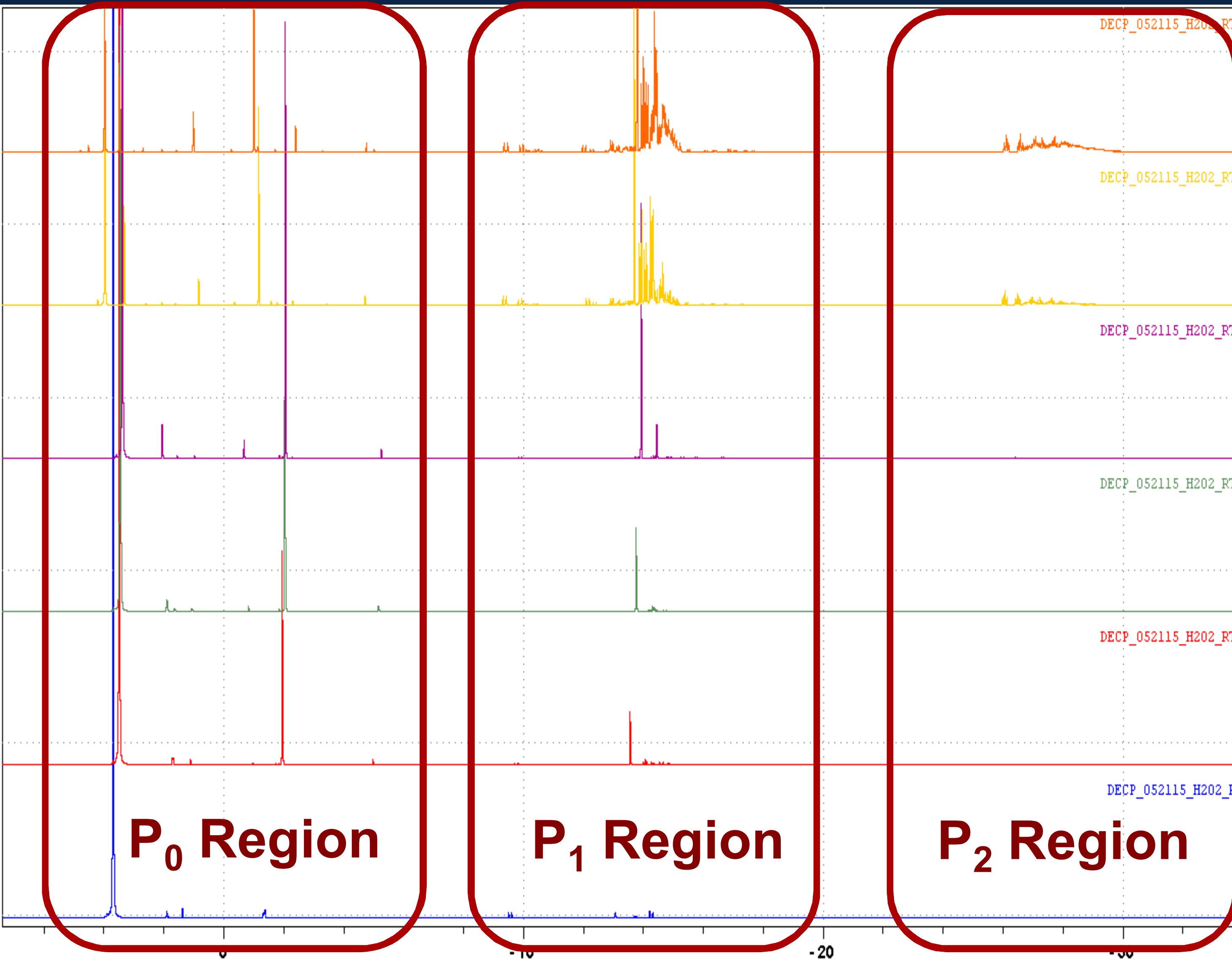


Why ^{31}P NMR spectroscopy and not ^{1}H or ^{13}C?

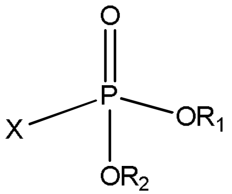
- The best answer: more distinction in chemical shift between different species and ^{31}P is 100% natural abundance as opposed to ^{13}C being 1.1%.



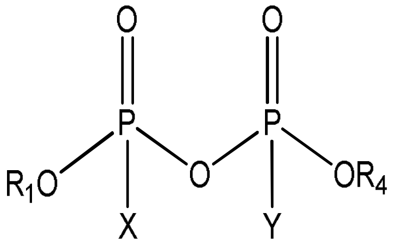
Why ^{31}P NMR spectroscopy and not ^{1}H or ^{13}C?



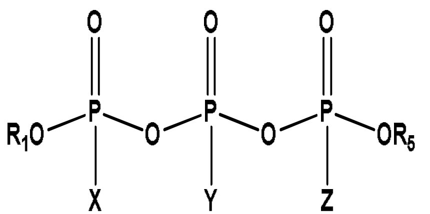
P_0 Species



P_1 Species



P_2 Species



X=Cl or OR_2, Y=Cl or OR_3, Z=Cl or OR_4

Reactions with DECP

Reaction	Conditions
10μL H_2O	323K
30μL H_2O_2 (30%)	Room Temperature
30μL 1N HCl	Room Temperature
30μL 1N NaOH	Room Temperature
10μL H_2O_2 (30%)	323K
10μL H_2O_2 (30%)	Room Temperature adding 10μL every 12 hours
10μL H_2O_2 (30%)	323K adding 10μL every 12 hours
10μL H_2O	Room Temperature adding 10μL every 12 hours
10μL H_2O	323K adding 10μL every 12 hours
30μL 3N NaOH	Room Temperature
30μL 3N HCl	Room Temperature
124μL H_2O_2 (30%)	Room Temperature
124μL H_2O	Room Temperature

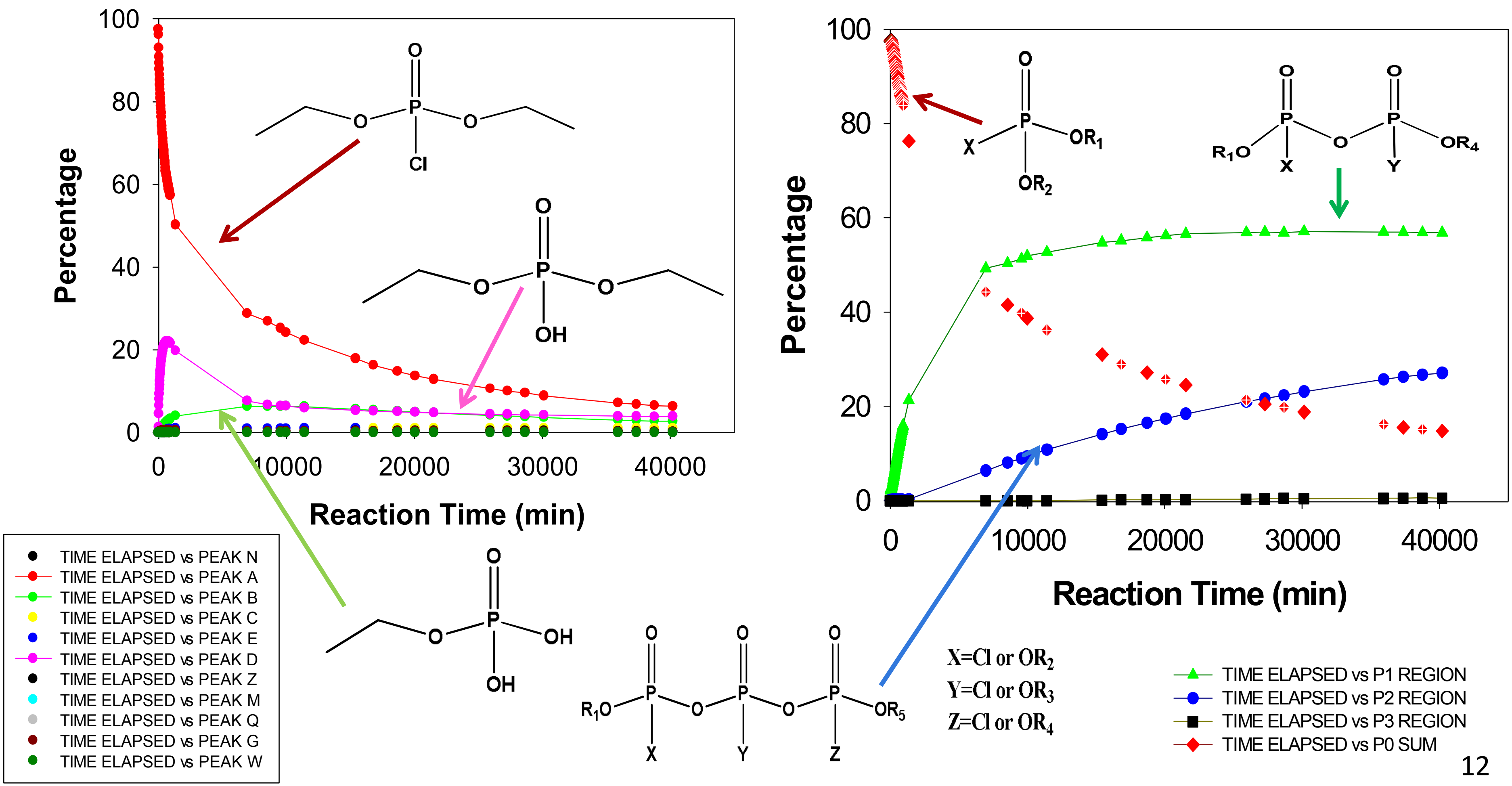
Other reaction with various reagents were pursed, but can not be discussed at this time.

All reactions employ 1.0mL of DECP

30μL H_2O_2 (30%) at RT

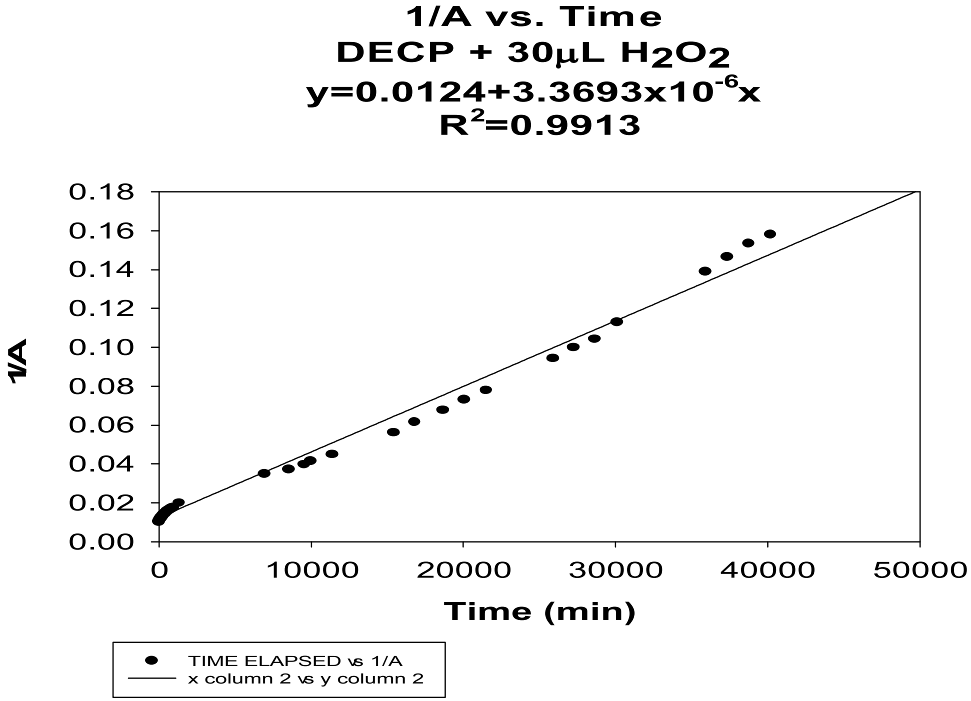
P_0 Species vs. Time
DECP + 30μL H_2O_2 at Room Temperature

P_n Species vs. Time
DECP + 30μl H_2O_2 at Room Temperature



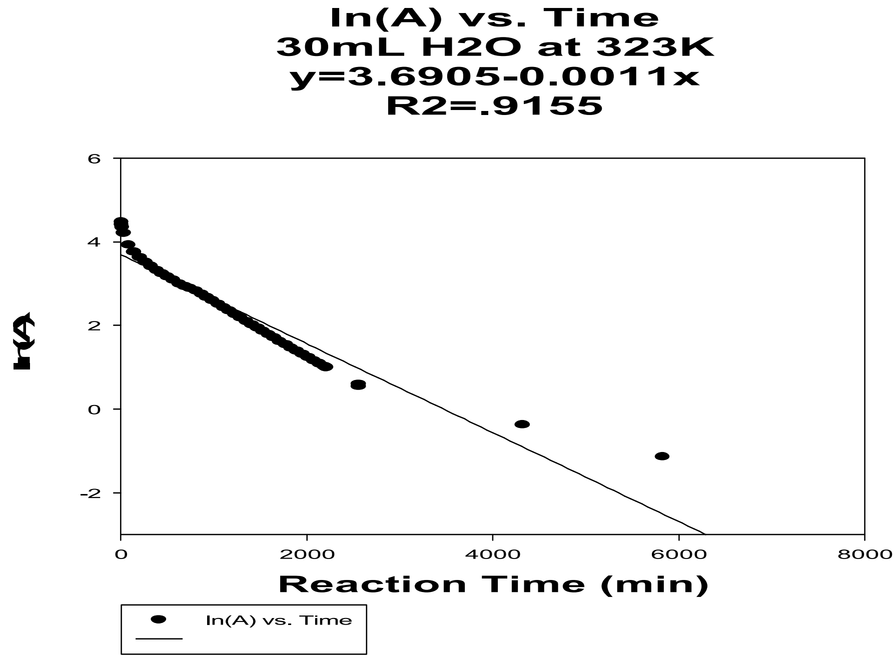
$30\mu L\ H_2O_2$ (30%) at RT Reaction “Kinetics”

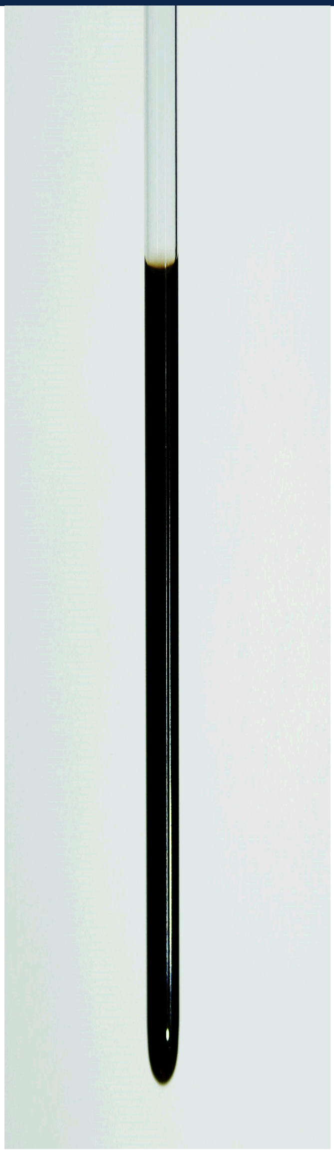
- Appears to be 2nd with respect to DECP and H_2O_2.
- Estimated $t_{1/2} = 1343\ min$.
- Estimated $k = 1.6847 \times 10^{-6} \frac{1}{\% \cdot min}$.



30μL H_2O at 323K Reaction "Kinetics"

- Appears to be 1st order with respect to DECP.
- Estimated $t_{1/2} = 85\, min$.
- Estimated $k = 0.0011 \frac{1}{min}$.





Stoichiometric Equivalents

- 1.0mL DECP $\approx 4.16 \times 10^{21}$ *molecules* $\approx$ 7 mmoles.
- 10μL $\approx 3.34 \times 10^{20}$ *molecules* $\approx$ .6 mmoles.
    - Roughly 12:1 DECP:H_2O (molecules).
- 30μL $H_2O \approx 1.0025 \times 10^{21}$ *molecules* $\approx$ 2 mmoles.
    - Roughly 4:1 DECP: H_2O (molecules).
- 124μL $H_2O \approx 4.14 \times 10^{21}$*molecules* $\approx$ 7 mmoles.
    - Roughly 1:1 DECP:H_2O (molecules)
- 30μL $H_2O_2 \approx 1.76 \times 10^{20}$ *molecules* $\approx$ .3 mmoles.
    - Roughly 23:1 DECP:H_2O_2 (molecules).
- 124μL $H_2O_2 \approx 7.31 \times 10^{20}$*molecules* ≈ 1.2 *mmoles*.
    - Roughly 6:1 DECP:H_2O_2 (molecules)

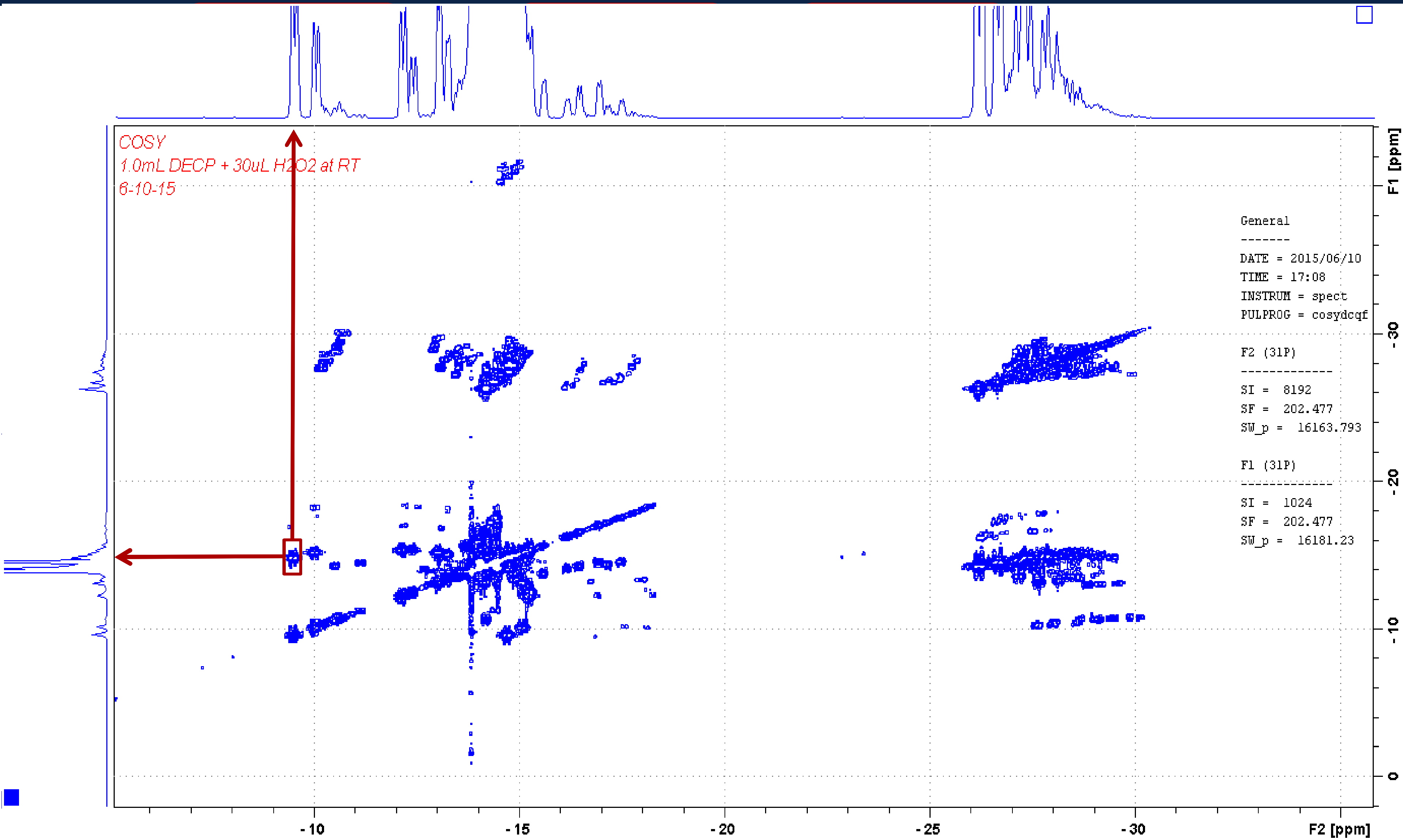
Summary of "Kinetics"

Reaction Conditions	Estimated Half-Life	Estimated $t_{1/4}$ of P1 Generation	Estimated Rate Constant	Rate Order Model
1.0 mL DECP + 10μL H_2O @ 323K	4390 min	976 min	$1.5786 \times 10^{-4} \frac{1}{min}$	1st
1.0 mL DECP + 30μL H_2O @ 323K	85 min	990 min	0.0011$\frac{1}{min}$	1st
1.0 mL DECP + 30μL H_2O_2 @ RT	1343 min	1000 min	$1.42132 \times 10^{-6} \frac{1}{\% \cdot min}$	2nd
1.0 mL DECP + 30μL 1N HCl @ RT	3162 min	2684 min	$1.0938 \times 10^{-6} \frac{1}{\% \cdot min}$	2nd
1.0 mL DECP + 30μL 1N NaOH @ RT	2642 min	2147 min	$1.3582 \times 10^{-6} \frac{1}{\% \cdot min}$	2nd
1.0 mL DECP + 30μL 3N HCl @ RT	2570 min	2075 min	$1.4915 \times 10^{-6} \frac{1}{\% \cdot min}$	2nd
1.0 mL DECP + 30 μL 3N NaOH @ RT	2129 min	1600 min	$1.3159 \times 10^{-6} \frac{1}{\% \cdot min}$	2nd
1.0 mL DECP + 3N HCl @ RT	2570 min	1971 min	$1.0041 \times 10^{-6} \frac{1}{\% \cdot min}$	2nd
1.0mL DECP + 124μL H_2O_2 @ RT	166 min	Not Reached	$1.7588 \times 10^{-5} \frac{1}{\% \cdot min}$	2nd
1.0mL DECP + 124μL H_2O @ RT	153 min	Not Reached	0.0003$\frac{1}{min}$	1st

Other reaction with various reagents were pursed, but can not be discussed at this time.

*Half-life's and rate constants were found using the interpolation function in SigmaPlot.

2D NMR Spectroscopy ^{31}P-^{31}P COSY



Advantages and Use of ^{31}P-^{31}P COSY

- Both axes correspond to ^{31}P Spectrum (homonuclear correlation).
- A cross-peak indicates a correlation (communication between nuclei).
- The coupling values are specific to each molecule. Allows for more exact measure of the coupling constants.
- In the P_1 and P_2 regions it shows which phosphorous compounds are corrlated by ^{31}P-^{31}P *J*-coupling; each compounds coupling is unique.

Conclusions

- The fastest reactions involved a peroxide species.
- The reaction mechanism and the complexity of the reaction is dependent on the initial concentration of DECP
- Using ^{13}C NMR it was possible to confirm the presence of EtCl and not EtOH as a byproduct of the hydrolysis reaction.
- ^{31}P-^{31}P COSY allows examination of which ^{31}P containing species are correlated.

Acknowledgements

- Dr. Todd Alam and the NMR group: Kim, Randi, and Dan.
- Sandia National Laboratories
- Department of Homeland Security

This research was supported in part by an appointment with the HS-STEM Summer Internship Program sponsored by the U.S. Department of Homeland Security (DHS) Science & Technology (S&T) Directorate Office of University Programs. This program is administered by the Oak Ridge Institute for Science and Education (ORISE) through an interagency agreement between the U.S. Department of Energy (DOE) and DHS. ORISE is managed by Oak Ridge Associated Universities (ORAU) under DOE contract number DE-AC05-06OR23100.

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2. Ledgard, Jared. 2006. A Laboratory History of Chemical Warfare Agents.
3. Derome, Andrew. 1986. 6. 133-143. Modern NMR Techniques for Chemistry Research

A Side Project: INEPT Optimization for ^{19}F-^{31}P

- **I**nsensitive **N**uclei **E**nhanced by **P**olarization **T**ransfer

- This types of sequence is used in many 2D experiments.
  - Also can be used as a filter to see only compounds with ^{19}F-^{31}P *J*-couplings.

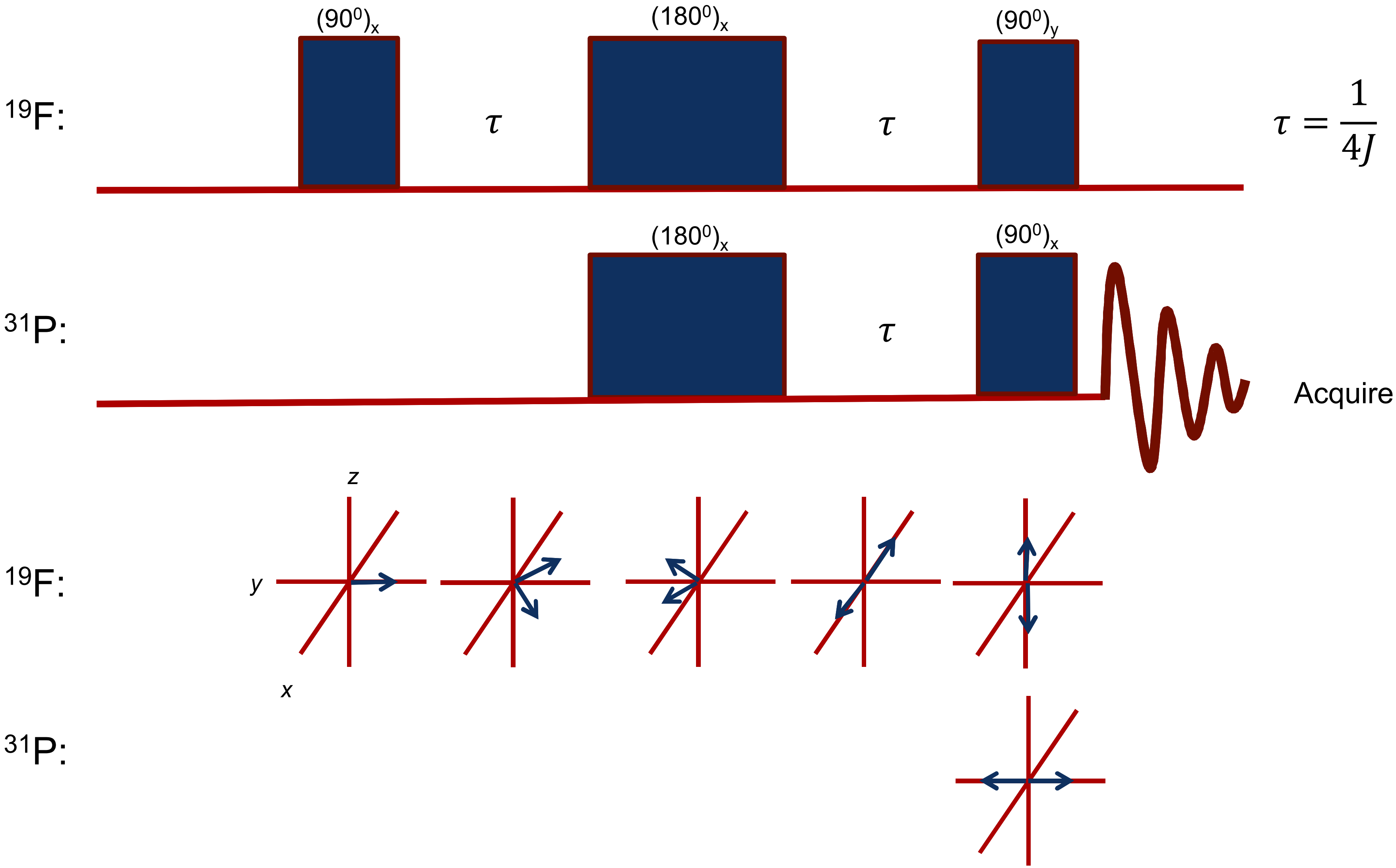
- Enhances the signal of an insensitive NMR active nuclei by a factor of the ratio of gyromagnetic ratios[3]:

$$I = I_0 \left|\frac{\gamma_S}{\gamma_I}\right|$$

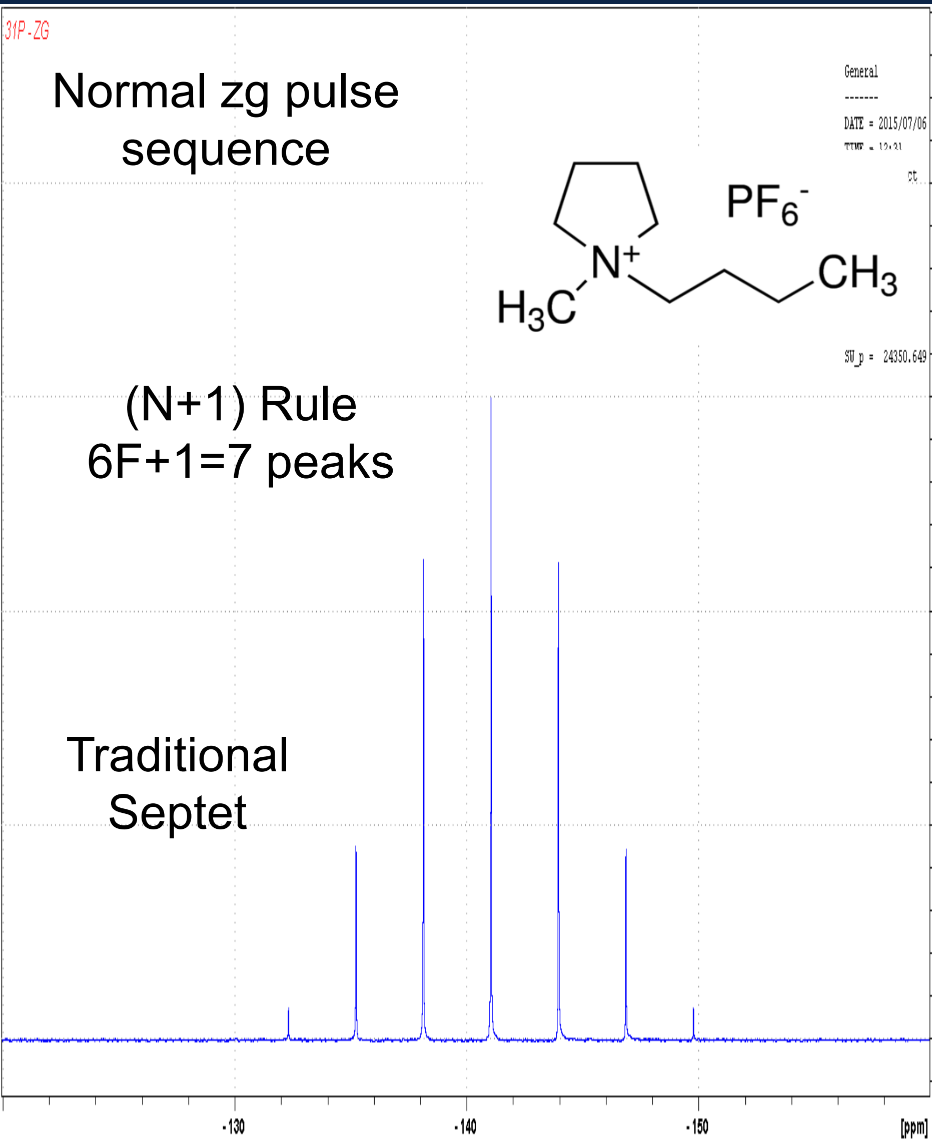
$$171699.06 * \left|\frac{40.0593}{17.235}\right| = 399080.02 \text{ (Theoretical Absolute Intensity)}$$

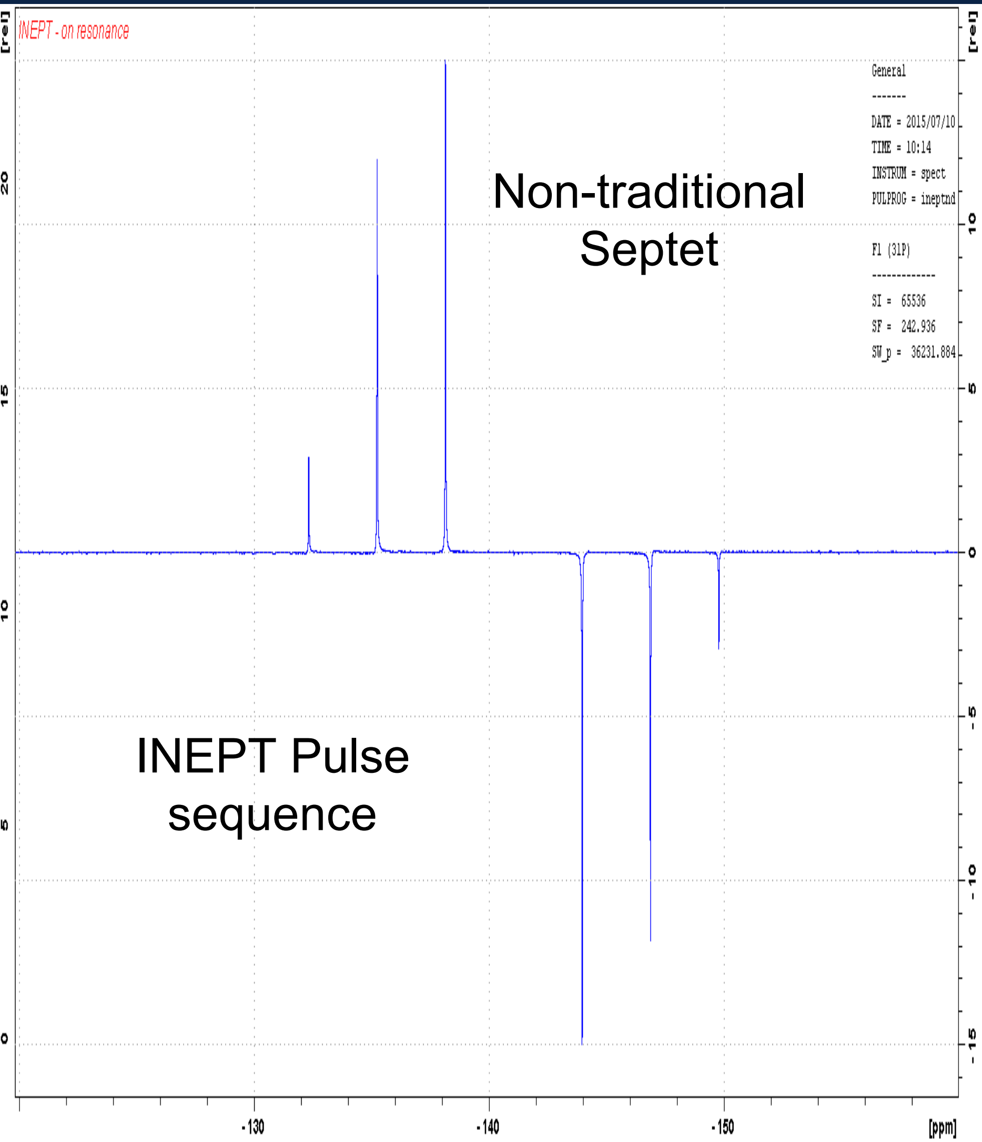
- Issues with this technique that can cause loss of signal:
  - Large ^{19}F-^{31}P *J*-coupling values $\sim 700Hz$ (or larger).
  - Large spectral width for ^{19}F (1000ppm range).
  - Large spectral width for ^{31}P (535ppm range).
  - Can’t use a shaped pulse do to power needed for a long range of time.

A Side Project: INEPT Optimization for ^{19}F-^{31}P



Comparison with INEPT



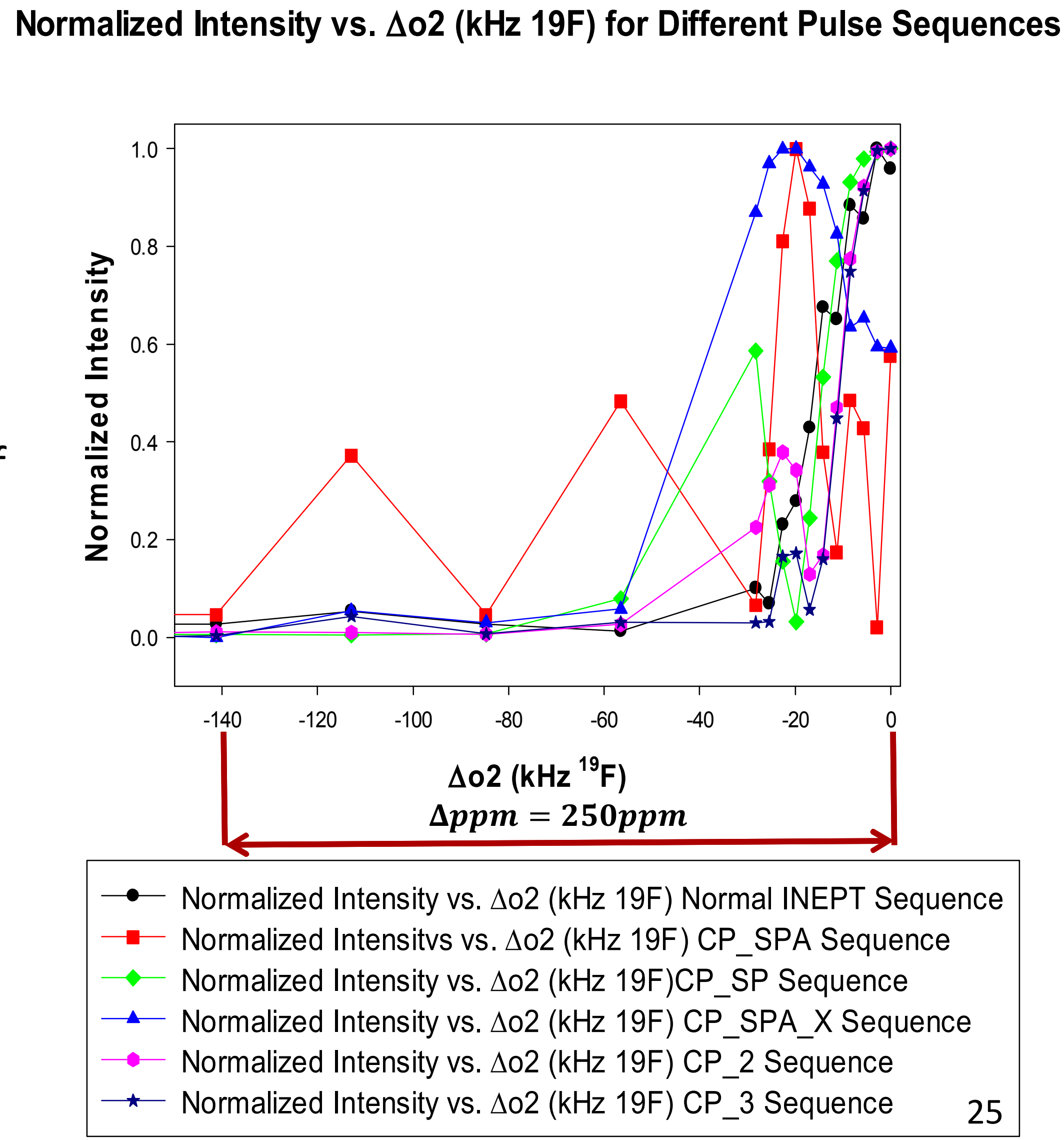


INEPT Optimization for ^{19}F-^{31}P Experiments

- Compound used: 1-Butyl-1-methylpyrrolidinium hexafluorophosphate in CD_3CN

- Different pulse programs were used to try to optimize signal intensity as a function of the offset frequency of the non-observed pulse channel (o2 ^{19}F).

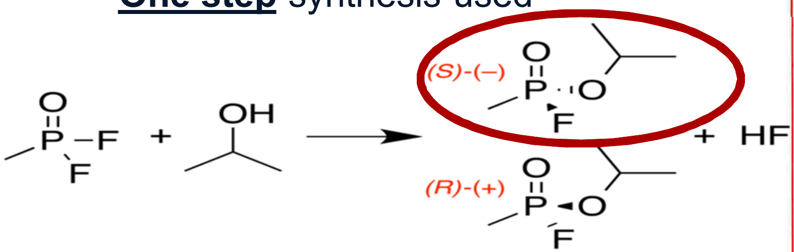
- There is still more work to be done to find a way to generalize the program.

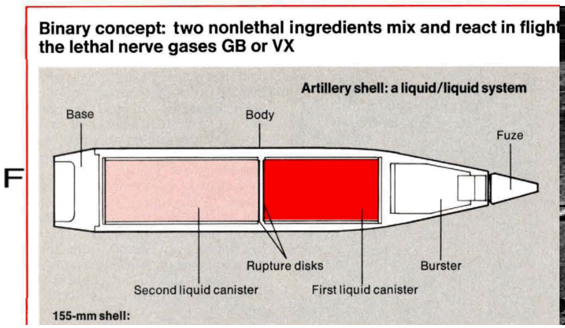


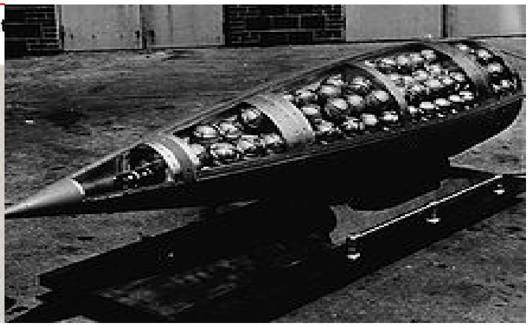
Recent Cases

In **<u>2004</u>** sarin (a CWA) was found in a roadside bomb that exploded near a US convoy in Iraq.

- Stored in a "binary shell" which contained holding two different nonlethal chemicals that synthesize sarin on impact.
- **<u>One step</u>** synthesis used



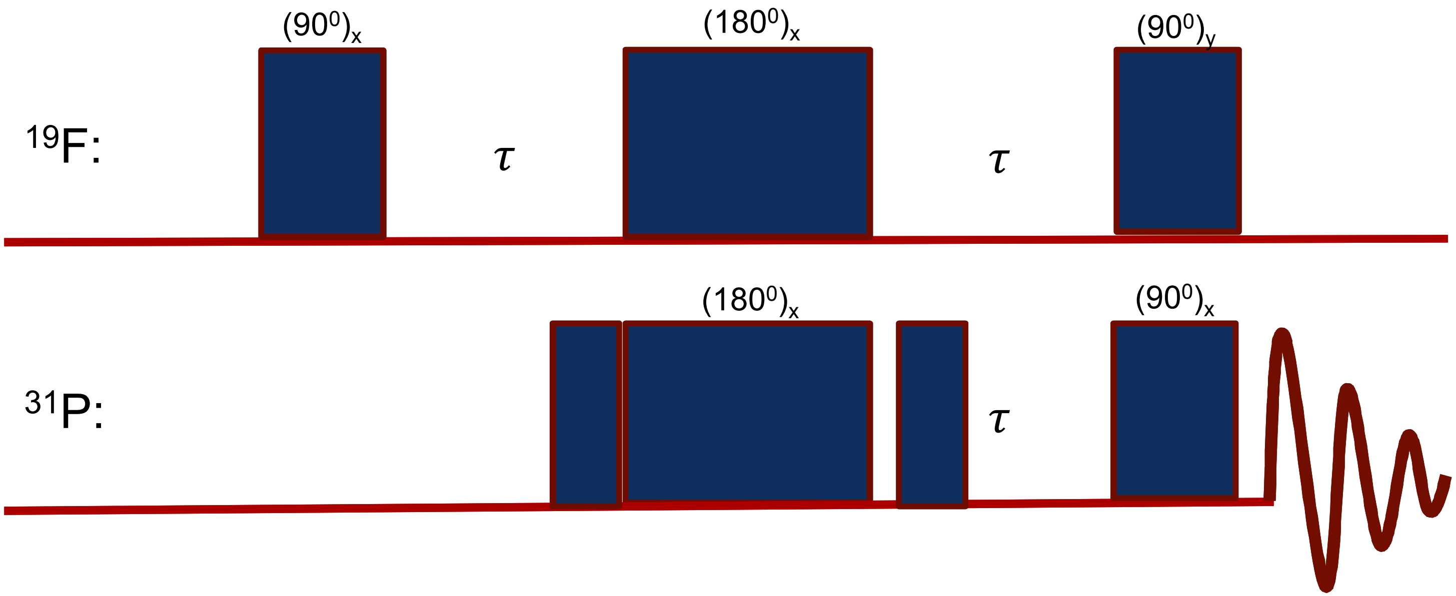




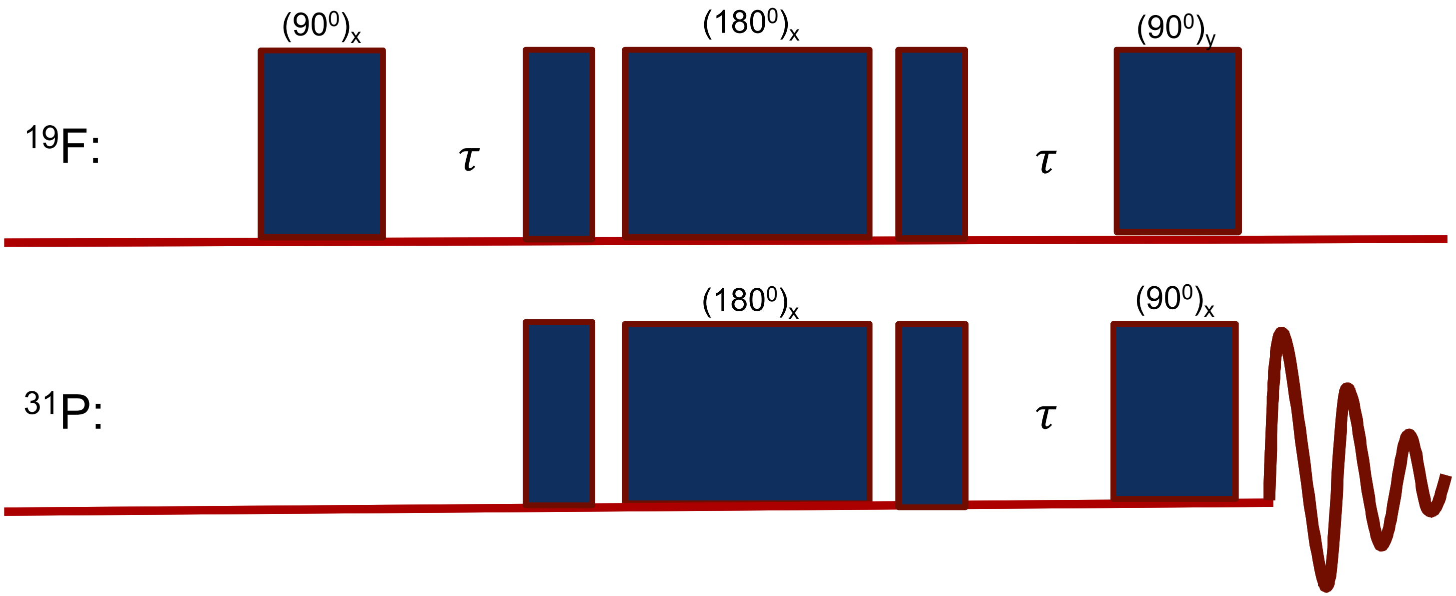
Sarin was used in Ghouta, Syria on **<u>August 21, 2013</u>**

- The US estimates 1,429 people were killed.

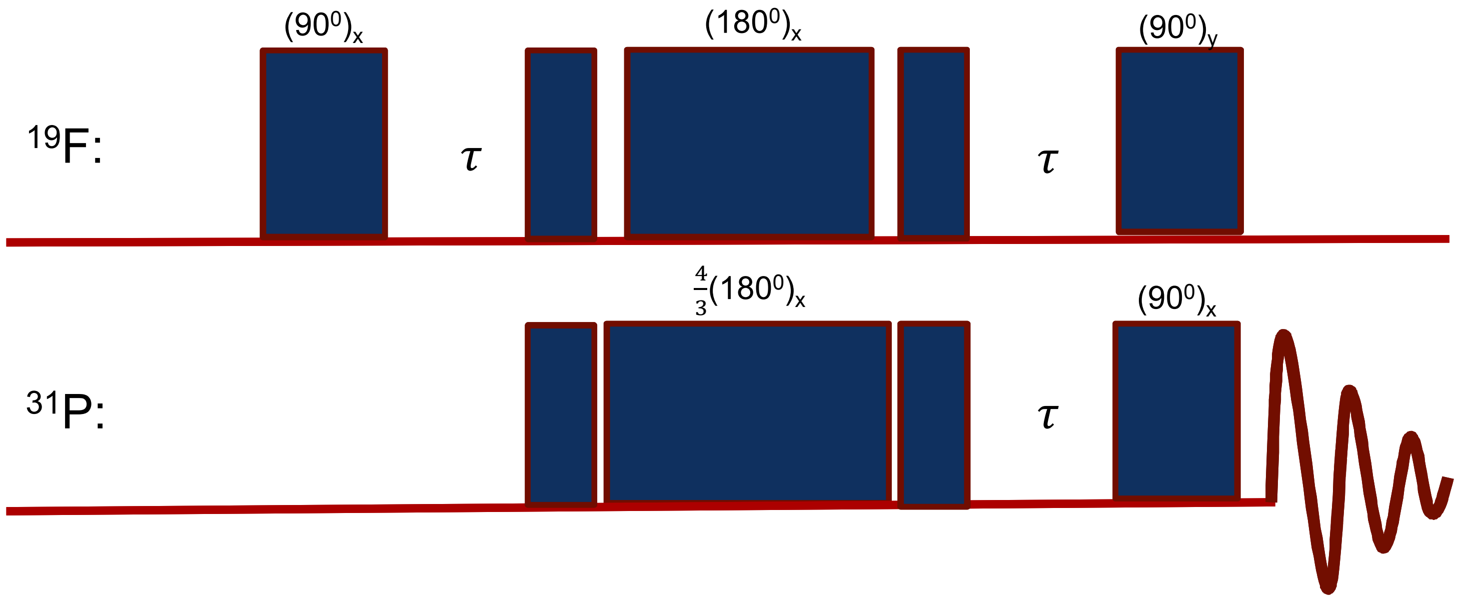
CP



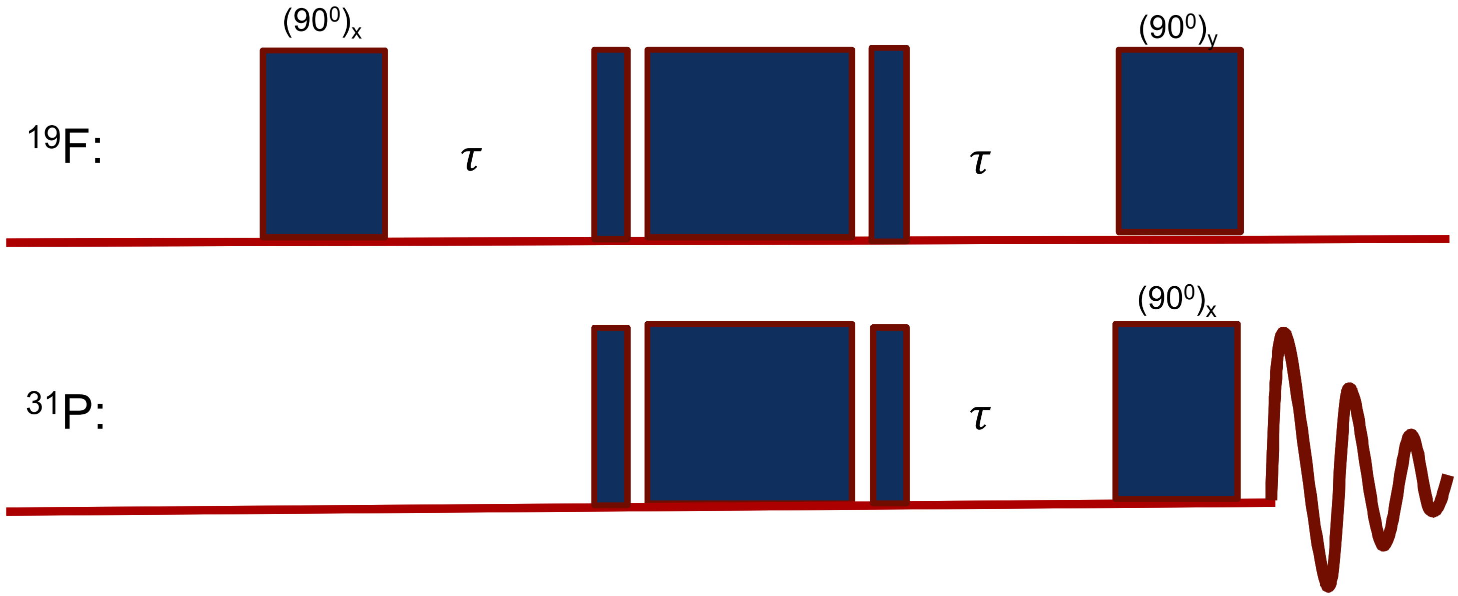
CP_2



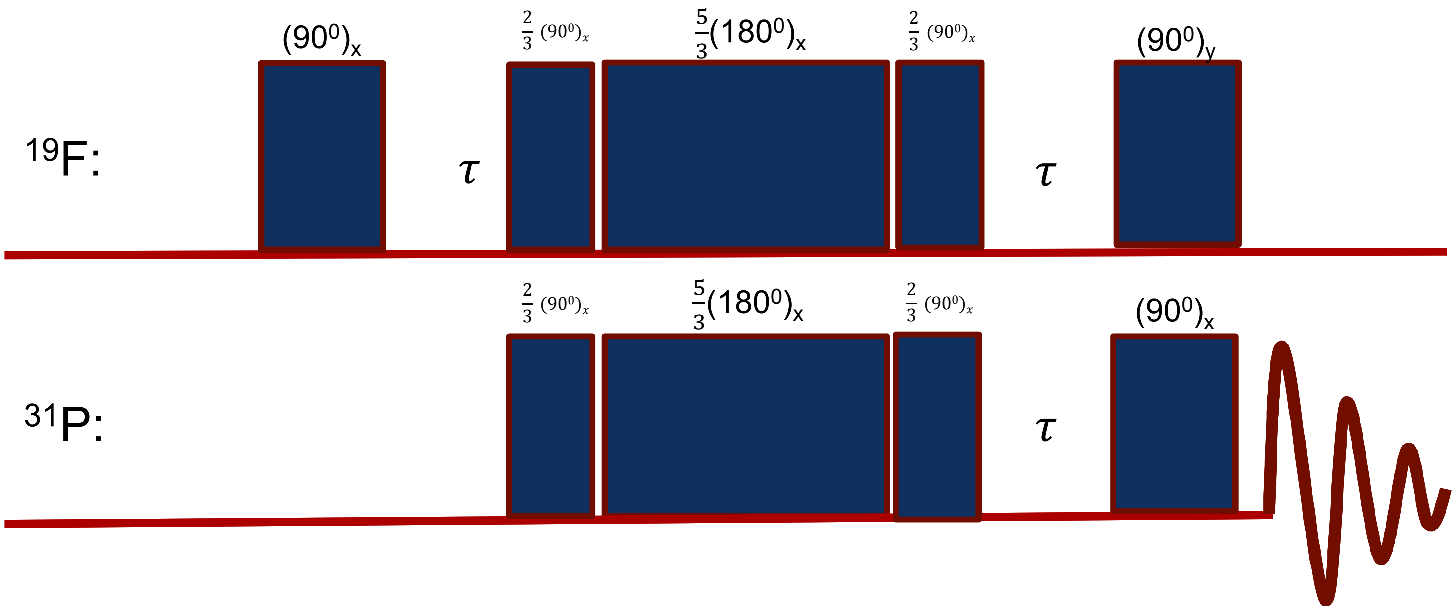
CP_3



CP_SPA



CP_SP



$(90^0)_x$
$\frac{2}{3}(90^0)_x$
$\frac{5}{3}(180^0)_x$
$\frac{2}{3}(90^0)_x$
$(90^0)_y$
^{19}F:
τ
τ
$\frac{2}{3}(90^0)_x$
$\frac{5}{3}(180^0)_x$
$\frac{2}{3}(90^0)_x$
$(90^0)_x$
^{31}P:
τ

CP_SPA_X