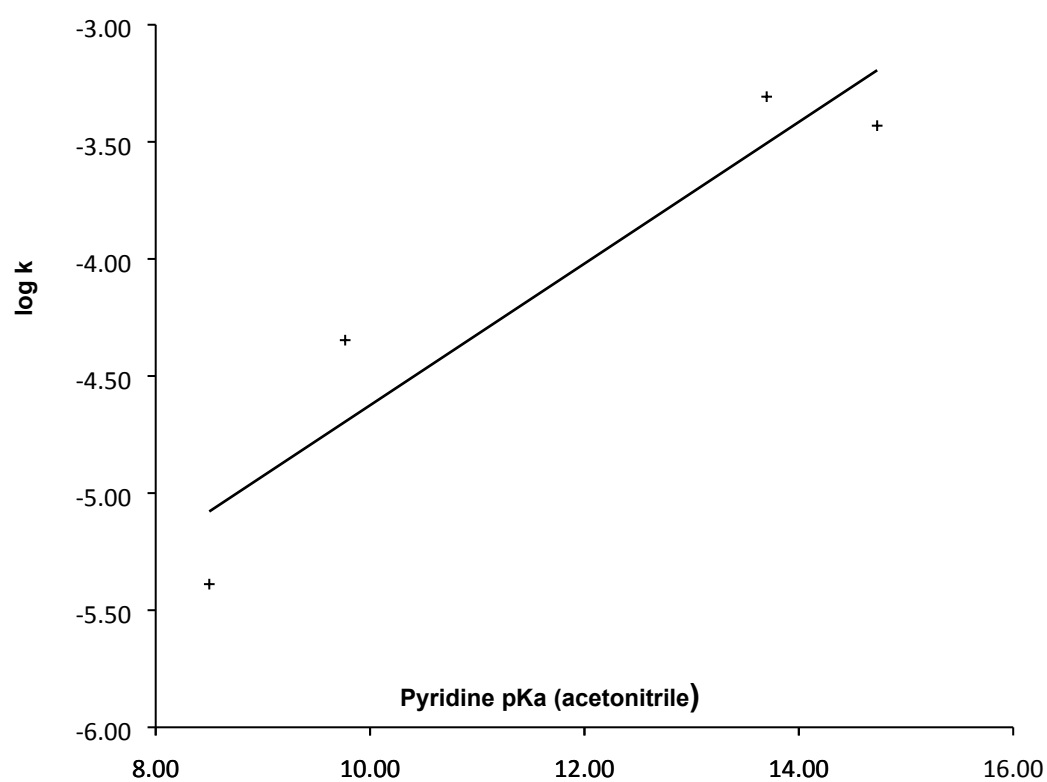


Electronic Supplemental Information

Phosphorothioate Anti-sense Oligonucleotides: The Kinetics and Mechanism of the Sulfurisation of Phosphites by Phenylacetyl Disulfide (PADS)

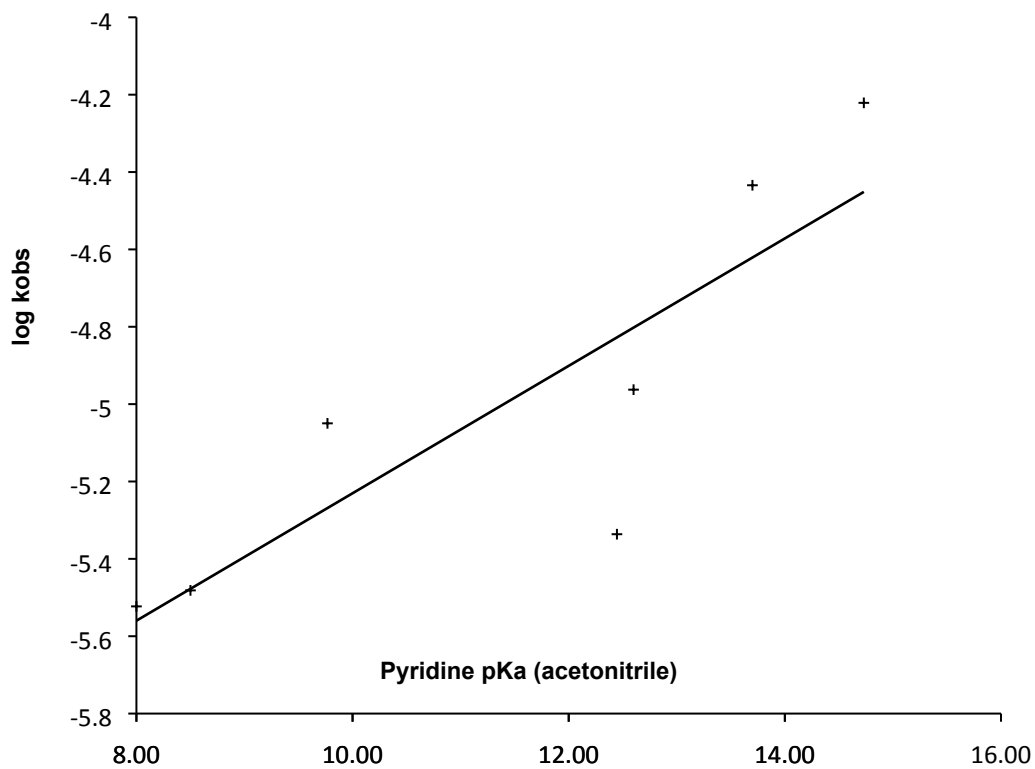
James L. Scotson, Benjamin I. Andrews, Andrew P. Laws and Michael I. Page

1. Brønsted plot for k_{obs} sulfurisation of $\text{P}(\text{PhO})_3$ with 2,2,2',2'-tetramethyl-2,2'-phenylacetyl disulfide as a function of pyridine pK_a



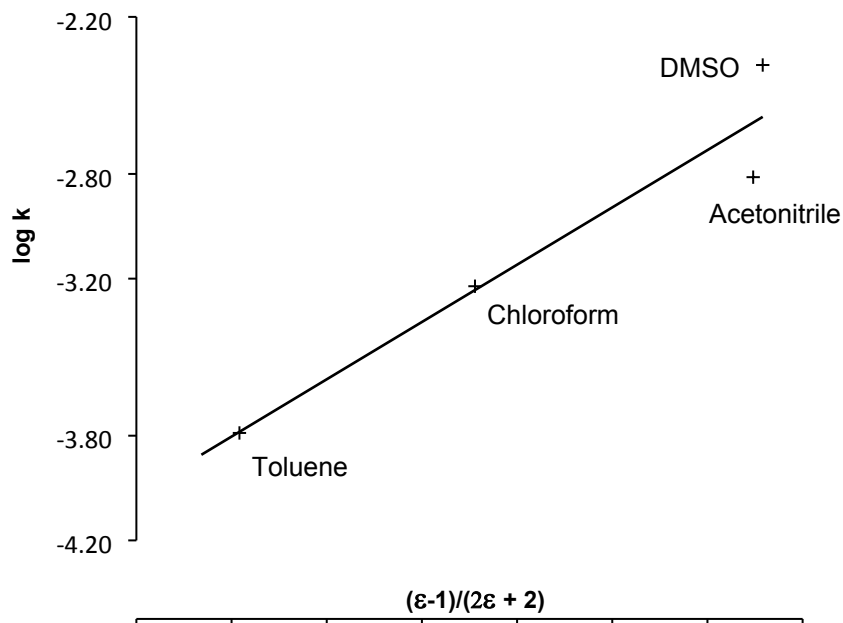
Substituent	pK_a ACN	k_{obs} (s^{-1})	$\log k$
4MeO	14.73	3.71×10^{-4}	-3.43
3Me	13.70	4.93×10^{-4}	-3.31
3Cl	9.77	4.50×10^{-5}	-4.35
4CN	8.50	4.09×10^{-6}	-5.39

2. Brønsted plot for k_{obs} sulfurisation of $\text{P}(\text{PhO})_3$ with dibenzoyl disulfide as a function of pyridine pK_a

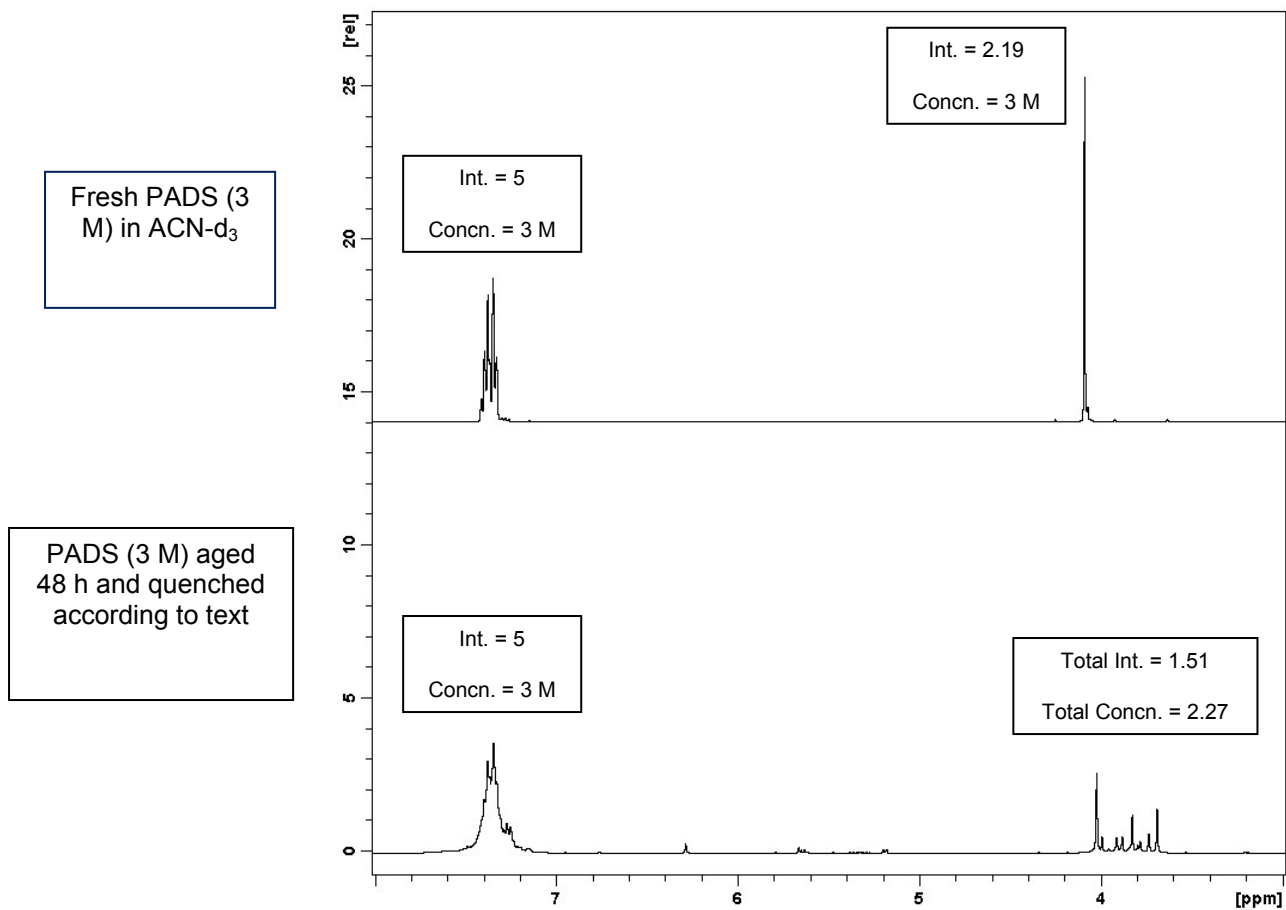


Substituent	pK_a ACN	K_{obs} (s^{-1})	log k
4MeO	14.73	6.01×10^{-5}	-4.22
3Me	13.70	3.68×10^{-5}	-4.43
H	12.60	1.09×10^{-5}	-4.96
3MeO	12.45	4.61×10^{-6}	-5.34
3Cl	9.77	8.92×10^{-6}	-5.05
3CN	8.00	3.00×10^{-6}	-5.52
4CN	8.50	3.30×10^{-6}	-5.48

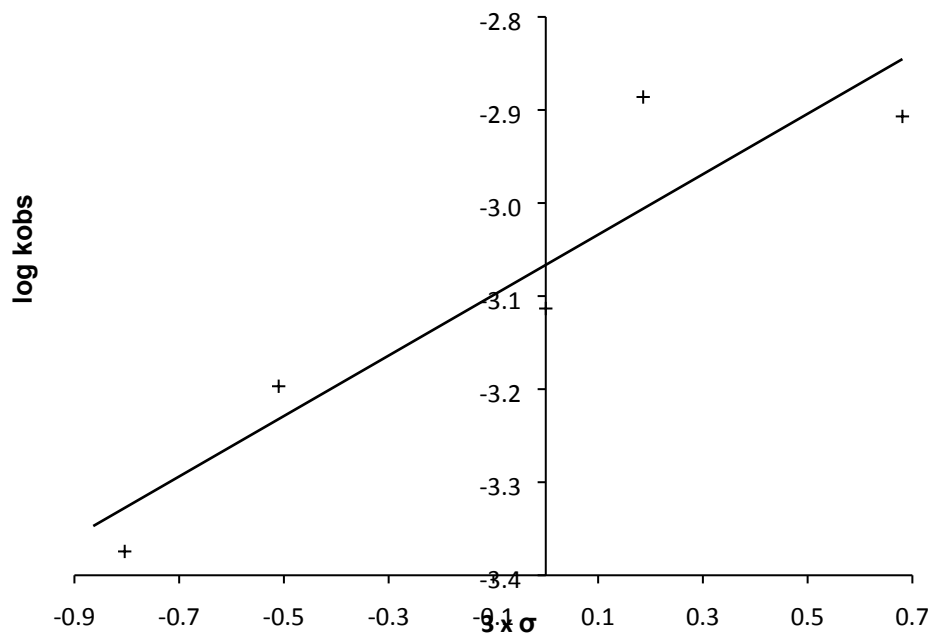
3. Rate of sulfurisation of P(PhO)₃ using fresh PADS in various solvents –plot of log rate constant against dielectric constant ϵ



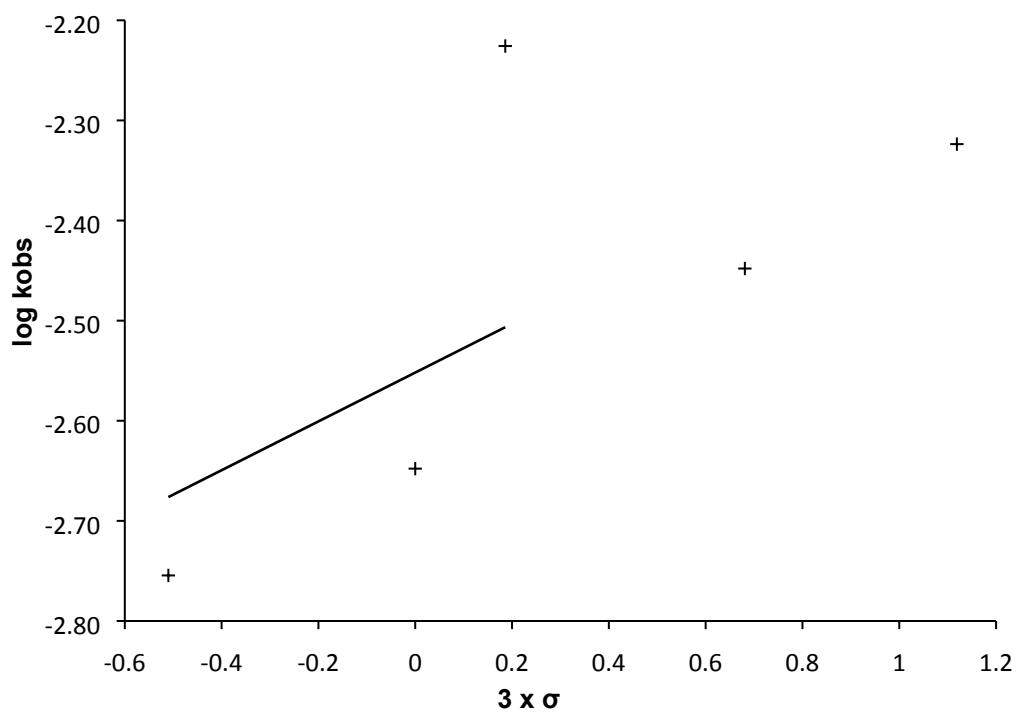
4. Concentration quantification of 48 h aged PADS



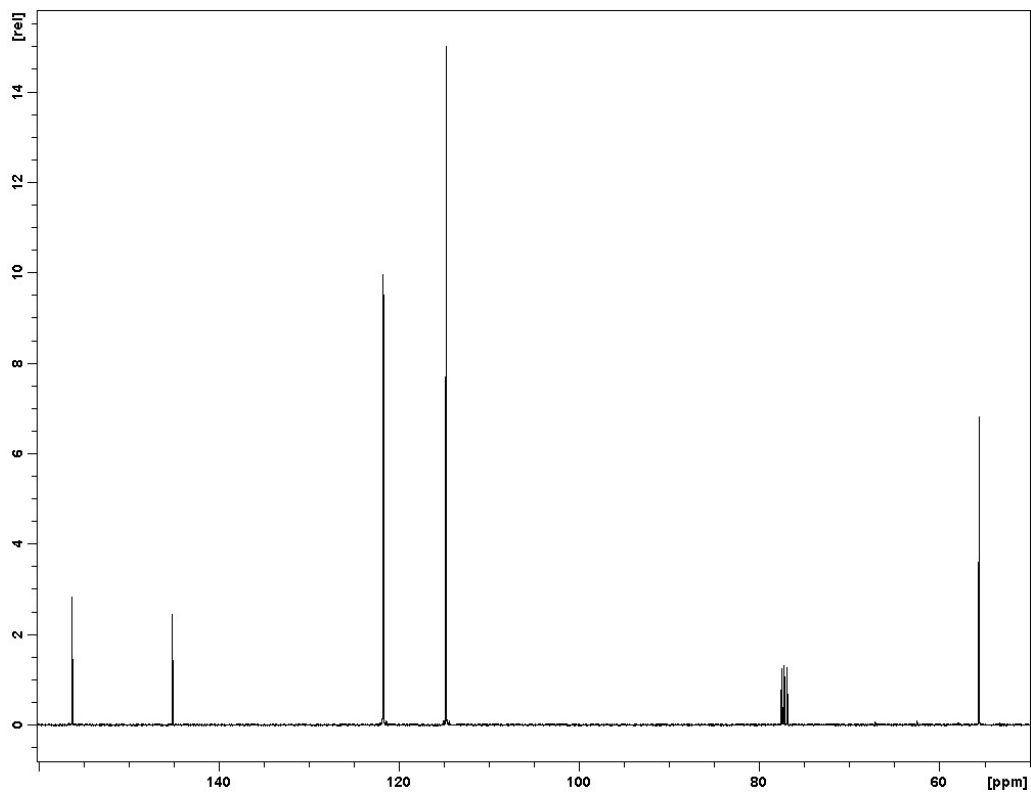
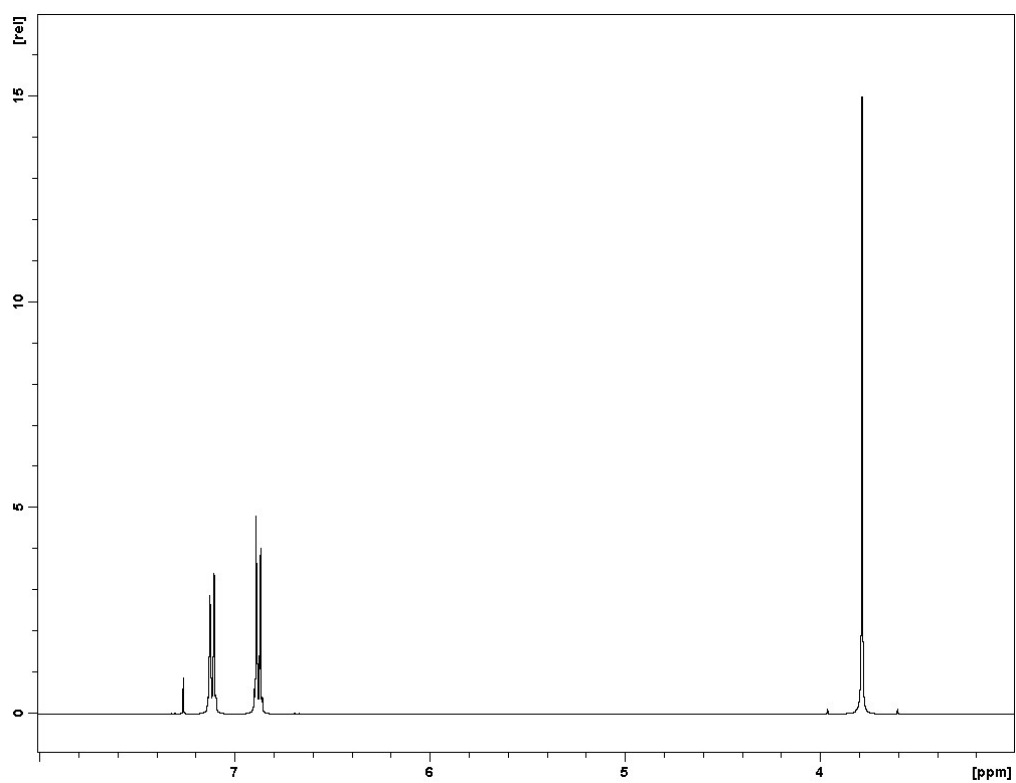
5. Sulfurisation of various substituted aryl phosphites (0.1 M) with fresh PADS (1 M) and 3-picoline (2 M) against substituent Hammett σ value

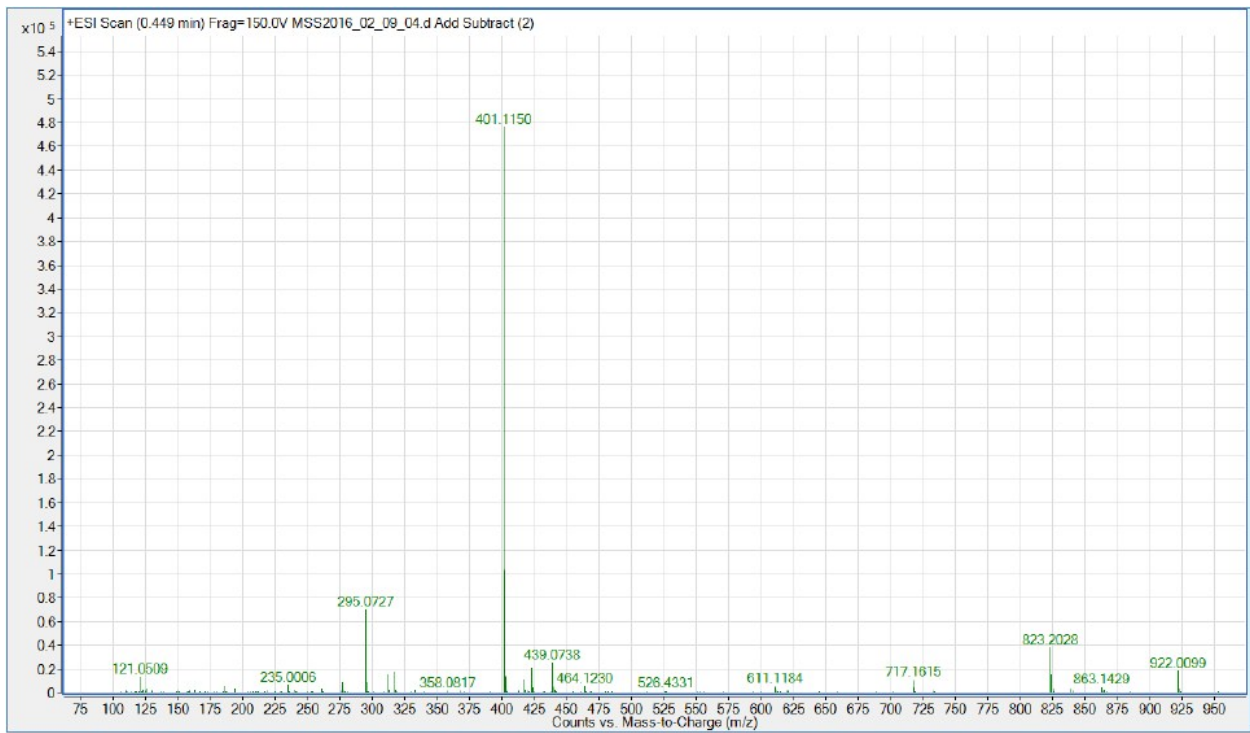
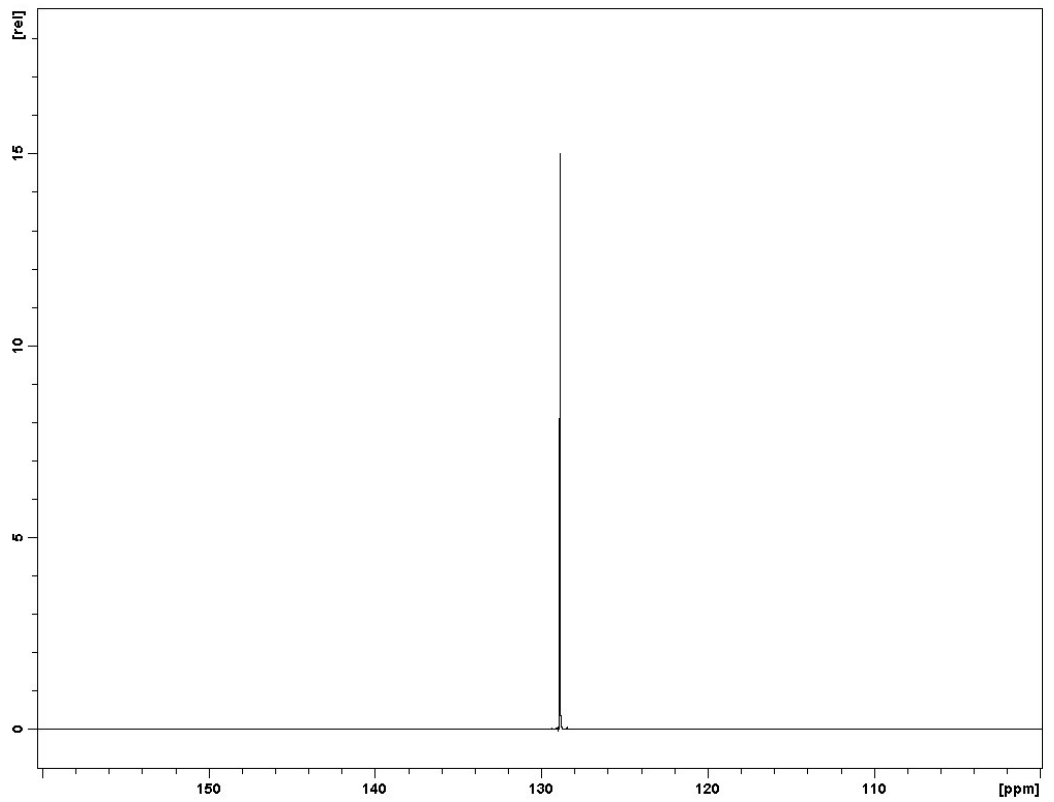


6. Sulfurisation of various substituted aryl phosphites (0.1 M) with PADS (1 M) aged for 18 hours and 3-picoline (2 M) against substituent Hammett σ value

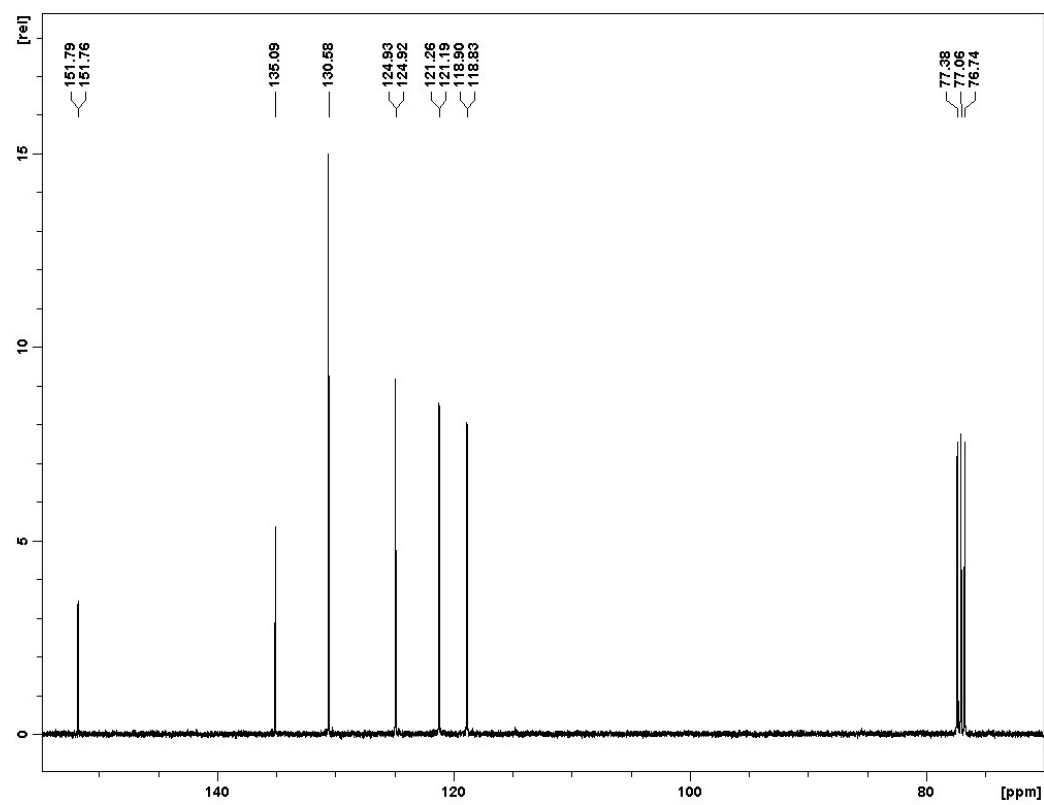
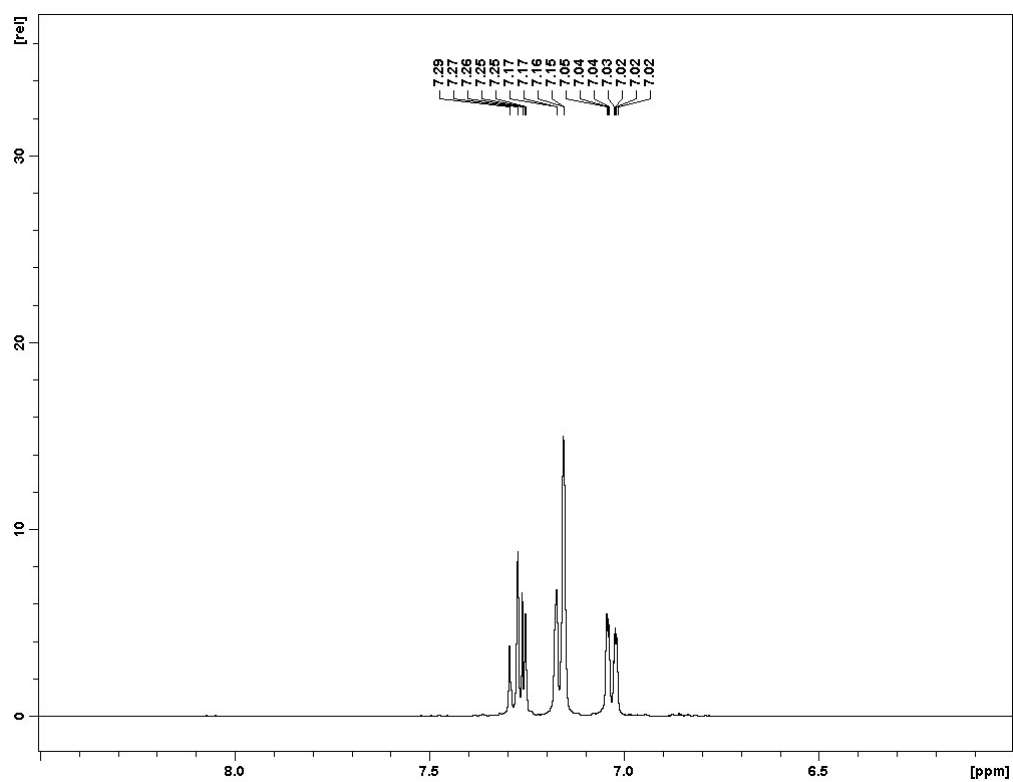


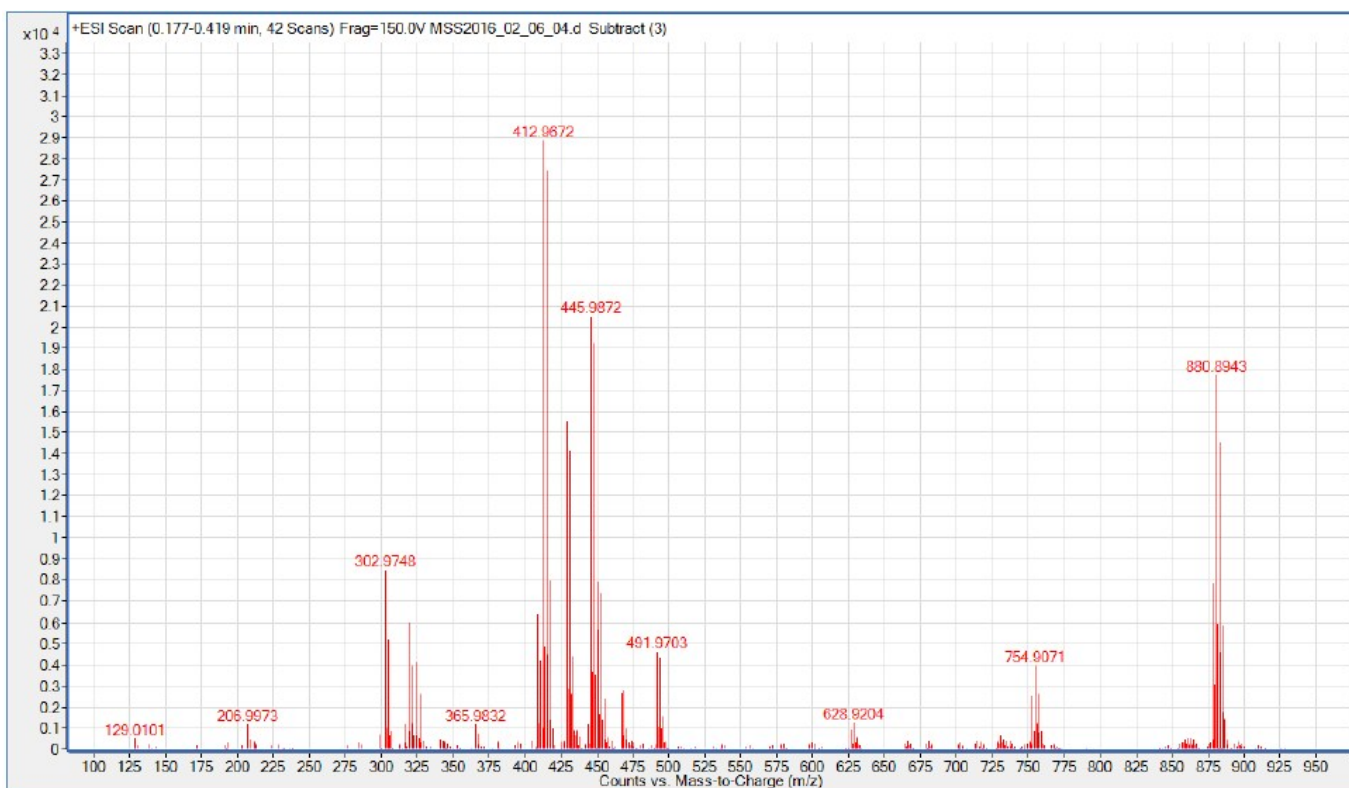
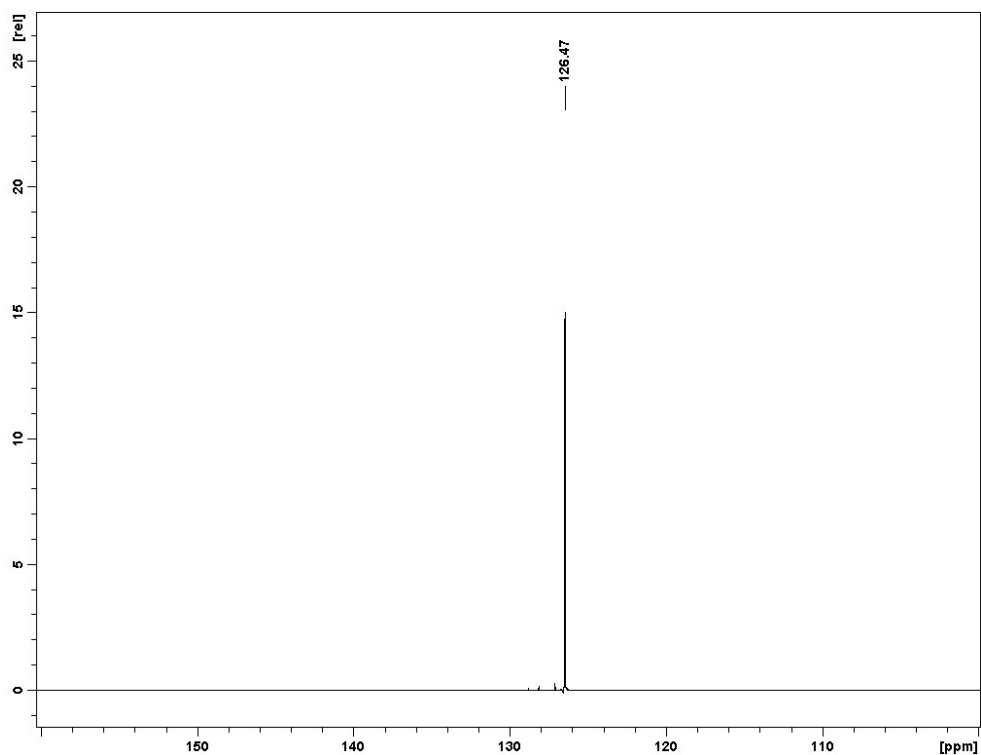
7. ^1H , ^{13}C and ^{31}P NMR of tris-(4-methoxyphenyl)phosphite



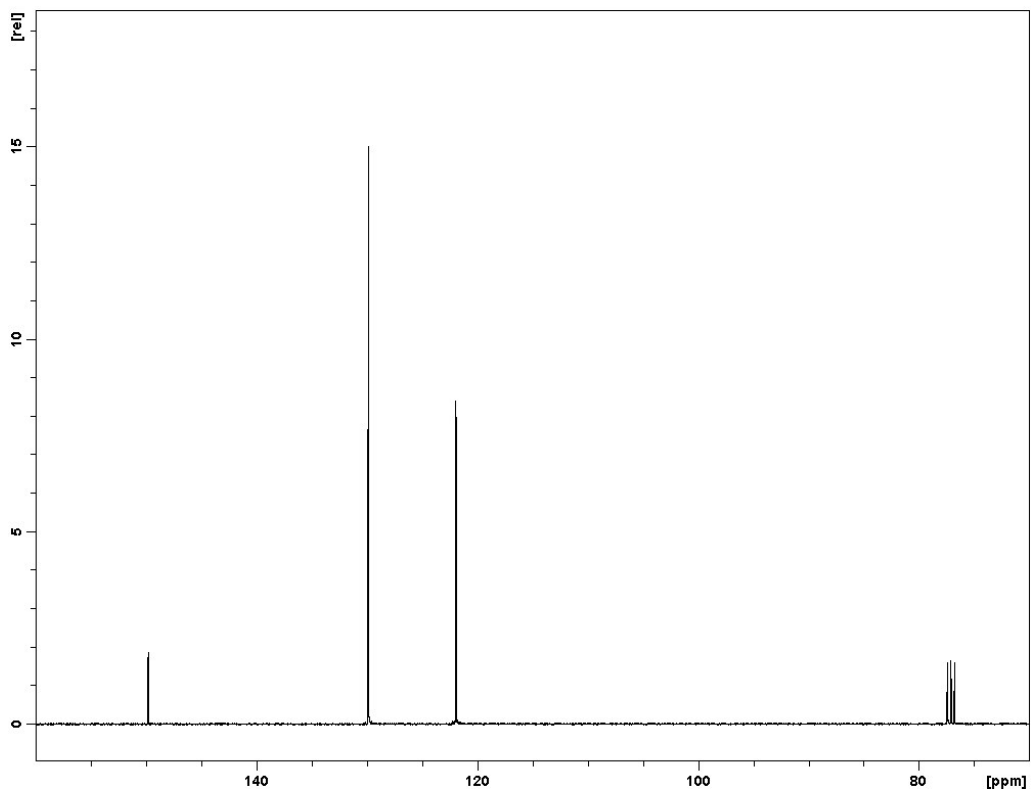
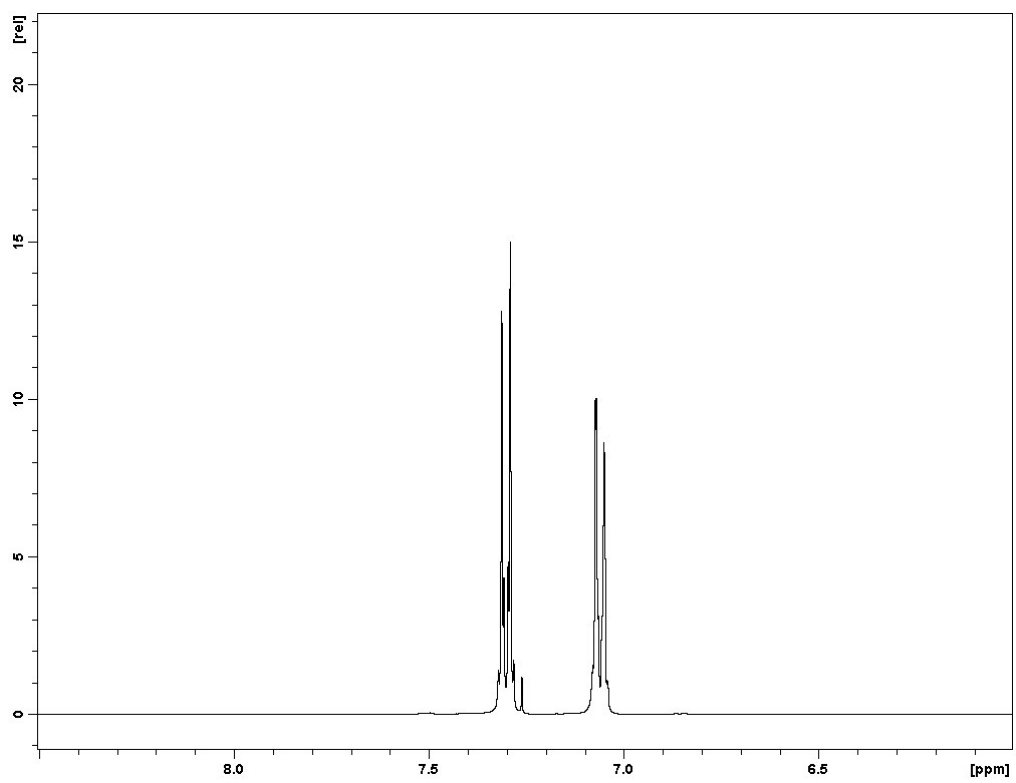


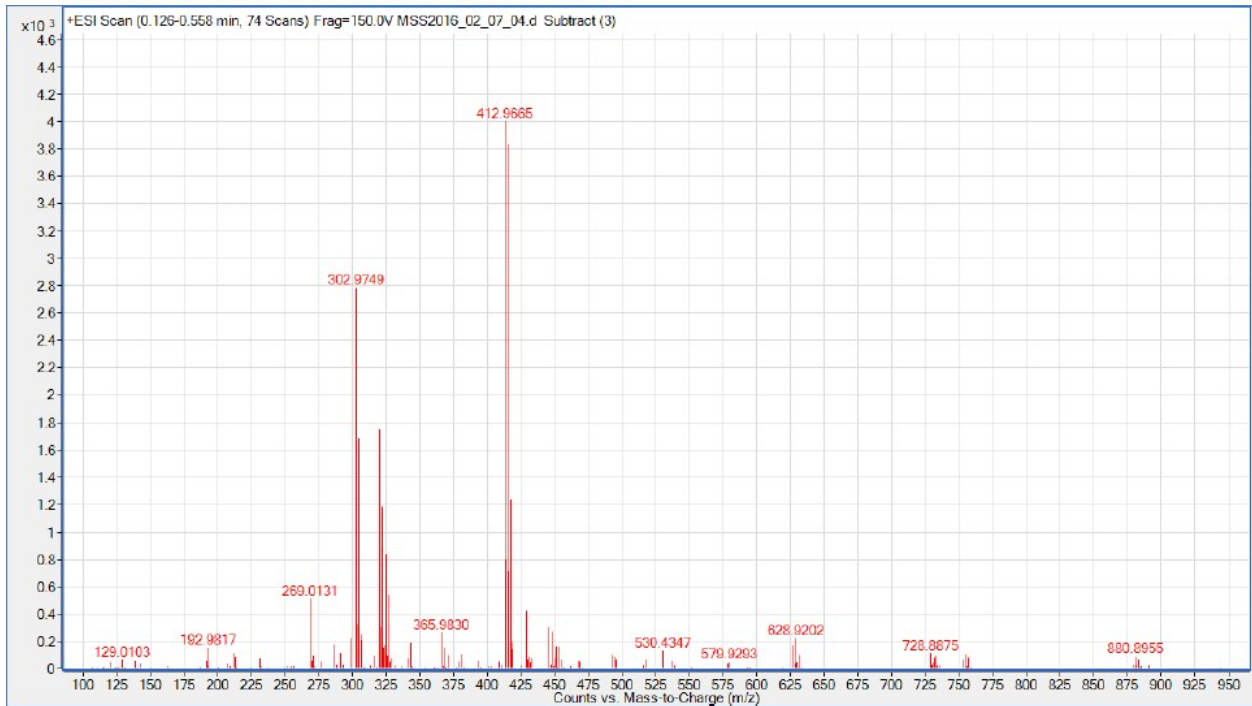
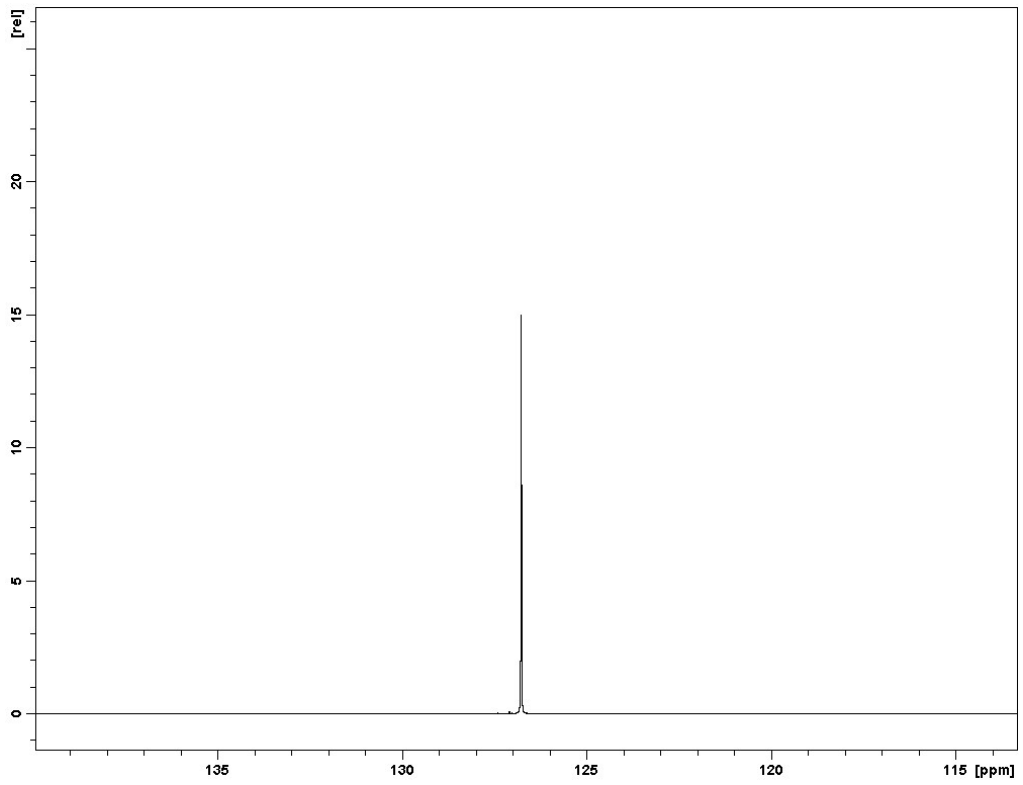
8. ^1H , ^{13}C and ^{31}P NMR of tris(3-chlorophenyl)phosphite



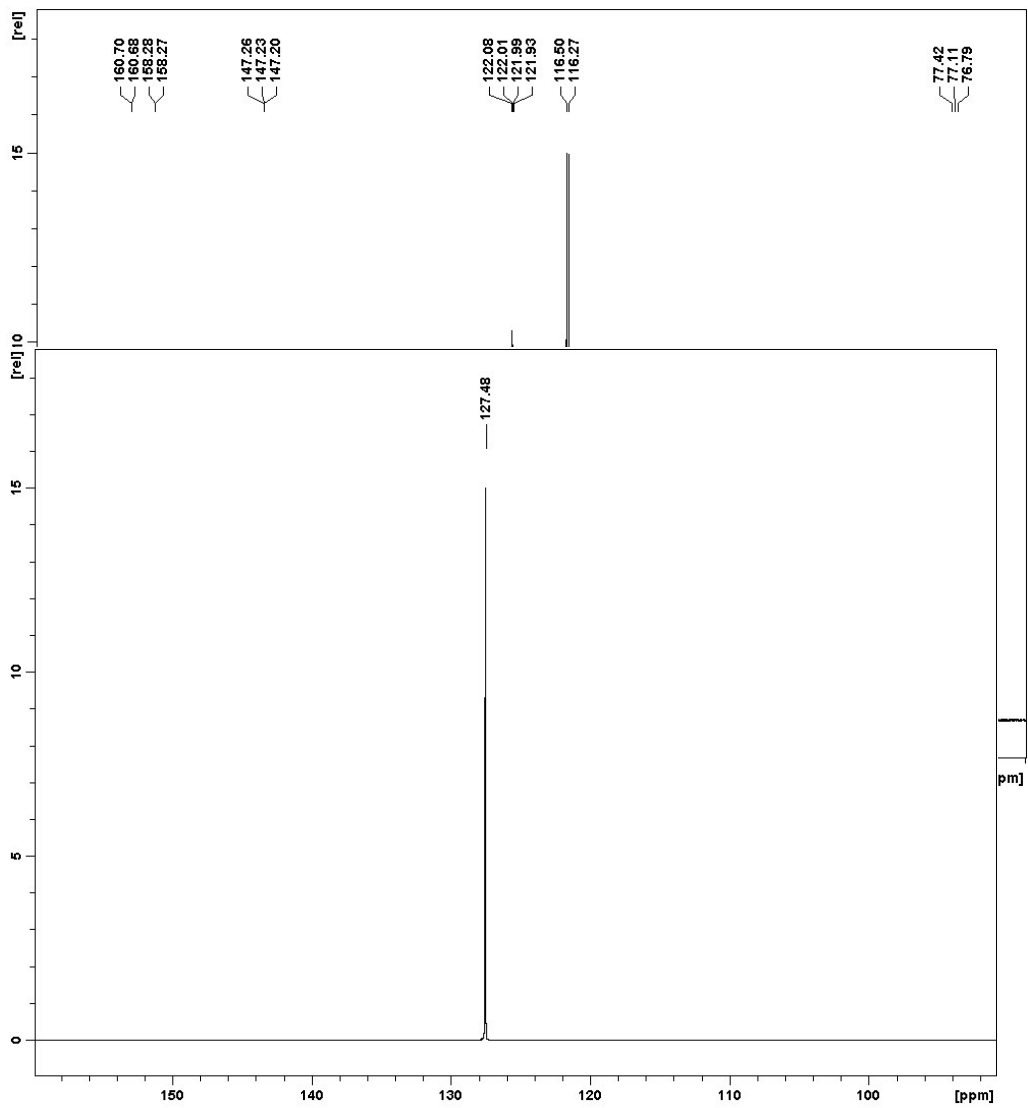
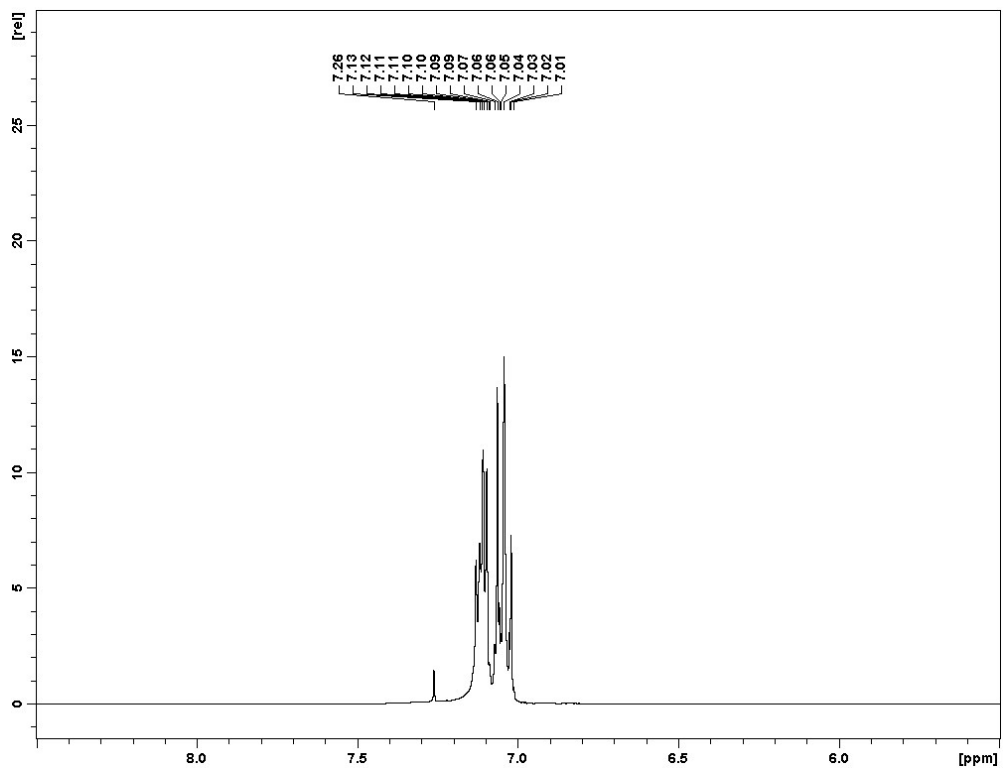


9. ^1H , ^{13}C and ^{31}P NMR of tris(4-chlorophenyl)phosphite





10. ^1H , ^{13}C and ^{31}P NMR of tris (4-fluorophenyl)phosphite



[ppm]

[ppm]

