2 2D Experiments
2.2 H,H COSY

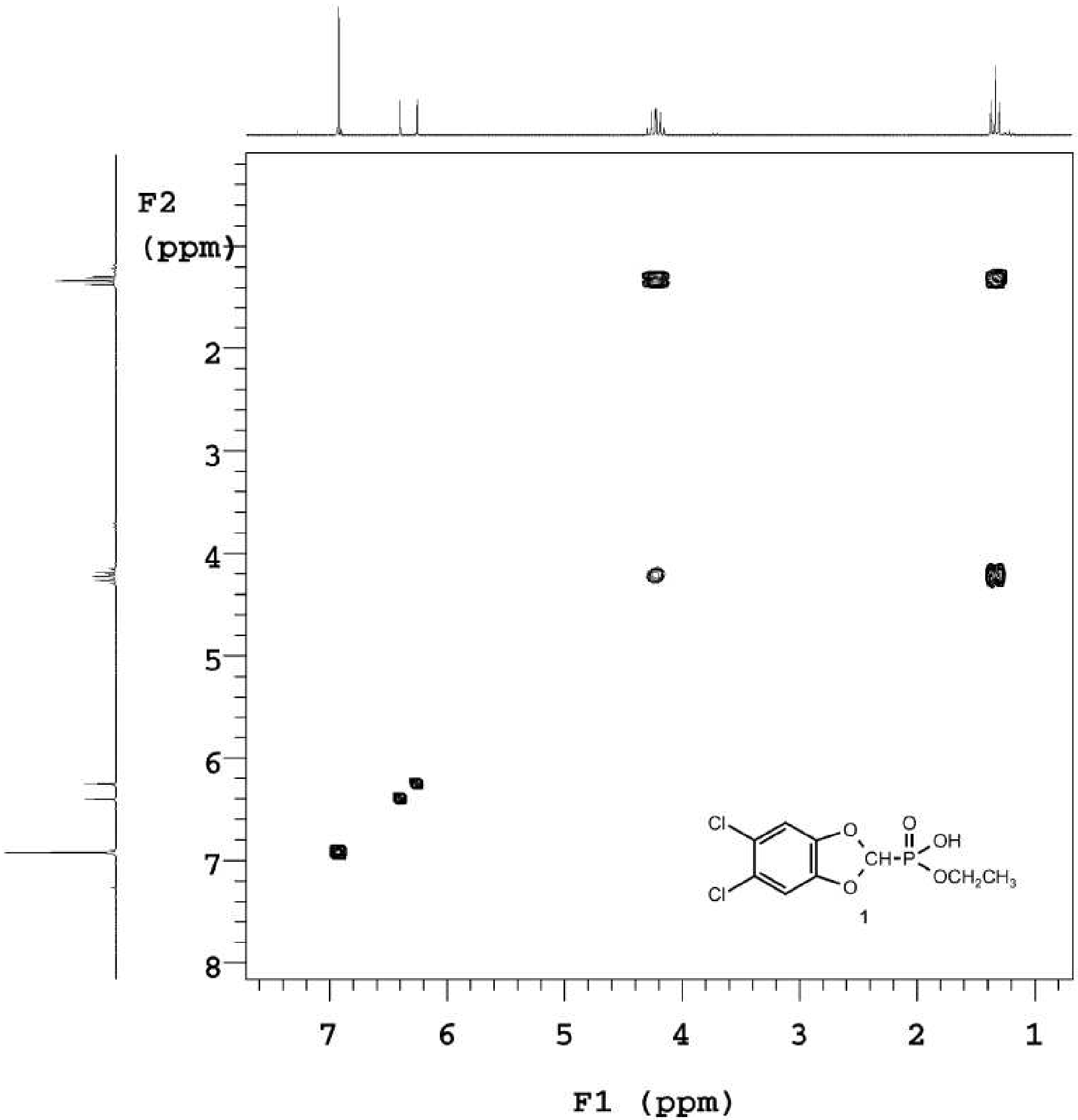
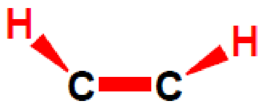


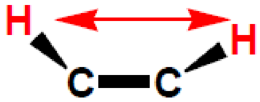
Fig. 24 H,H COSY spectrum of compound 1 in $CDCl_3$, measurement time 3.5 min

Αλληλεπίδραση δίπόλο-δίπολο

Εκτός από την αλληλεπίδραση μέσω των δεσμικών ηλεκτρονίων, τα πυρηνικά σπίν αλληλεπιδρούν και μέσω του χώρου. Αυτή η αλληλεπίδραση ονομάζεται αλληλεπίδραση δίπολο-δίπολο.



Σύζευξη σπιν-σπιν



Αλληλεπίδραση δίπολο-δίπολο

Η μέγιστη τιμή του NOE μεταξύ δύο πυρήνων I και S δίνεται από τη σχέση:

$$\mathrm{NOE(max)} = \frac{\gamma_S}{2\gamma_I}$$

γ_I γυρομαγνητικός λόγος πυρήνα I

γ_S γυρομαγνητικός λόγος πυρήνα S

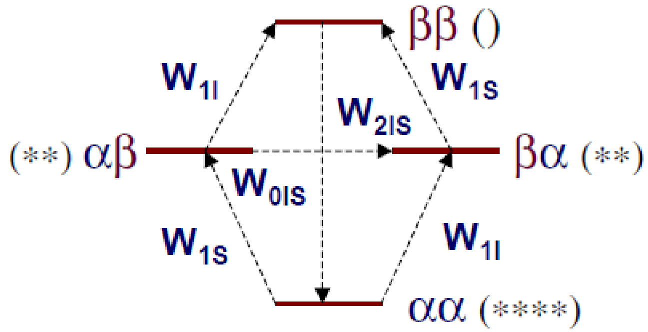
Το αποτέλεσμα της αλληλεπίδρασης δίπολο-δίπολο είναι γνωστό ως φαινόμενο NOE (Nuclear Overauser Enhancement) και επηρεάζει την εμφάνιση του φάσματος NMR.

Το NOE εξαρτάται από το αντίστροφο της έκτης δύναμης της απόστασης μεταξύ π.χ. δύο πρωτονίων, r^6. Έτσι, για να εμφανίζουν δύο πρωτόνια NOE θα πρέπει να βρίσκονται αρκετά κοντά το ένα με το άλλο. Επίσης, επειδή το NOE οφείλεται στην αλληλεπίδραση μέσω του χώρου, είναι ανεξάρτητο από το εάν τα πρωτόνια εμφανίζουν σύζευξη ή όχι.

Nuclear Overhauser Effect (NOE)

- The ***NOE*** is one of the ways in which the system (a certain spin) can release energy. Therefore, it is profoundly related to relaxation processes. In particular, the NOE is related to exchange of energy between two spins that are not scalarly coupled ($J_{IS} = 0$), but have ***dipolar coupling***.

- The NOE is evidenced by enhancement of certain signals in the spectrum when the equilibrium (or populations) of other nearby are altered. We use a two spin system energy diagram to explain it:



- **W** represents a ***transition probability***, or the rate at which certain transition can take place. For the system in equilibrium we can have $\mathbf{W_{1I}}$ and $\mathbf{W_{1S}}$ transitions, which represents ***single quantum*** transitions.

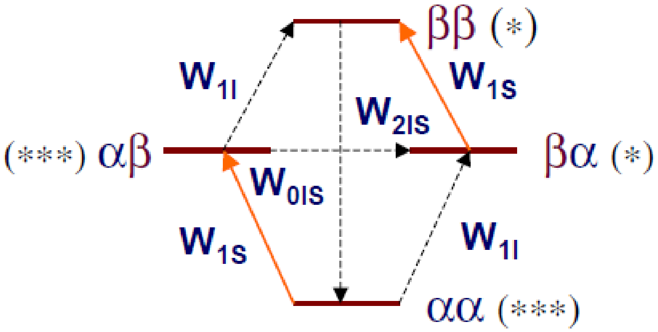
- $\mathbf{W_{0IS}}$ and $\mathbf{W_{2IS}}$ are ***zero*** and ***double quantum*** transitions, are forbidden and have a much lower probability.

Nuclear Overhauser Effect (continued)

- The $\mathbf{W_{1I}}$ and $\mathbf{W_{1S}}$ transitions, are related to spin-lattice or longitudinal relaxation.

- Here we see that relaxation due to dipolar coupling takes place when the spins give away energy by processes that occur at frequencies close to $\omega = \gamma * B_o$, which include the movement (translation, rotation) and collision of spins.

- We now ***saturate*** the **S** transition, which means that we make both its energy levels equal. The populations of the **S** transitions are now the same:



- The $\mathbf{W_{1S}}$ transitions are not possible (we have the same populations in these levels), and the $\mathbf{W_{1I}}$ is not happening (we have not affected the equilibrium for this spin). The $\mathbf{W_{0IS}}$ and $\mathbf{W_{2IS}}$ become the only way **S** can relax.

- These relaxation pathways for **S** also involve transitions of **I**, so thus the enhancement of this signal. $\mathbf{W_{2IS}}$ will give positive enhancement of **I**, and $\mathbf{W_{0IS}}$ will give negative enhancements.

Nuclear Overhauser Effect (even more…)

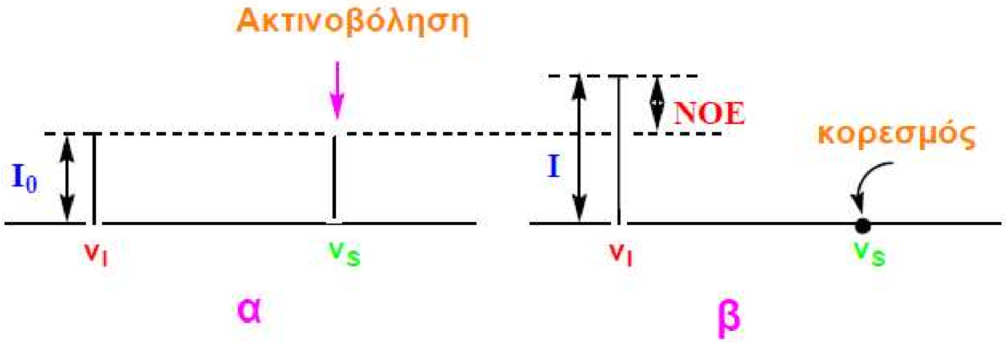
- We cannot detect $\mathbf{W_{2IS}}$ or $\mathbf{W_{0IS}}$, but they affect the way the spin system relaxes. One has a rate close to twice $\boldsymbol{\omega}$, while the other one is almost zero. So one will be related to very slow motions, and the other one to fast tumbling...

- If we now put all this in a big equation (the Solomon equation) we get something that will help us see several things.

. We have:

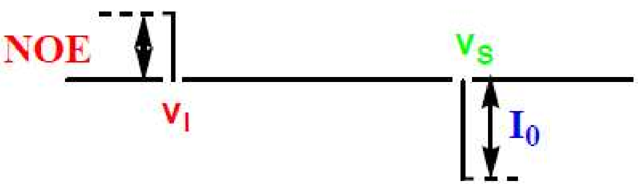
$$\eta = \gamma_I / \gamma_S * \frac{W_{2IS} - W_{0IS}}{2 * W_{1S} + W_{2IS} + W_{0IS}}$$

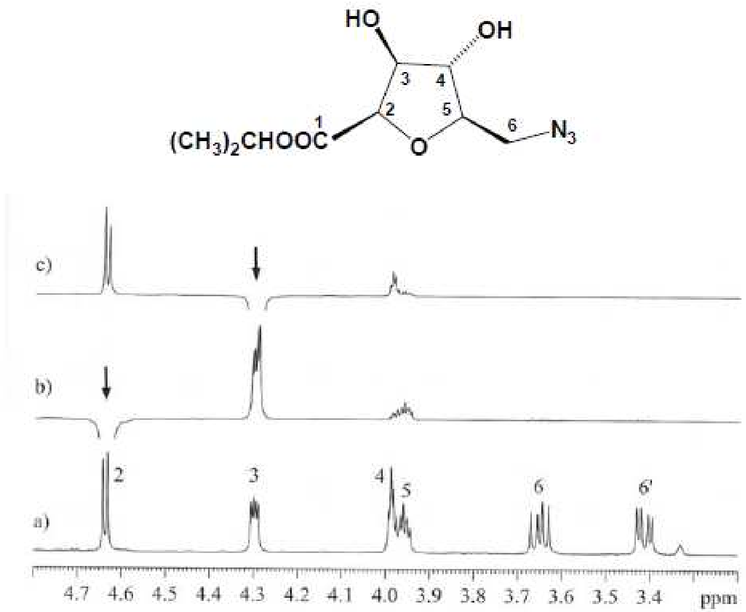
Μέτρηση του NOE



$$\text{NOE} = f_I(S) = \frac{I - I_0}{I_0}$$

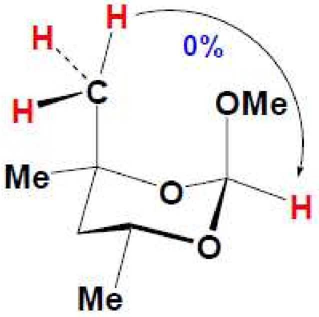
Φάσμα (β) – Φάσμα (α) = Φάσμα διαφοράς

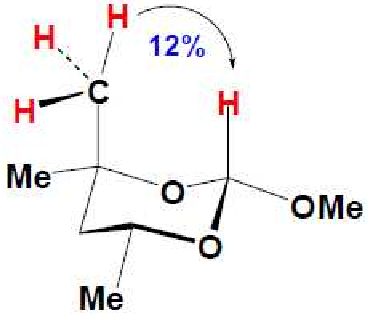


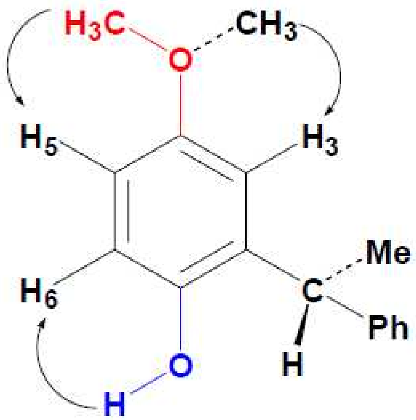


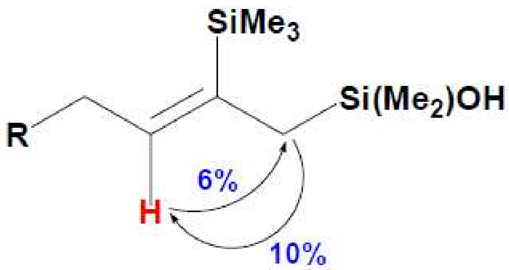
Η τεχνική λήψης φασμάτων διαφοράς NOE χρησιμοποιείται στην περίπτωση που το NOE είναι πολύ μικρό (< 1%).

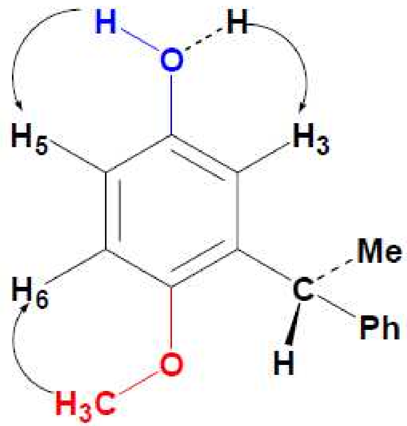
Εφαρμογές του NOE

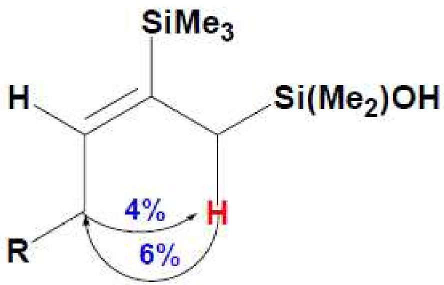




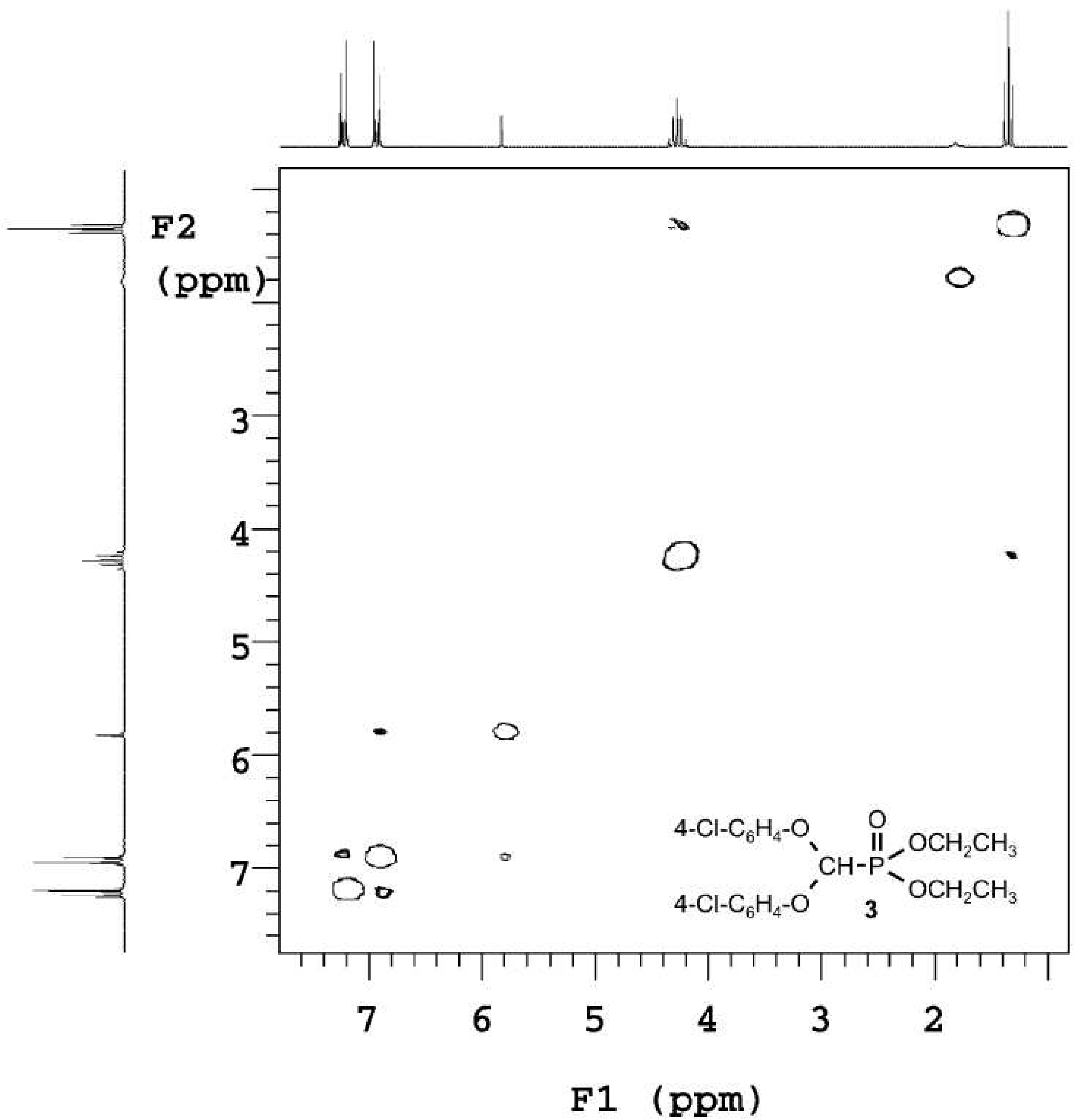








2.3 2D NOE - H,H NOESY



2.3 2D NOE - H,H NOESY

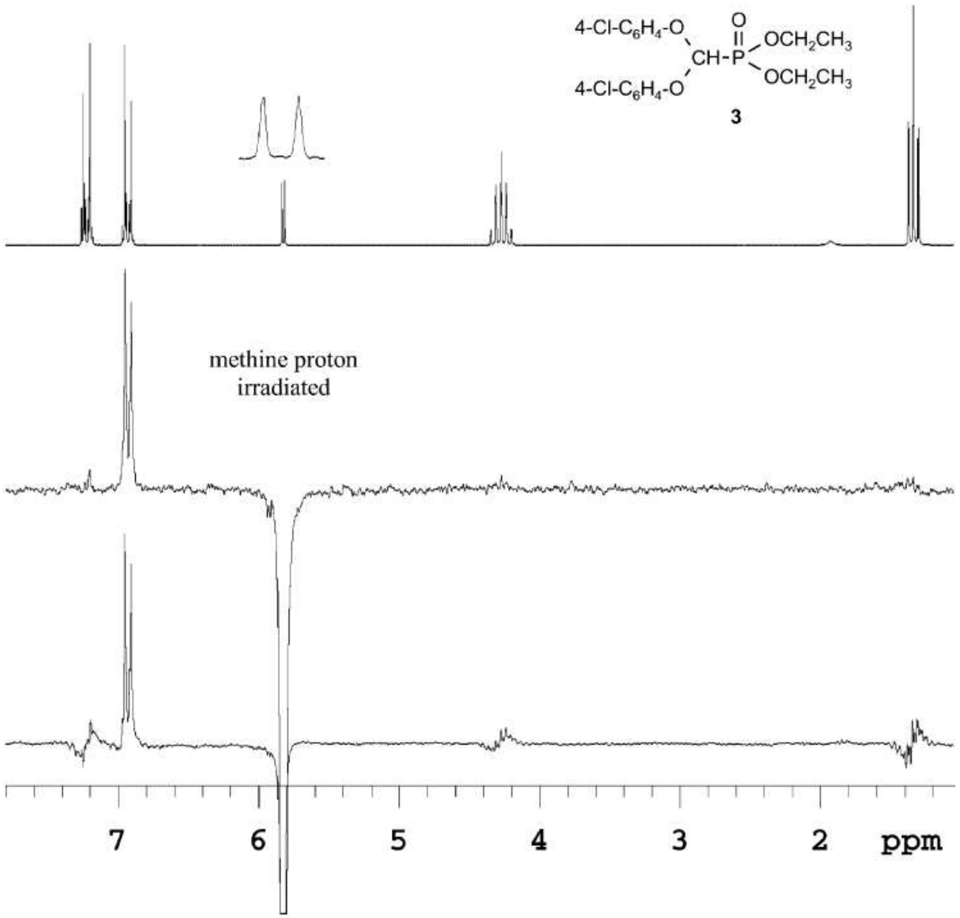
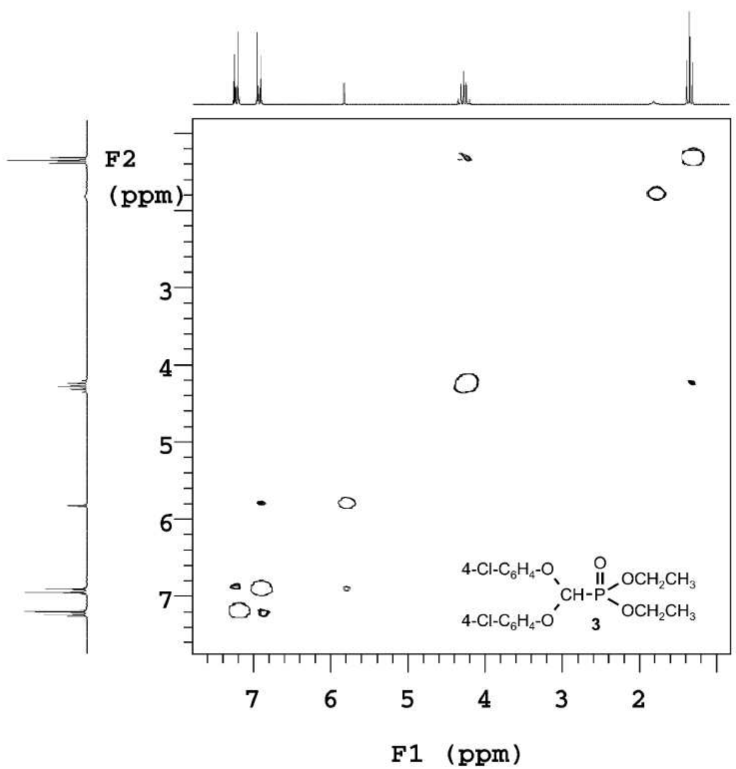
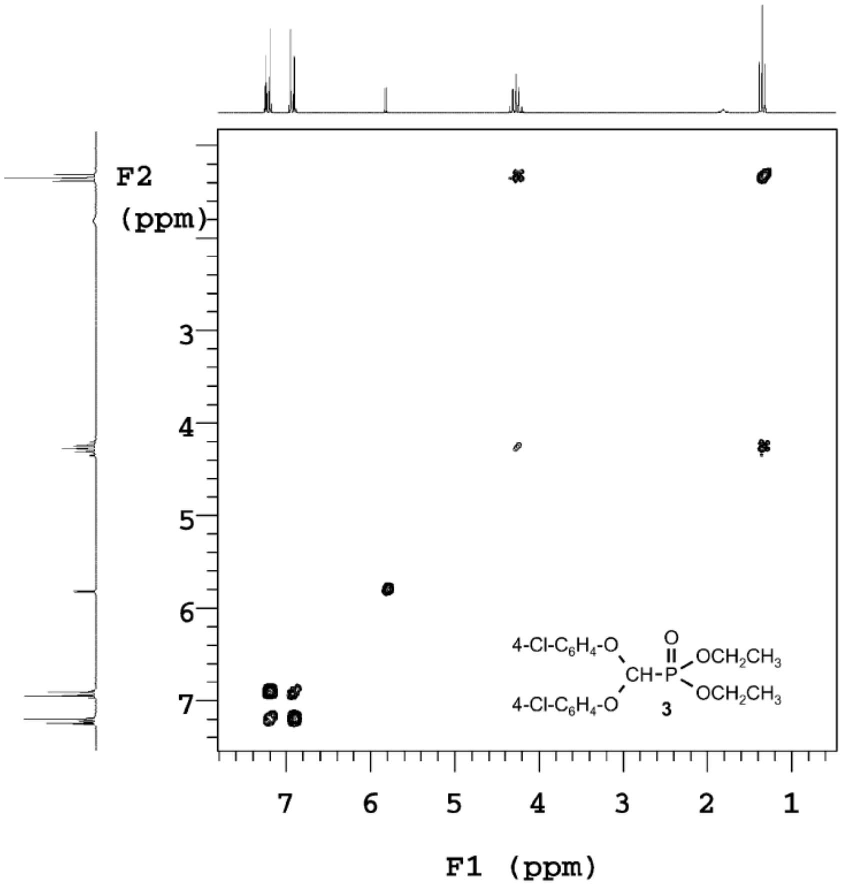


Fig. 12a–c NOE experiments carried out at 200 MHz on compound 3. a Normal spectrum, with expansion of methine doublet; b selective NOE spectrum, total time required 18 min; c NOE difference spectrum, total time required (preparation, measurement) 42 min



2.3 2D NOE - H,H NOESY

COSY



NOESY

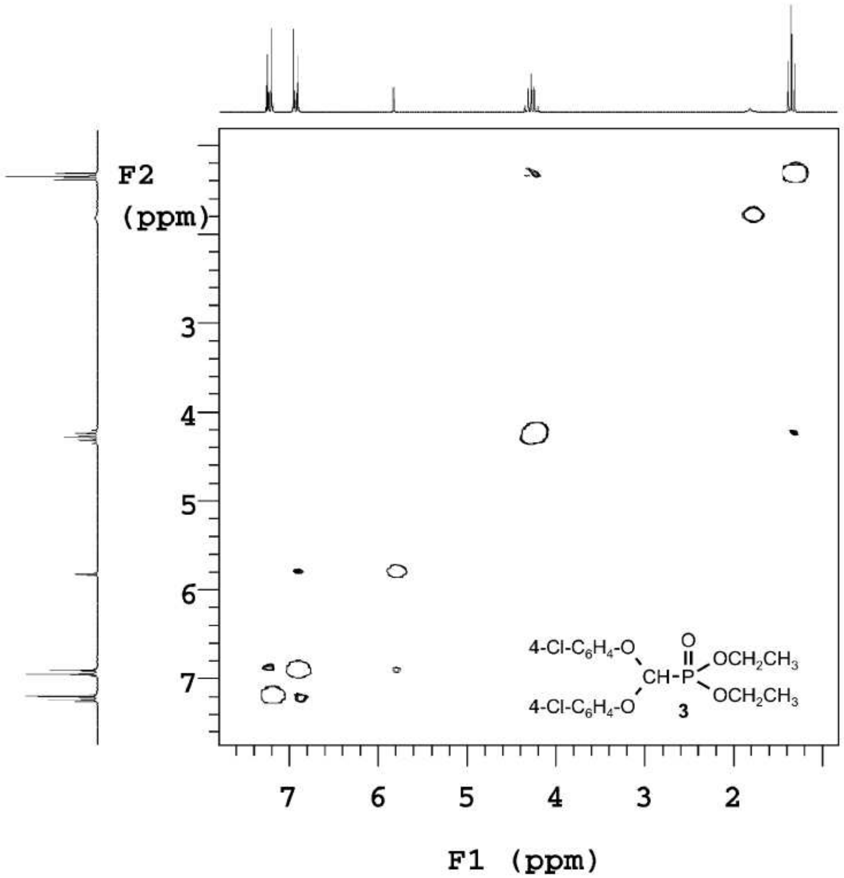
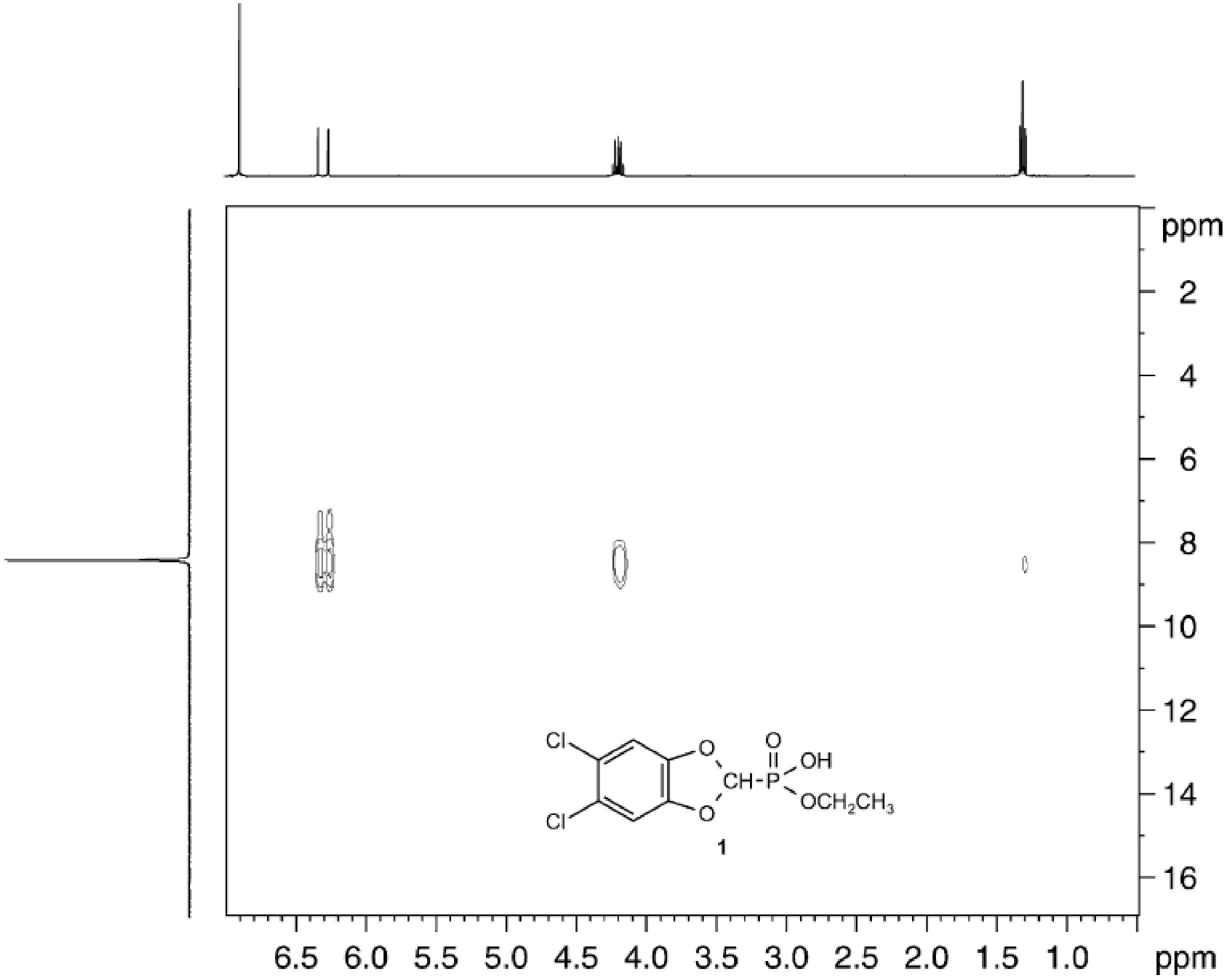


Fig. 25 2D spectra of compound **3**. *Top*: COSY (200 MHz, $CDCl_3$, measurement time 15 min); *below*: NOESY spectrum (200 MHz, $CDCl_3$, measurement time 40 min)

Ετεροπυρηνική Φασματοσκοπία NMR

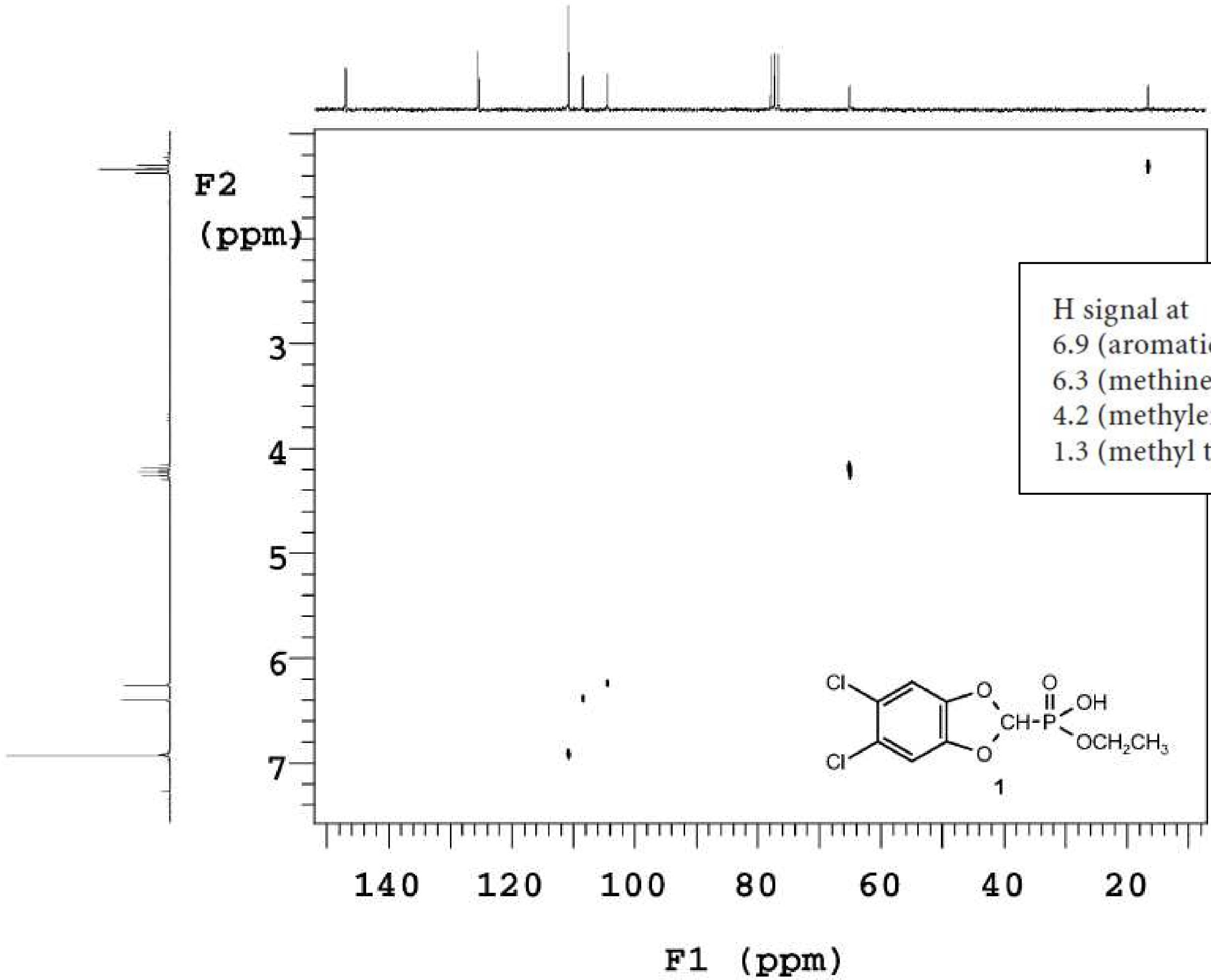
2.4
P,H COSY: with Varying Mixing Times for the Coupling



Chemical shift (ppm)	J_{HP} (Hz)
11.58	0
6.92	not observed
6.32	28.7
4.20	8.0
1.33	0.6

Fig. 26 P,H correlation spectrum of compound 1 (400 MHz, 5% in $CDCl_3$, delay set for J_{PH} = 1.65 Hz, measurement time 12 min)

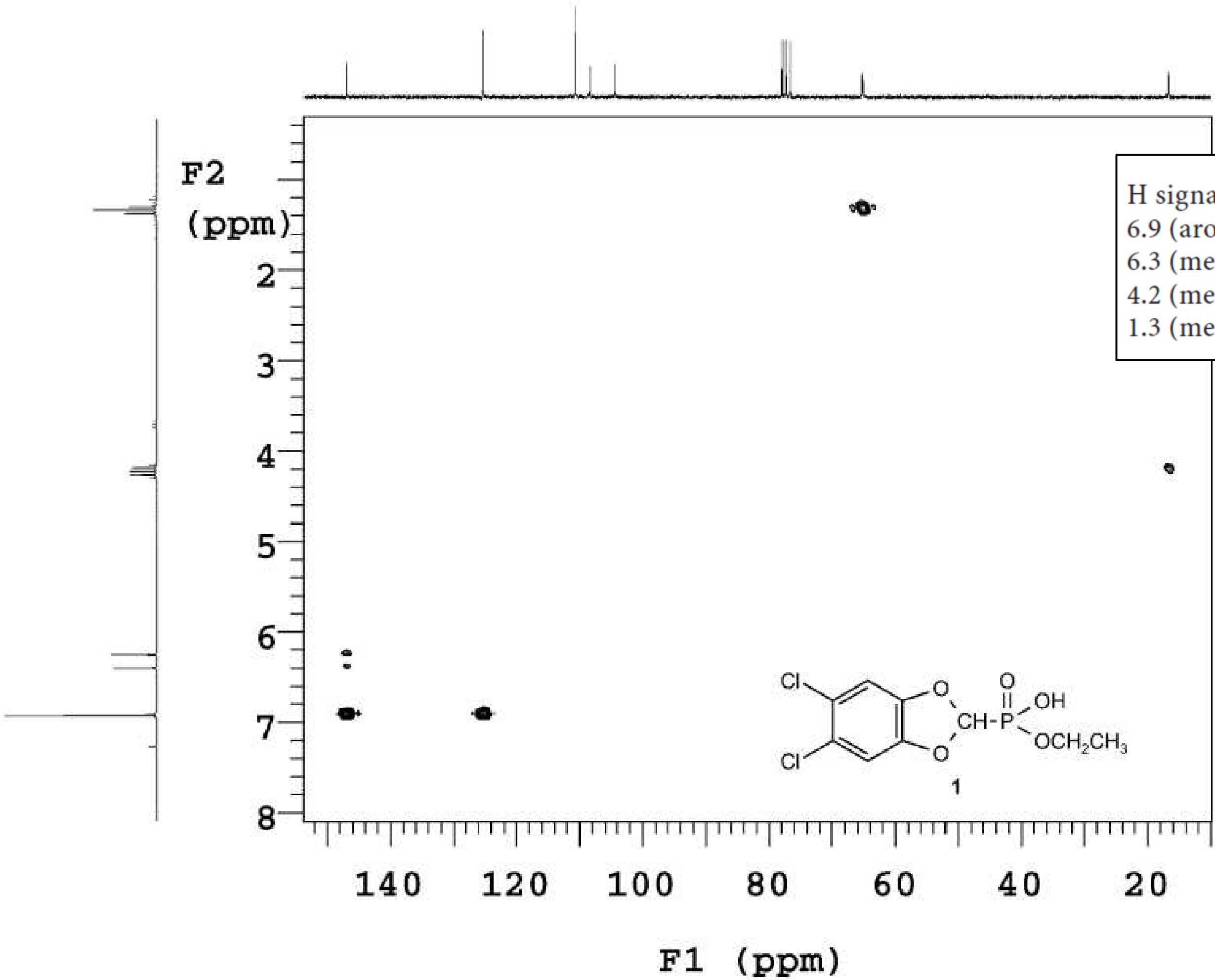
2.5
C,H Direct Correlation



H signal at	correlates with	C signal at
6.9 (aromatic)		110
6.3 (methine doublet)		106
4.2 (methylene multiplet)		65
1.3 (methyl triplet)		17

Fig. 27 C,H correlation spectrum for compound 1 (set for directly bonded hydrogens, 200 MHz, 5% in $CDCl_3$, measurement time 60 min, inverse detection)

2.6
C,H Long Range Correlation



H signal at	correlates with	C signals at
6.9 (aromatic)		147, 125
6.3 (methine doublet)		147
4.2 (methylene multiplet)		17
1.3 (methyl triplet)		65

Fig. 28 C,H correlation spectrum for compound 1 (set for long-range coupling, 400 MHz, 5% in $CDCl_3$, measurement time 18 min, inverse detection)

2.8
P,P Correlation

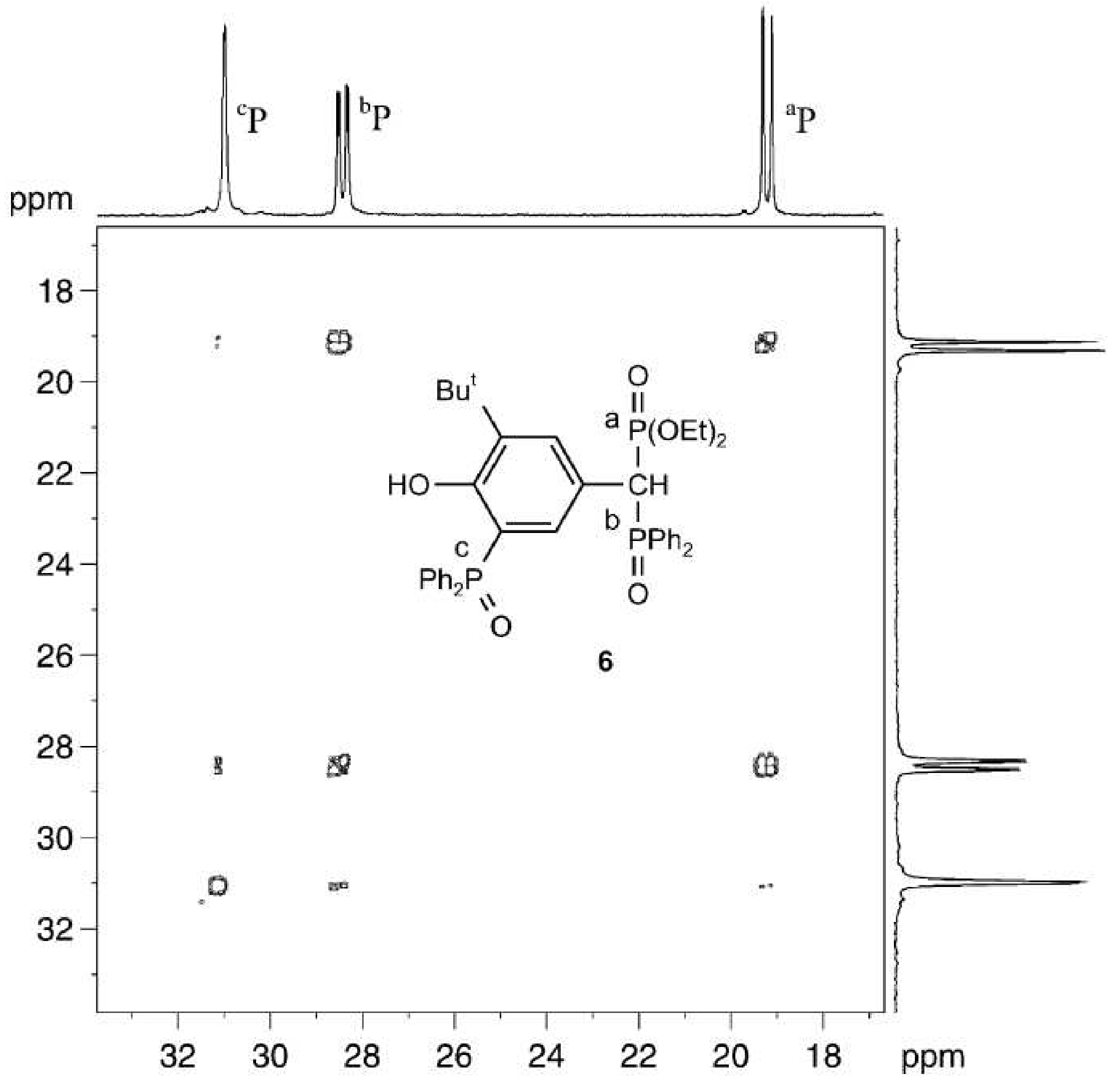


Fig. 30 P,P correlation spectrum for compound 6 (202 MHz, measurement time 15 min)