SUPPORTING INFORMATION

Effective Neutralization of Chemical Warfare Agents (HD, VX) By Me-DABCOF: A Small Molecule with Dual Action

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1. Experimental section

Caution: These experiments should only be performed by trained personnel using applicable safety procedures.

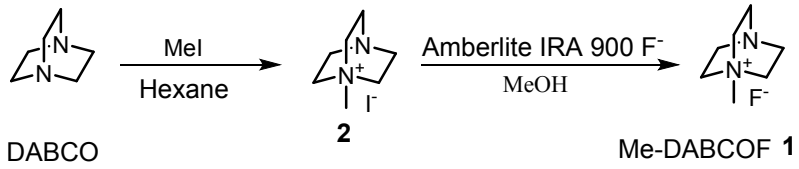
1.1 General

Unless otherwise stated, all reagents were obtained from commercial suppliers and were used without further purification. HD labeled with ^{13}C (HD*) was prepared (>98% purity) according to a literature procedure.[1] The ^{13}C labeling was evenly distributed among the carbons. VX was obtained locally at IIBR (>99% purity). ^{1}H, ^{13}C and ^{31}P NMR spectra were obtained using either a 11.7 T spectrometer (500, 125 and 202 MHz, respectively) or a 7.0 T spectrometer (300, 75 and 121 MHz, respectively). Chemical shifts for ^{13}C and ^{31}P were referenced to external TMS and trimethyl phosphate (TMP), respectively, as 0 ppm. SS-MAS NMR measurements were recorded at 125 and 202 MHz for ^{13}C and ^{31}P NMR respectively, on 11.7 T (500 MHz) spectrometer, equipped with a 0.4 cm standard CP-MAS probe using direct polarization (i.e., no cross polarization (CP) was used). Typical spinning rates were 5 kHz. The number of transients per spectrum varied between 100 to 2000.

HRMS analysis: HRMS analysis of samples like **4** is not at all trivial because it holds multiple charges of quaternary ammonium centers. Therefore, we used the following procedure: The sample was diluted in water to a concentration of 1 μg/mL and was syringe infused (15 μL/min) into an Orbitrap QE + MS (Thermo Scientific), operated in the positive ESI mode, scanning in the range of 50-500 *m/z* a mass resolution of 35000, obtaining $\Delta m/z$<2ppm.

1.2 Synthetic procedures

Preparation of 1



Me-DABCOF (**1**) was prepared according to our previously reported procedure.[2] The product was characterized by ^{1}H and ^{13}C NMR which were identical to the reported ones.

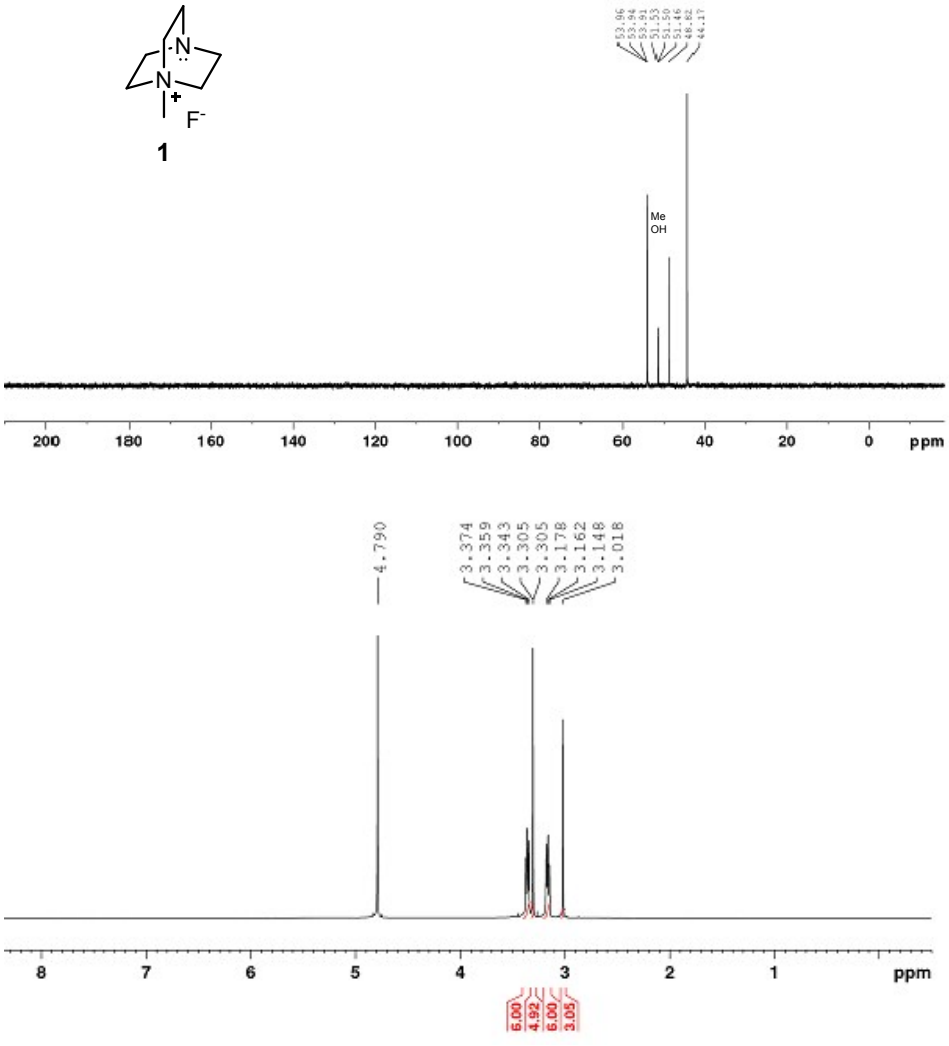
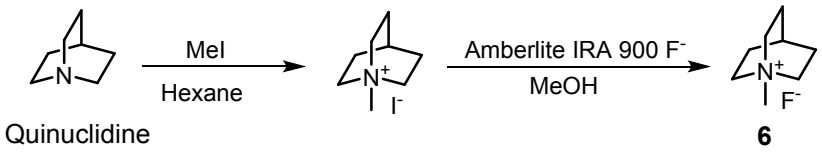


Figure S1: ^{1}H and ^{13}C NMR spectra of Me-DABCOF **1** in D_2O.

Preparation of 6



N-Me-quinuclidinium **6** was prepared according to our previously reported procedure.[2] The product was characterized by ^{1}H and ^{13}C NMR which were identical to the reported ones.

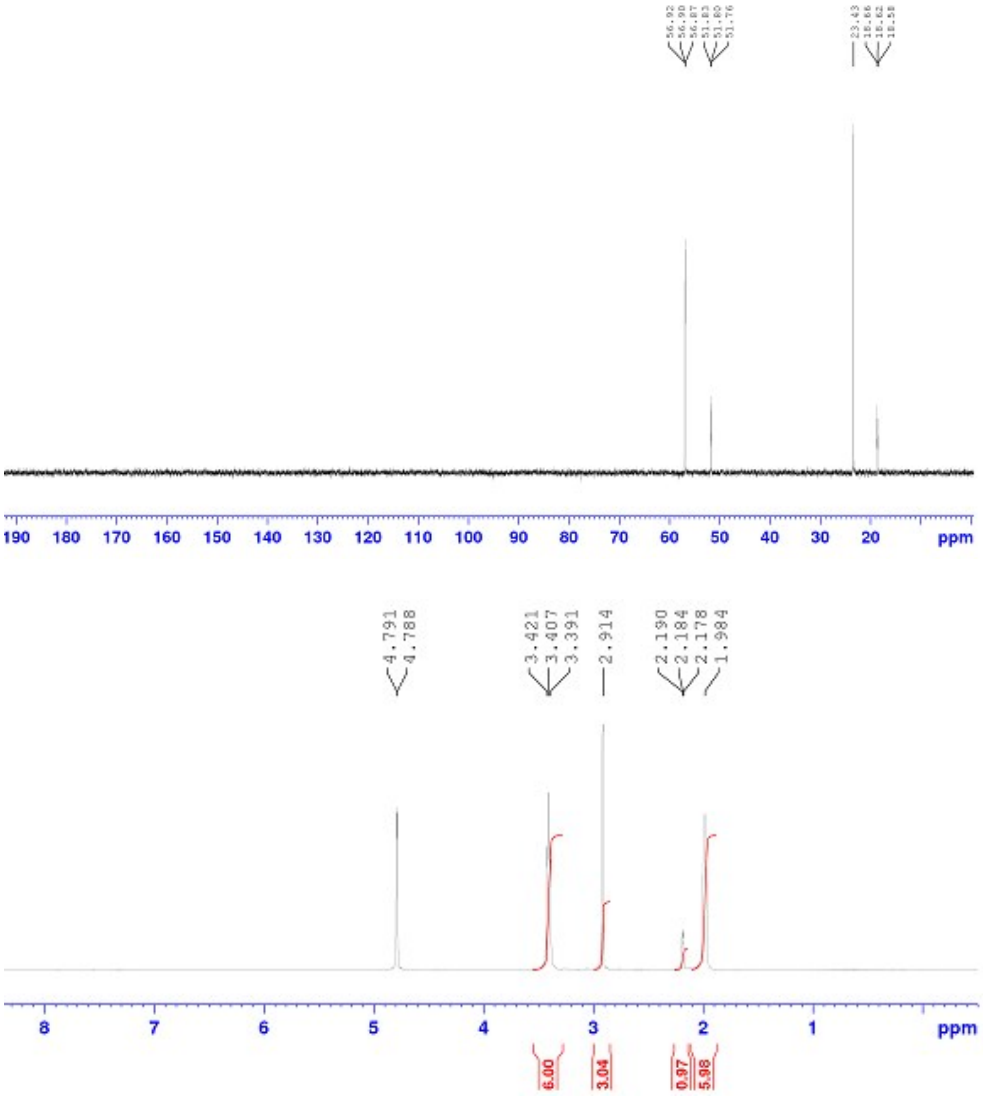
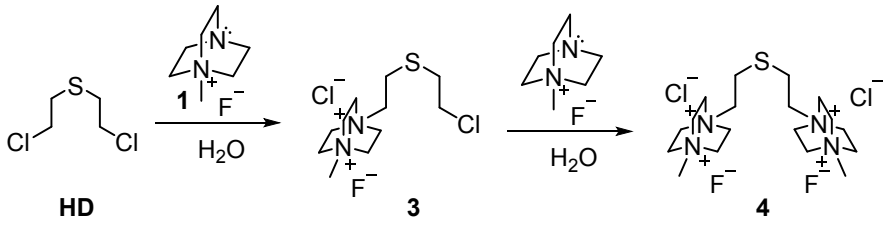


Figure S2: ^{1}H and ^{13}C NMR spectra of N-Me-quinuclidinium **6** in D_2O.

Neutralization of HD using 8 eq. of 1; Formation of product 4



In order to fully characterize product **4**, the following reaction was performed: 467mg of **1** were fully dissolved in 2 mL of D_2O in a 25 mL conical flask and the solution was stirred with a small magnet at room temperature. Non ^{13}C labeled HD was then added to the flask in 3 portions of 17 µL over 6 hours (total of 51 µL). Following HD addition, the reaction was kept stirring overnight for a total of 24h, after which the samples were taken directly for NMR and mass spectra analyses.

Product 4

^{1}H-NMR (500MHz, D_2O): δ 3.10 (m, 4H); 3.34 (s, 6 H); 3.85 (m, 4H); 4.03 (s, 24H).

^{13}C-NMR (125MHz, D_2O): δ 23.75; 51.53; 52.66; 53.36; 63.89.

HRMS (ESI$^+$) m/z calculated for $C_{18}H_{36}N_4S$ $(M^{+4}-2H^+)^{+2}$ 170.1325 found 170.1327 for the monoisotopic peak; calculated for the 1st natural isotope peak 170.6342 found 170.6344 (22%); calculated for the 2nd natural isotopic peak 171.1305 found 171.1307 (5%).

Preparation of a 20% Me-DABCOF/Al_2O_3 powder

The above powder was prepared following similar protocols, reported previously.[3] Briefly, 0.2 g of **1** were dissolved in 8 ml of dry ethanol to achieve a homogenous solution. Dry alumina (0.8 g dried overnight at 160 °C) was added to that solution, which was placed on an evaporator for stirring and heating (45 min at 45 °C) without vacuum. Following that time, vacuum and heating to 60 °C was applied for 45 min. The dry powder was then ground using a glass rod, 7 mL of dry ethanol

were added and evaporation while heating to 60 °C was performed. Once dried, the powder was ground again, and placed on an oil pump overnight to ensure dryness.

Preparation of a 20% Me-DABCOF/Al_2O_3 powder wetted with 10 wt% of water

The above dry powder, 90 mg, was placed in a glass vial and water, 10 mg, was added on top. The mixture was vortexed and ground thoroughly, using a glass rod (three cycles).

Preparation of a carboxymethylcellulose gel holding 1

250 mg of a commercially available carboxymethylcellulose with medium viscosity was added to a solution of 600 mg of **1** in 9.15 mL of tap water. The resulting solution was stirred over night to obtain a viscos clear gel.

1.3 Neutralization studies

1.3.1 Solution NMR

The neutralization studies were performed in an NMR tube by ^{13}C and ^{31}P NMR monitoring. For direct comparison between experiments, the scan number was maintained. A typical experiment was performed as follows: Calculated amounts of HD* or VX (corresponding to the required excess of reagents, tables 1 and 2) were added directly to an NMR tube followed by 0.5 mL of the appropriate reagent solution, prepared by dissolving 3% of **1**, DABCO or **6** in Tap water. For example, run 1, table 1: HD (0.028 mmol, 3.57µL) was added to an NMR tube followed by 0.5 mL of a solution containing 3% **1** (0.1mmol, 15 mg). For experiments holding 20 eq. of **1** as compared to the CWA (table 1 run 3 and table 2 run 3) a solution containing 6% of **1** was prepared. CWA's degradation experiments using the gel were performed in the same manner in an NMR tube using 0.5mL of gel.

1.3.2 Solid State – MAS NMR

Samples of the appropriate powders (~65 mg) were added to a 0.4 cm ZrO_2 rotor, and 1-1.1 and 1.9-2.2 µL of HD and VX respectively were applied via a dispenser to the center of the sample. The rotor was then sealed with a fitted Kel-F cap. Spectra were measured periodically to determine the remaining starting material and to identify degradation products. For comparison purposes, spectra were recorded under identical conditions.

2 Neutralization of ^{13}C-labeled HD (HD*) by 1

2.1 Neutralization of HD* by 3.6 equiv. **1**.

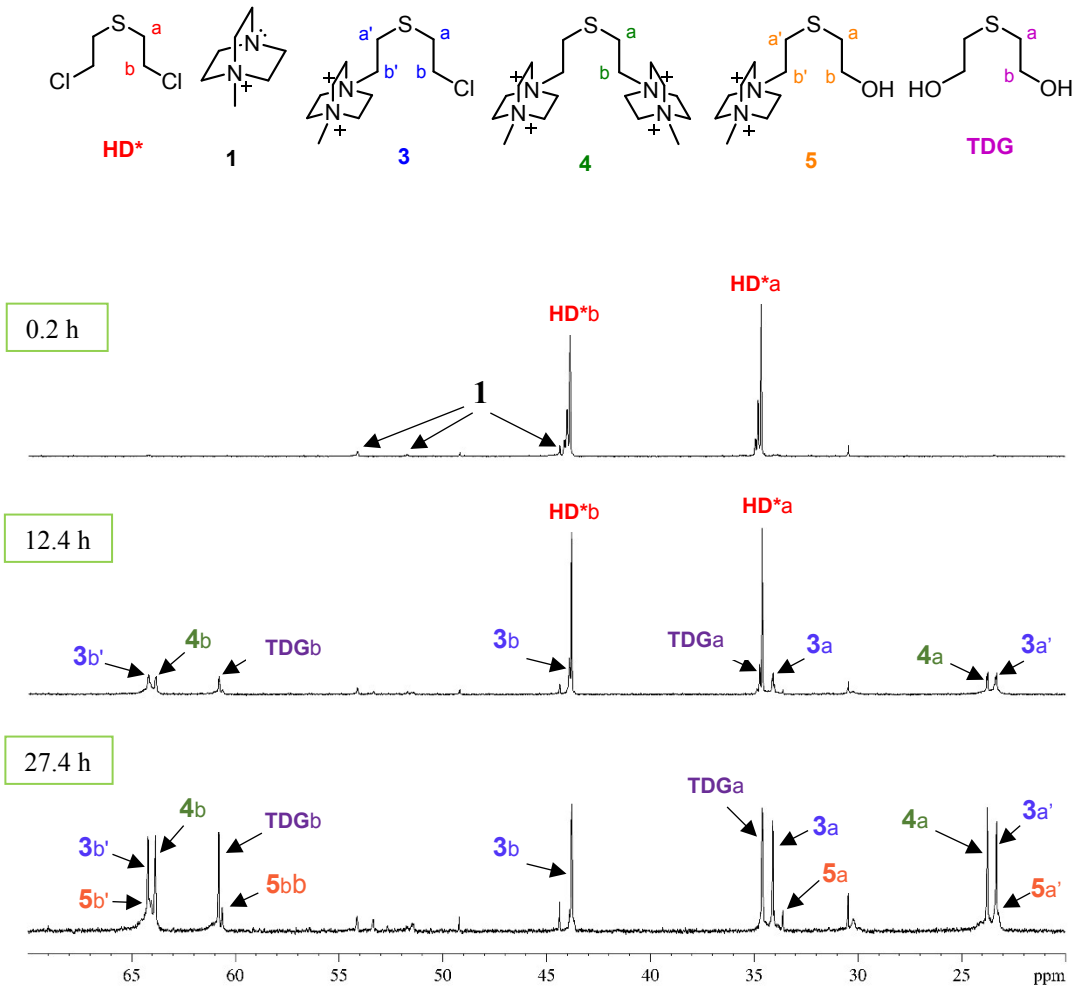


Figure S3. Selected ^{13}C-NMR spectra of HD* neutralization in the presence of 3.6 eq. of **1**.

2.2 Neutralization of HD* by 8.0 equiv. **1**.

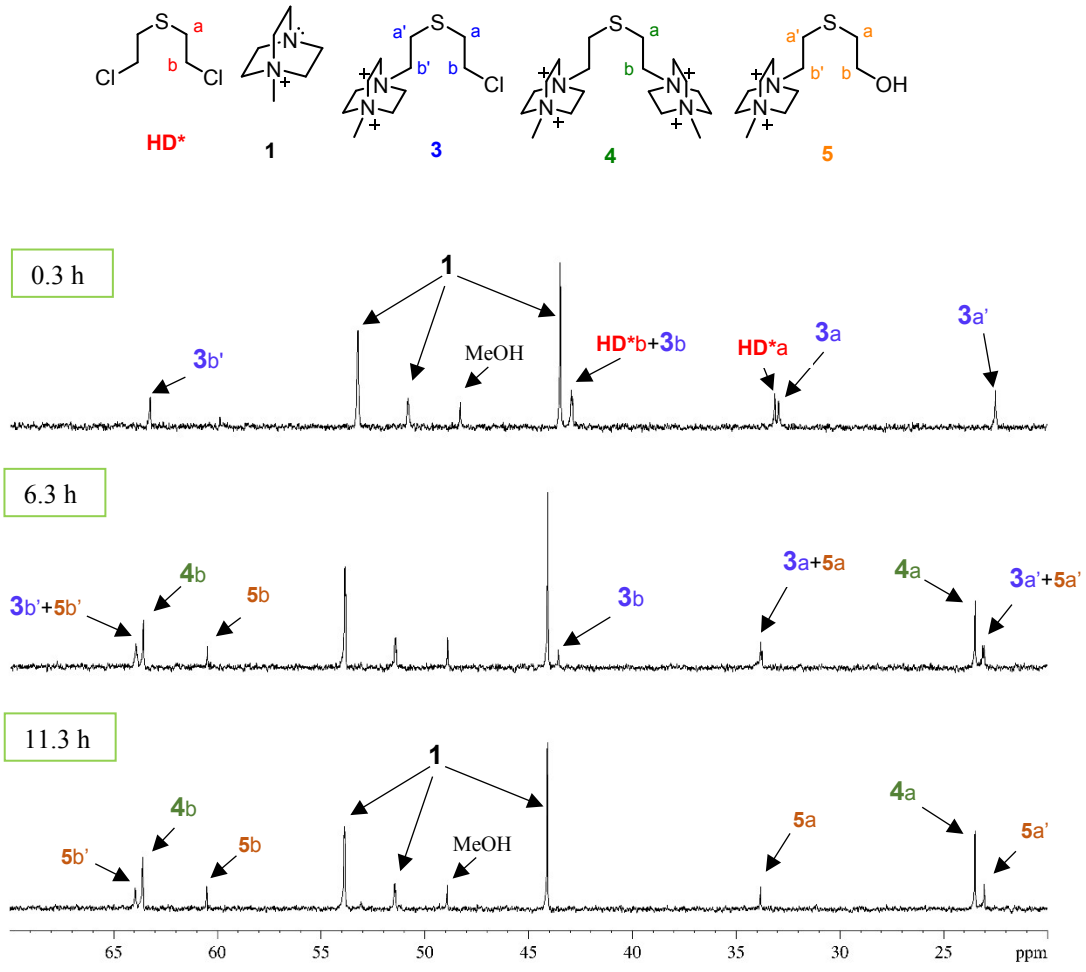


Figure S4. Selected ^{13}C-NMR spectra of HD* neutralization in the presence of 8 eq. of **1**.

2.3 Neutralization of HD* by 20.0 equiv. **1**.

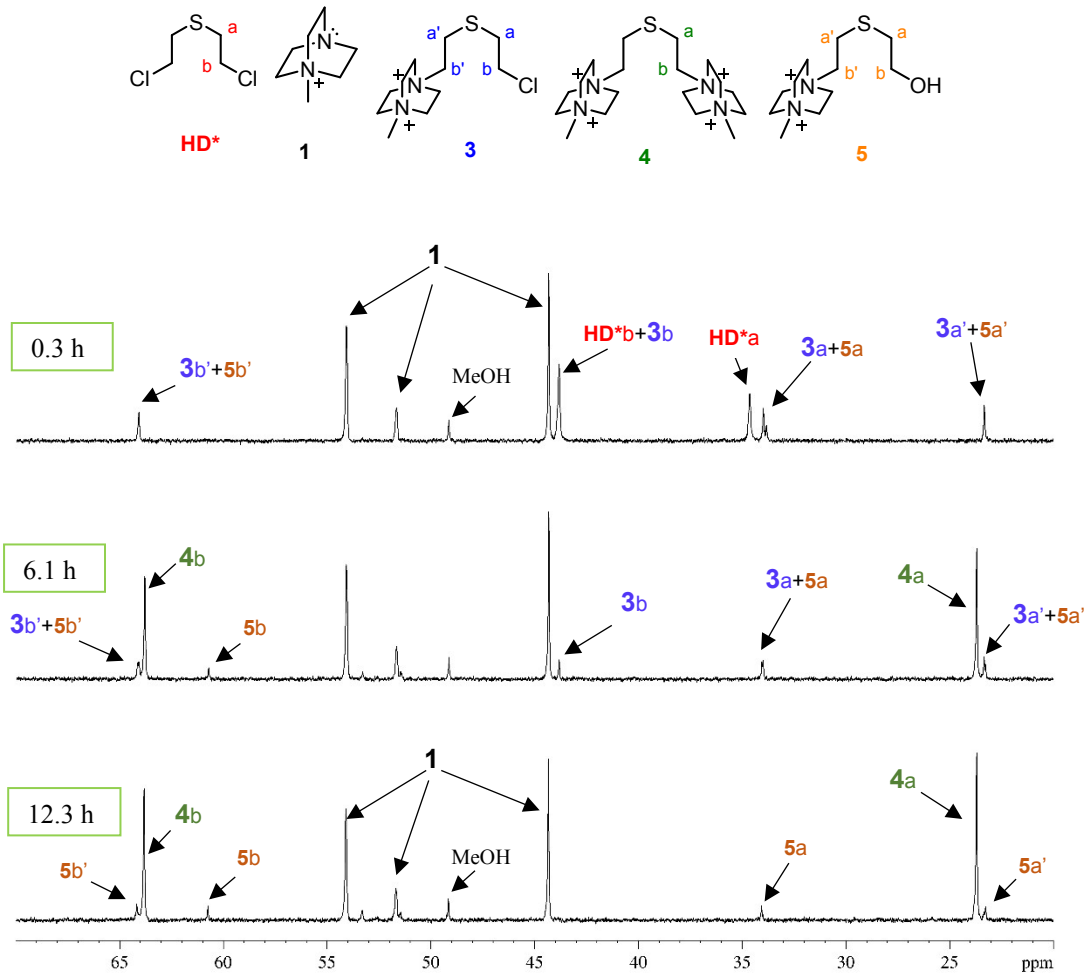


Figure S5. Selected ^{13}C-NMR spectra of HD* neutralization in the presence of 20 eq. of **1**.

2.4 Neutralization of HD* by 8.0 equiv. of DABCO.

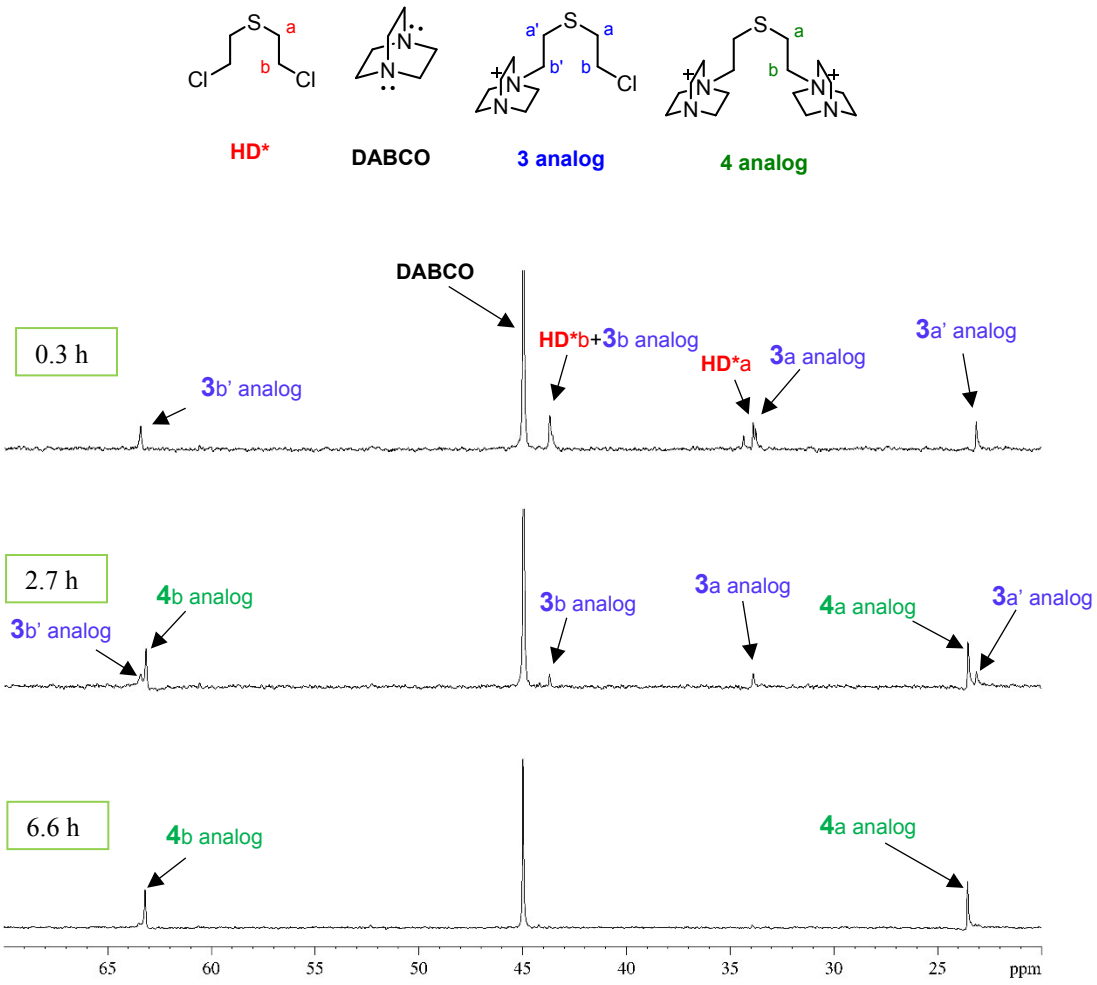


Figure S6. Selected ^{13}C-NMR spectra of HD* neutralization in the presence of 8 eq. of DABCO.

2.5 Neutralization of HD* by 3.6 equiv. of **6**.

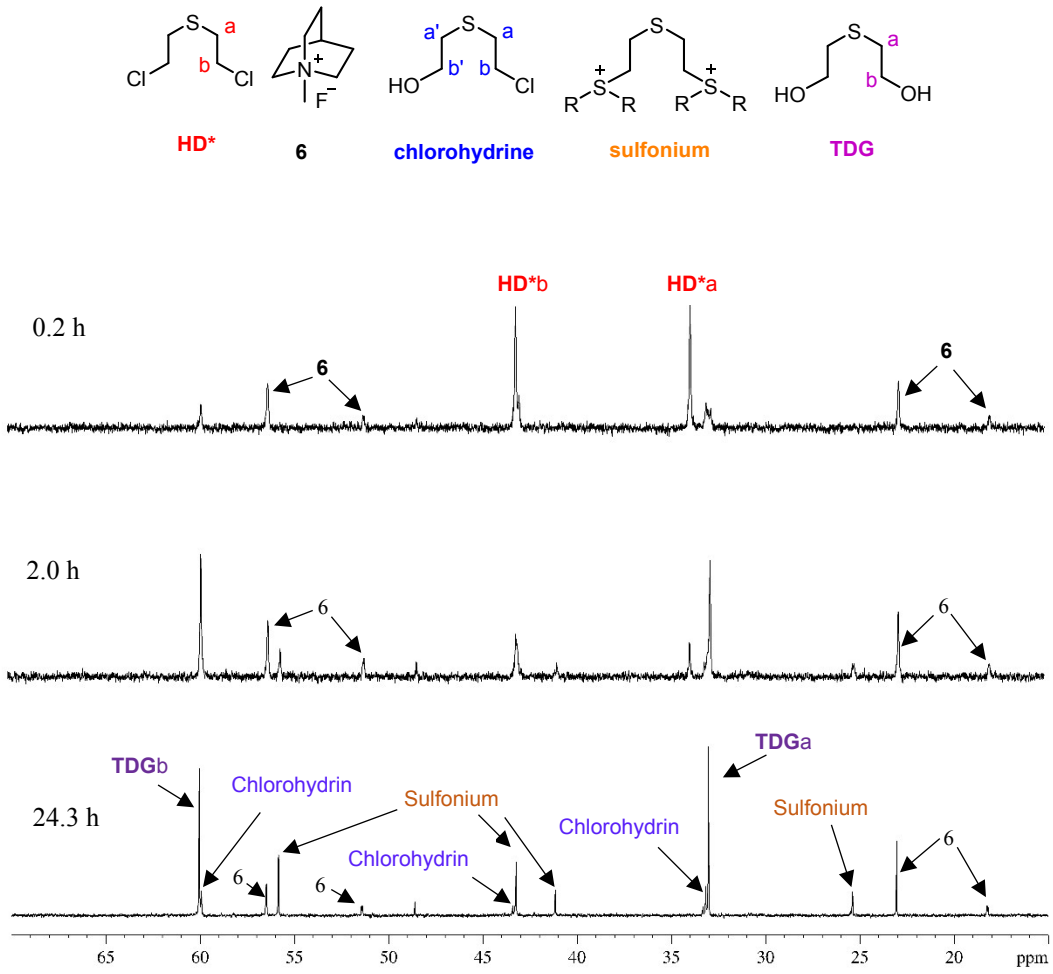


Figure S7. Selected ^{13}C-NMR spectra of HD* neutralization in the presence of 3.6 eq. of **6**.

3. Characterization of product 4

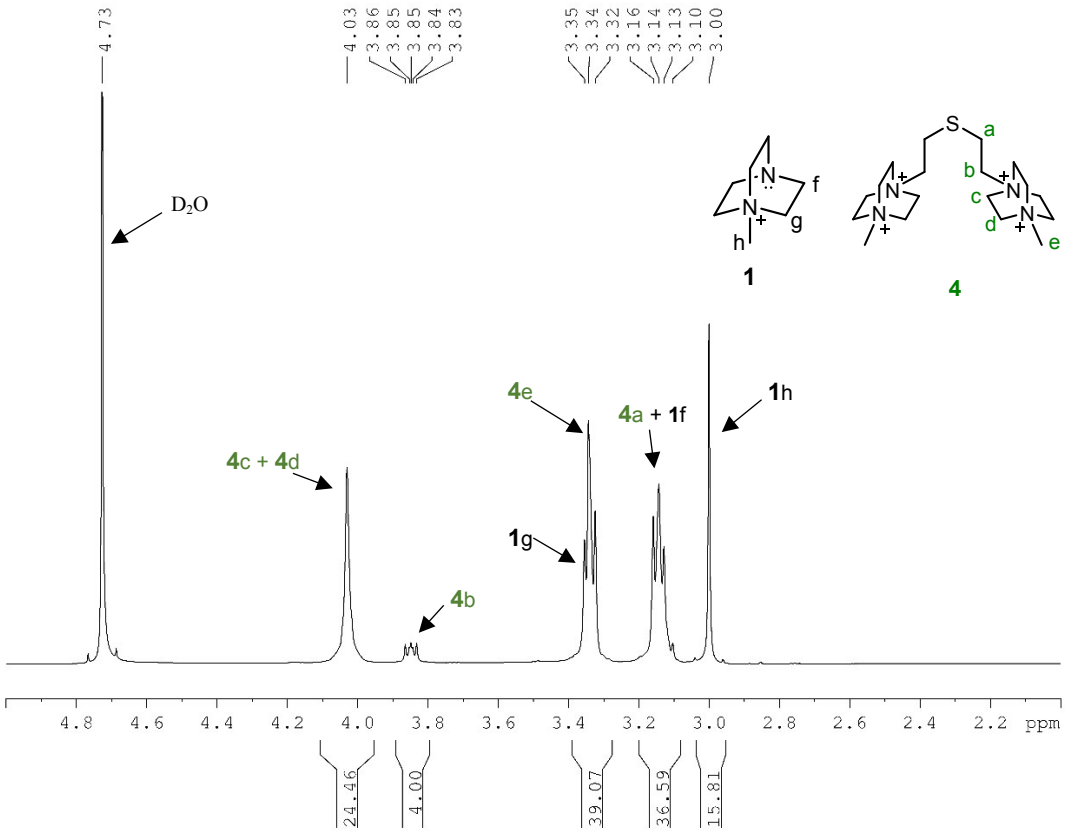


Figure S8. ^{1}H-NMR spectra of the reaction of 8 eq. of **1** and HD, large scale and slow addition.

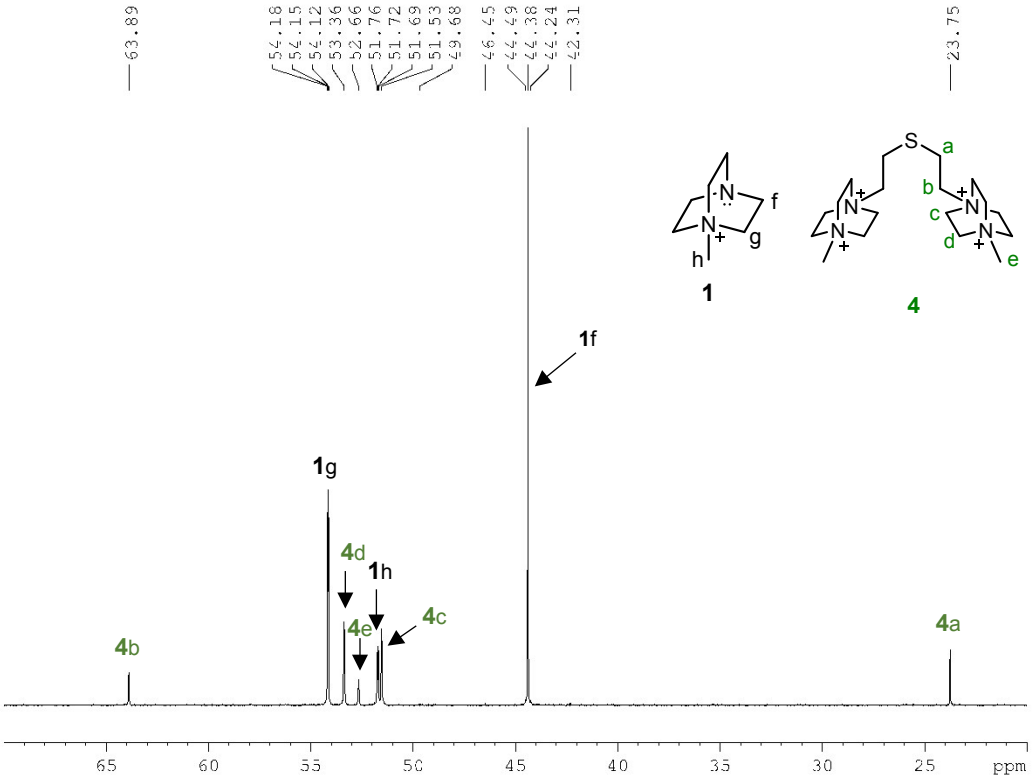


Figure S9. ^{13}C-NMR spectra of the reaction of 8 eq. of **1** and HD, large scale and slow addition.

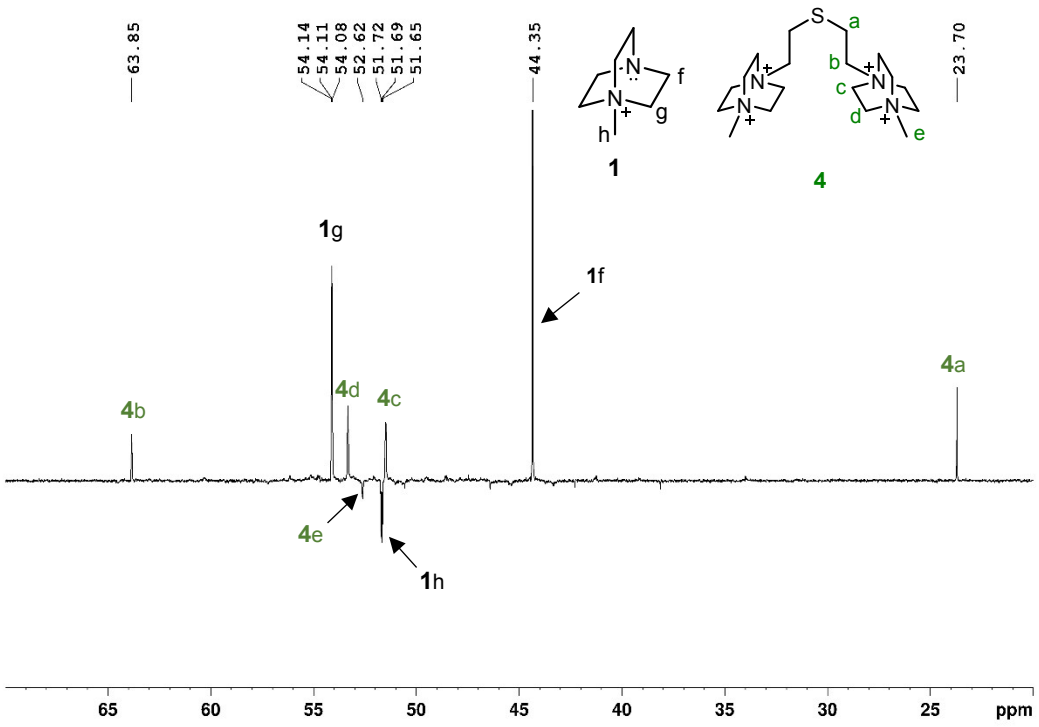


Figure S10. DEPT spectra of the reaction of 8 eq. of **1** and HD, large scale and slow addition.

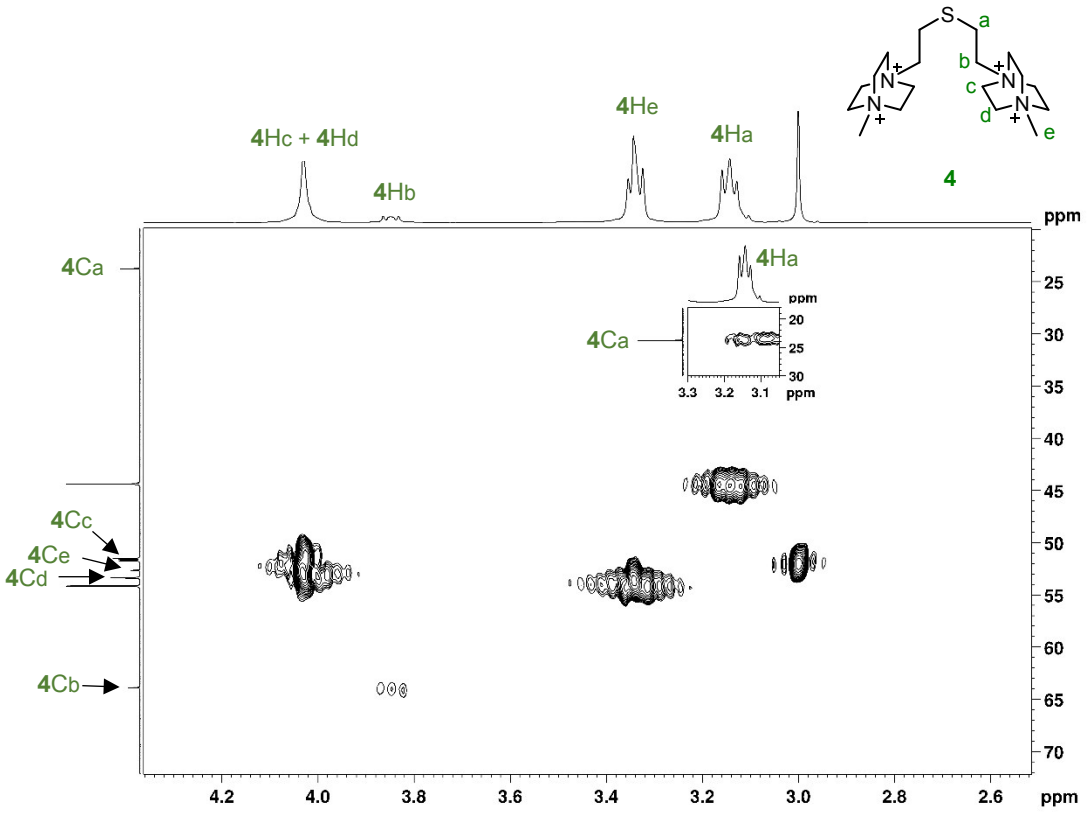


Figure S11. HMQC spectra of the reaction of 8 eq. of **1** and HD, large scale and slow addition.

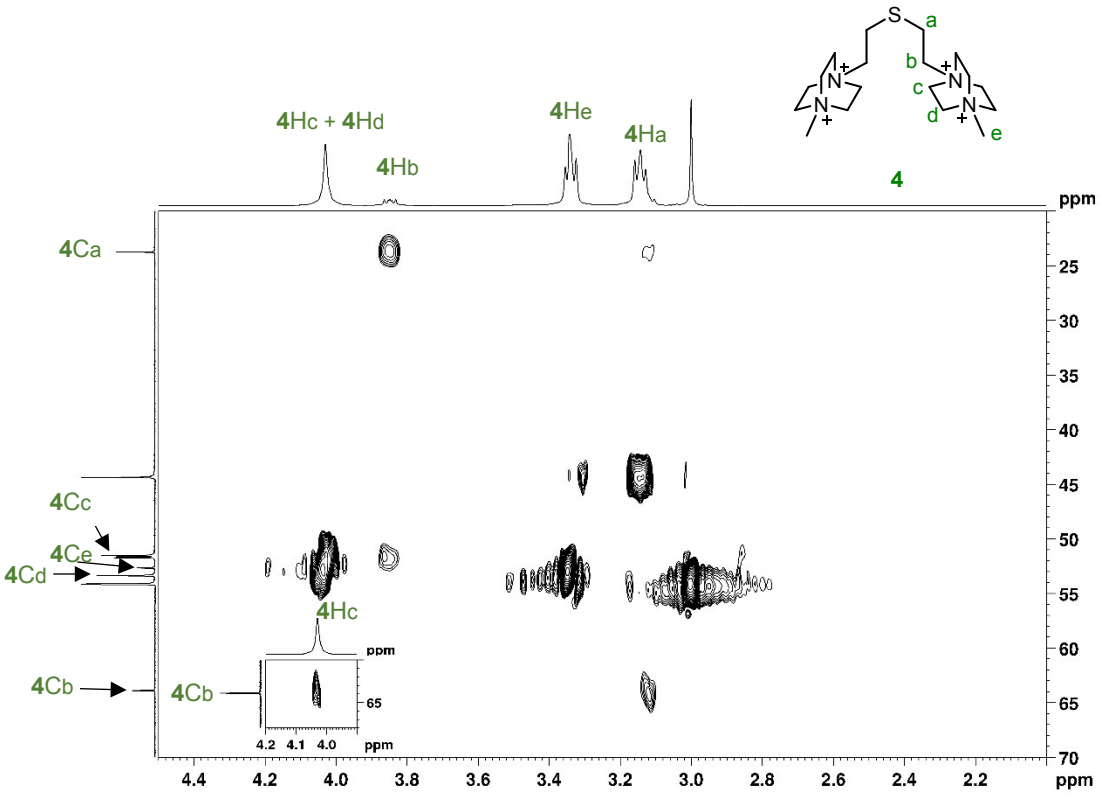


Figure S12. HMBC spectra of the reaction of 8 eq. of **1** and HD, large scale and slow addition.

4. Neutralization of HD* on Me-DABCOF/Al_2O_3

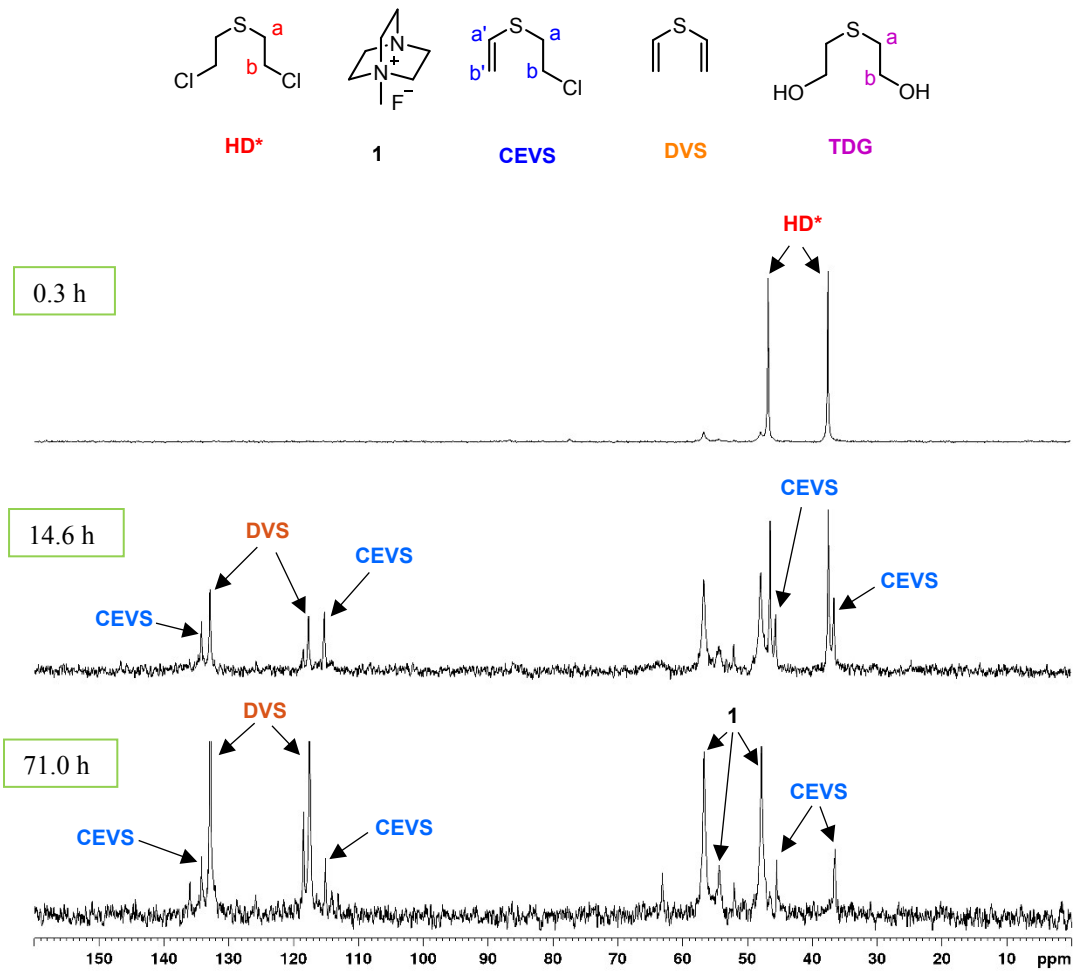


Figure S13. Selected ^{13}C- solid-state MAS NMR spectra of HD neutralization on dry Me-DABCOF/Al_2O_3.

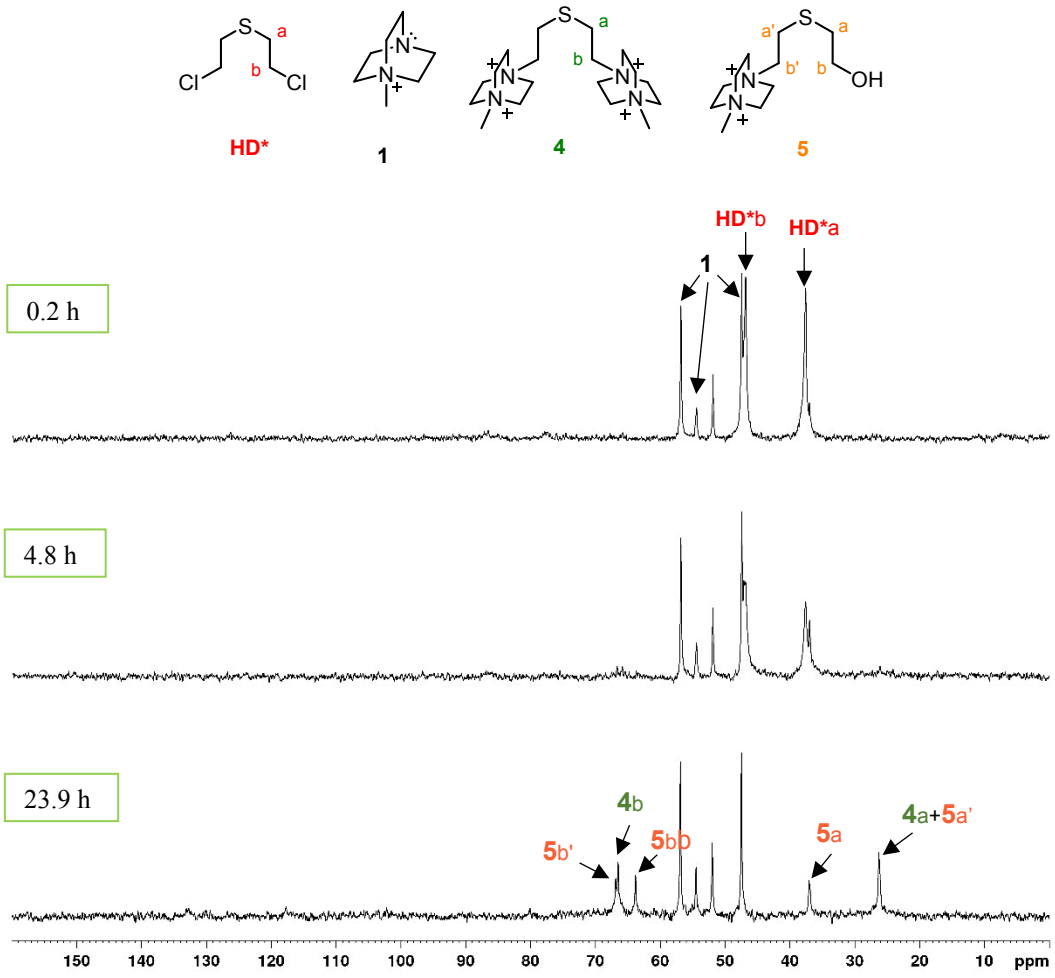


Figure S14. Selected ^{13}C- solid-state MAS NMR spectra of HD neutralization on Me-DABCOF/Al_2O_3 wetted with 10% of water.

5. **Neutralization of HD* by Carboxymethylcellulose/Me-DABCOF gel**

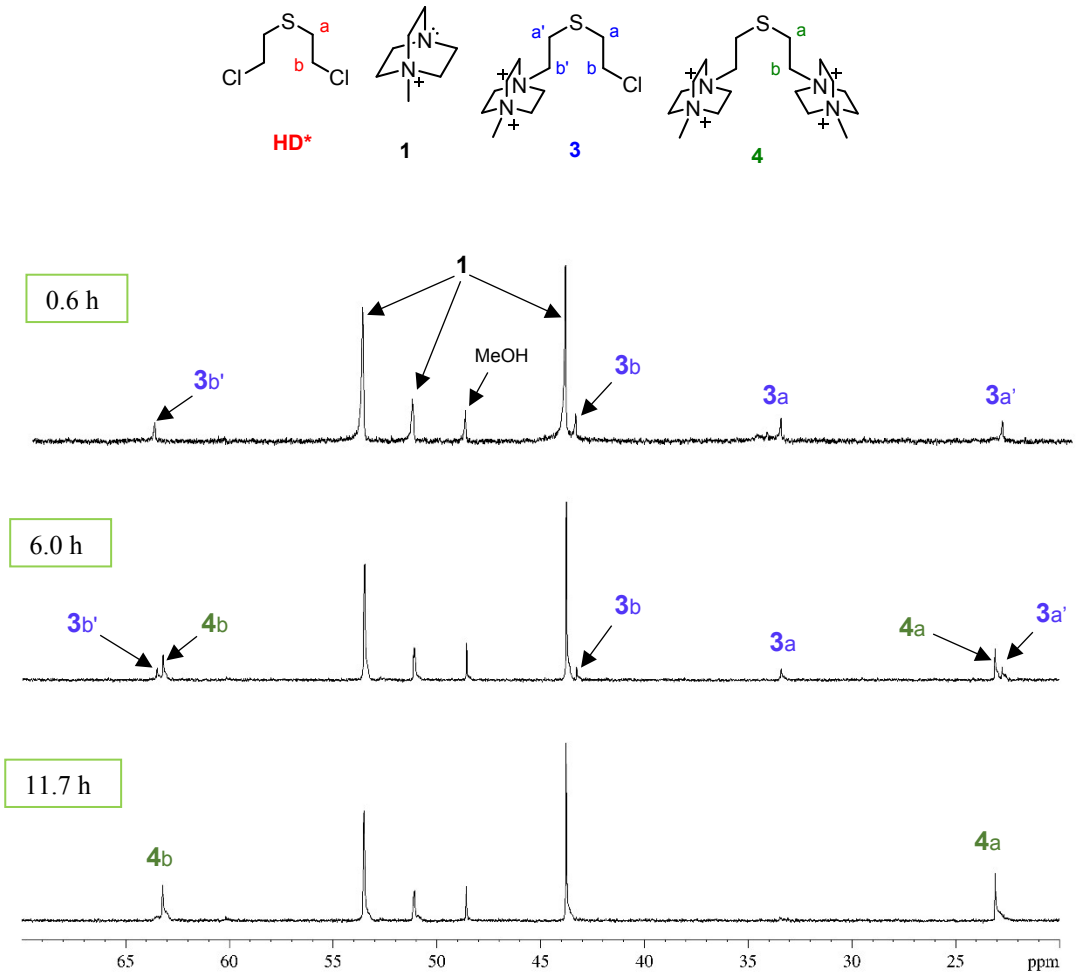


Figure S15. Selected ^{13}C NMR spectra of HD neutralization inside a carboxymethylcellulose gel holding **1**.

6. Neutralization of VX by 1

6.1 Neutralization of VX by 3.6 equiv. of **1**.

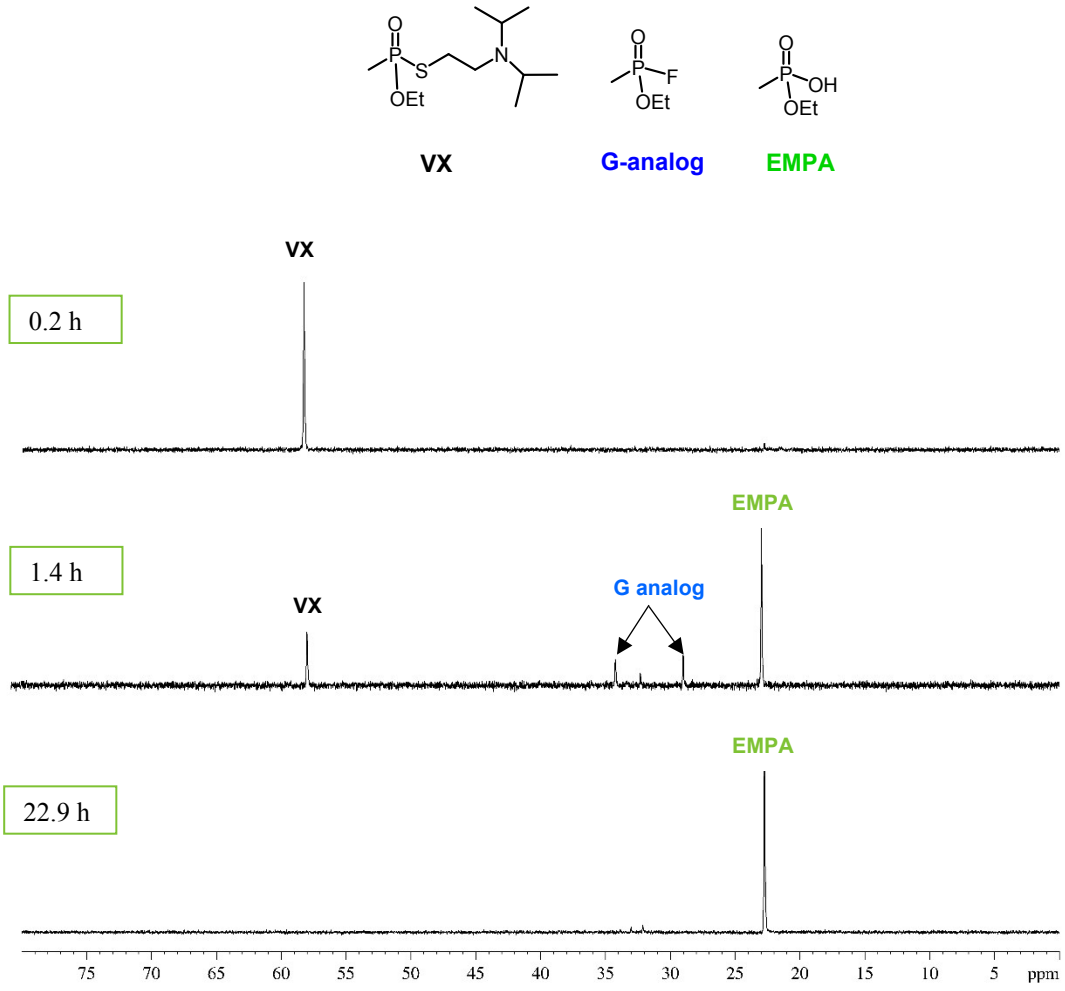


Figure S16. Selected ^{31}P-NMR spectra of VX neutralization in the presence of 3.6 eq. of **1**.

6.2 Neutralization of VX by 8.0 equiv. of **1**.

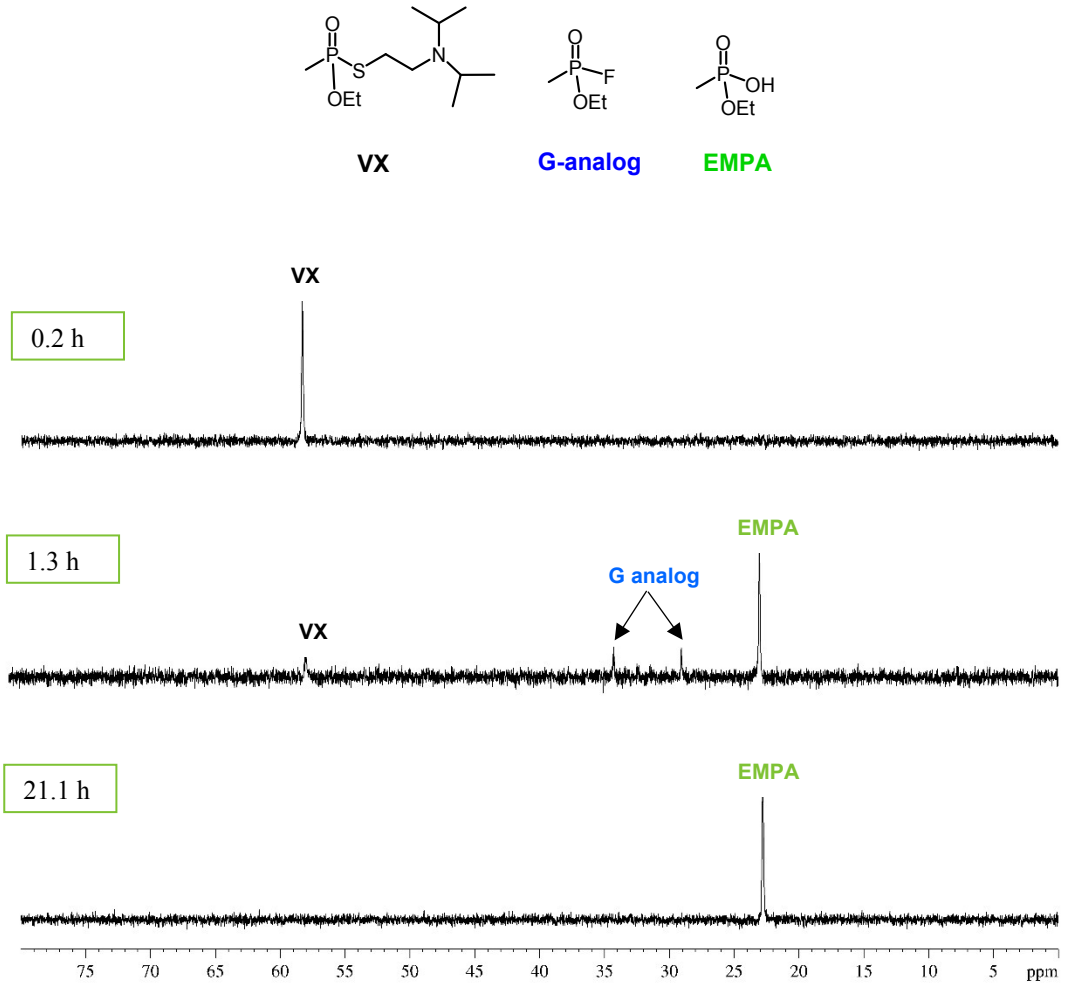


Figure S17. Selected ^{31}P-NMR spectra of VX neutralization in the presence of 8.0 eq. of **1**.

6.3 Neutralization of VX by 20 equiv. of **1**.

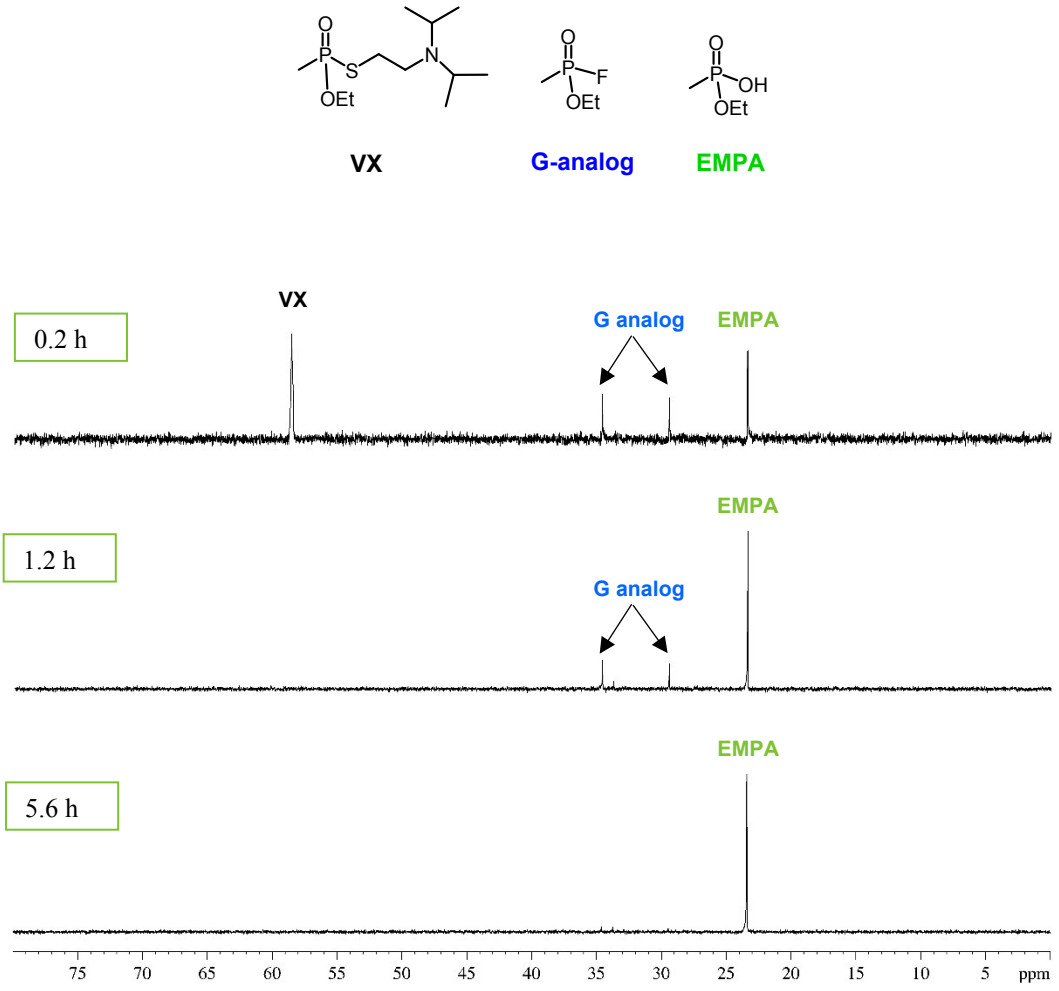


Figure S18. Selected ^{31}P-NMR spectra of VX neutralization in the presence of 20 eq. of **1**.

6.4 Reaction of VX with 8.0 equiv. of **DABCO**.

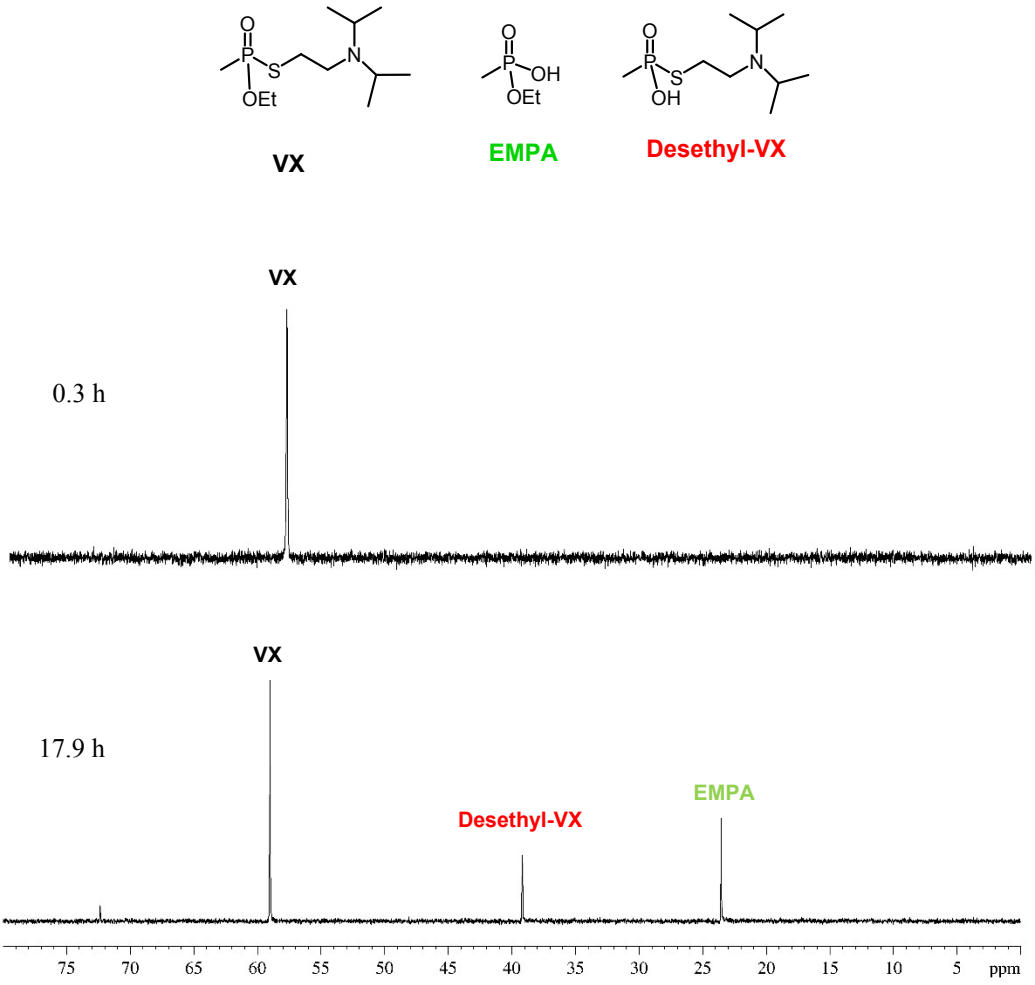


Figure S19. Selected ^{31}P-NMR spectra of VX partial neutralization in the presence of 8 eq. of DABCO.

7. Neutralization of VX on Me-DABCOF/Al_2O_3

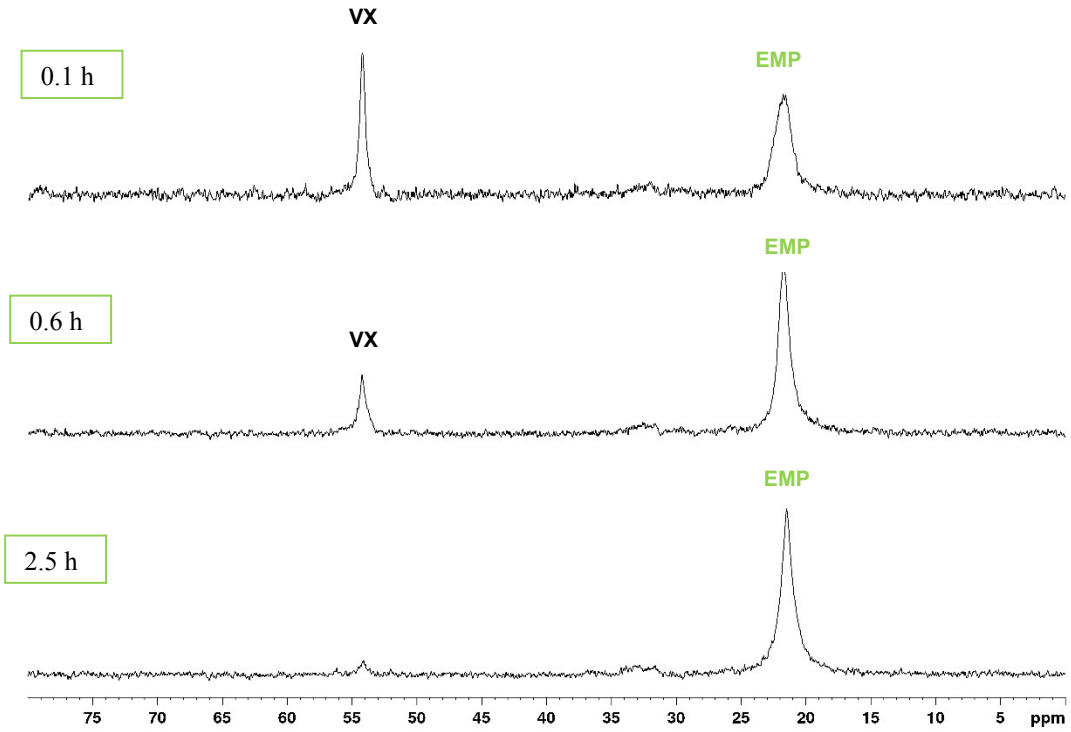


Figure S20. Selected ^{31}P- solid-state MAS NMR spectra of VX neutralization on dry Me-DABCOF/Al_2O_3.

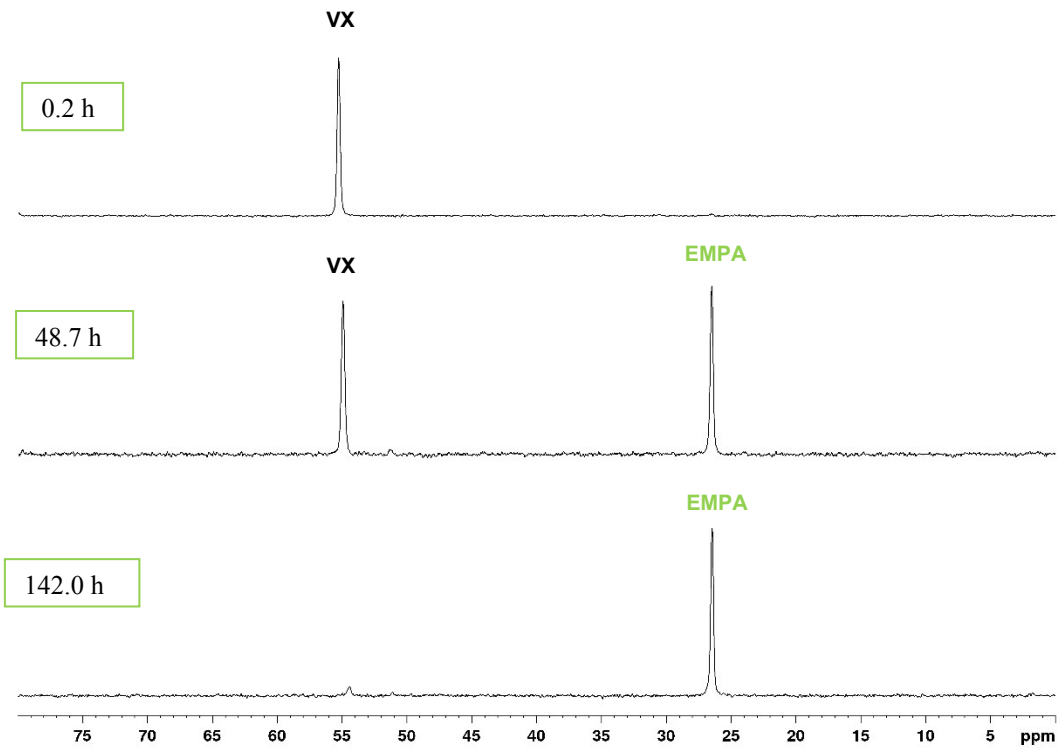


Figure S21. Selected ^{31}P- solid-state MAS NMR spectra of VX neutralization on Me-DABCOF/Al_2O_3 wetted with 10% of water.

8. Neutralization of VX by Carboxymethylcellulose/ Me-DABCOF gel

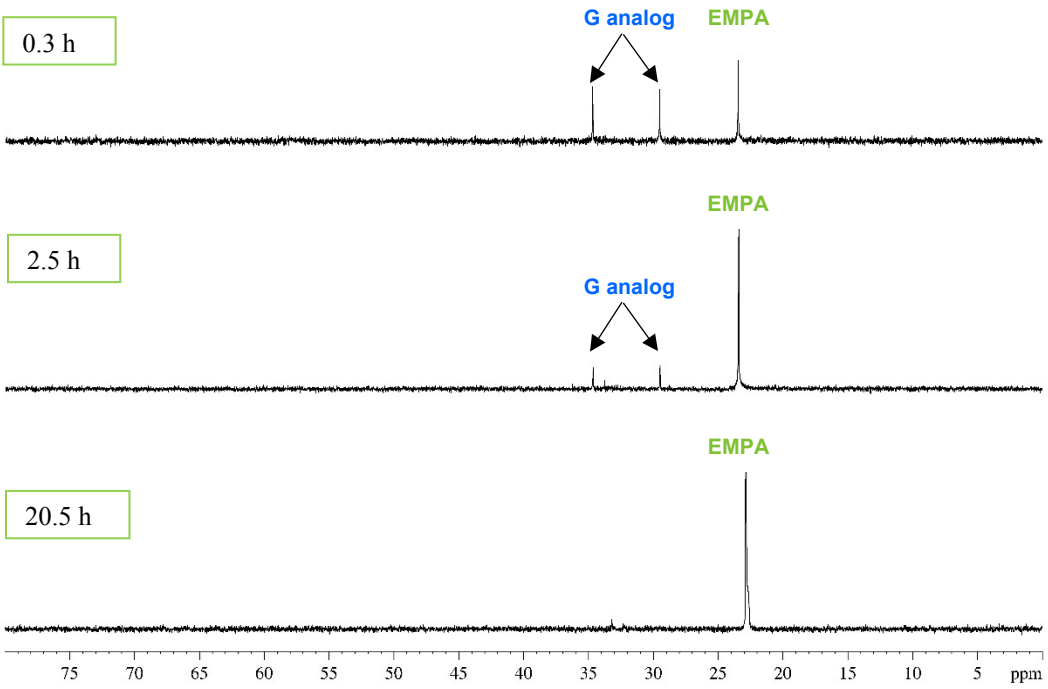


Figure S22. Selected ^{31}P NMR spectra of VX neutralization by a carboxymethylcellulose gel holding **1**.

9. References:

1. L. P. Reiff, D. F. Taber and L. Yet. Proceedings of the 1996 ERDEC Scientific Conference on Chemical and Biological Defense Research, 19-22 November, 1996, 799.
2. S. Elias, N. Karton-Lifshin, L. Yehezkel, N. Ashkenazi, I. Columbus and Y. Zafrani, *Org. Lett.*, 2017, **19**, 3039-3042.
3. a) E. Gershonov, I. Columbus and Y. Zafrani, *J. Org. Chem*., 2009, **74**, 329-338. b) G. Fridkin, L. Yehezkel, I. Columbus and Y. Zafrani, *J. Org. Chem*., 2016, **81**, 2154-2158.