# SUPPORTING INFORMATION (SI)

## An Unusual Double Beckmann Fragmentation Reaction under Physiological Conditions

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## I. MS and HPLC data

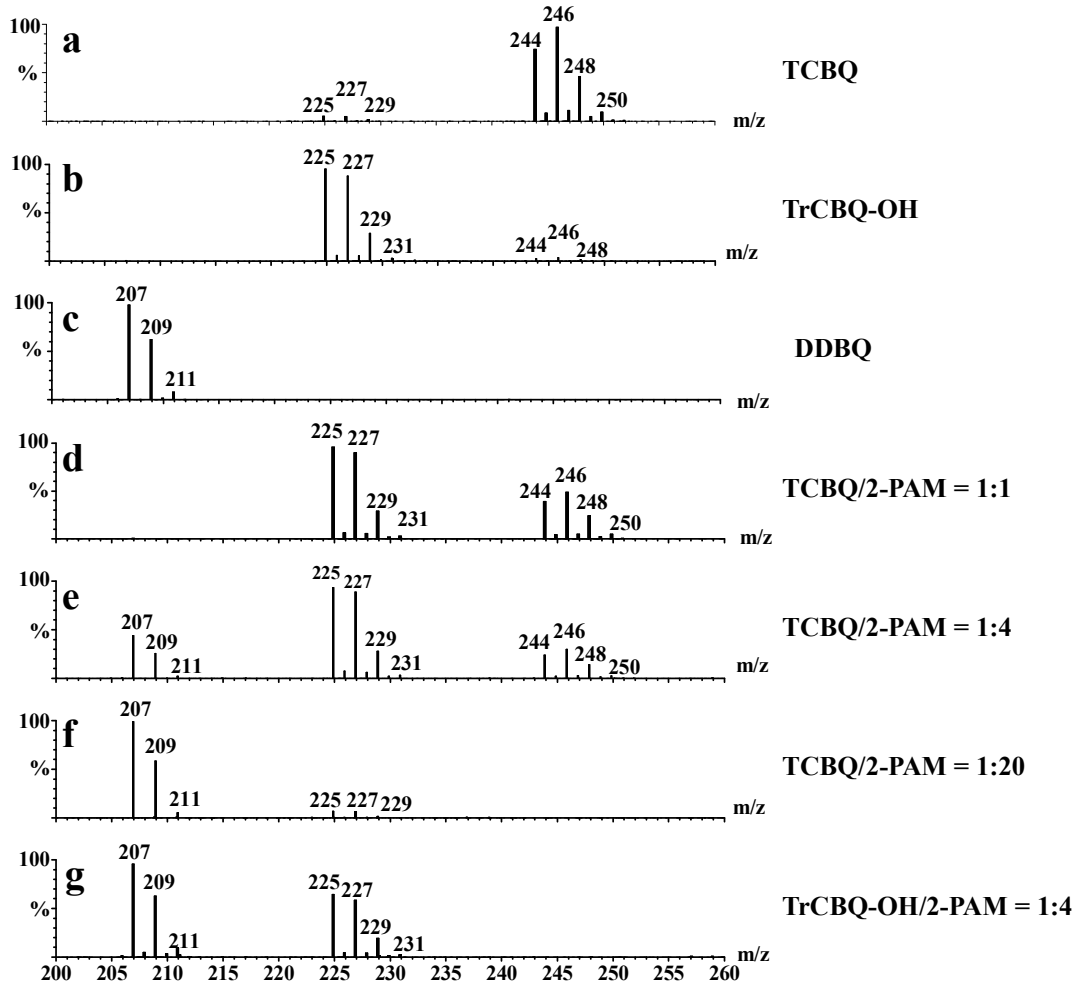


***Figure S1: Mass spectral analysis of the dechlorination and hydroxylation products for TCBQ.*** ESI-Q-TOF-MS spectra of TCBQ (a), TrCBQ-OH (b), DDBQ (c), TCBQ with 2-PAM at the ratio of 1:1 (d), 1:4 (e), 1:20 (f), and TrCBQ-OH with 2-PAM at the ratio of 1: 4 (g) in $CH_3COONH_4$ buffer (pH 7.4, 0.1 M) at room temperature, 6 min. TCBQ, 0.05 mM; TrCBQ-OH, 0.05 mM; 2-PAM, 0.05, 0.20 or 1 mM (for details, see Materials and Methods).

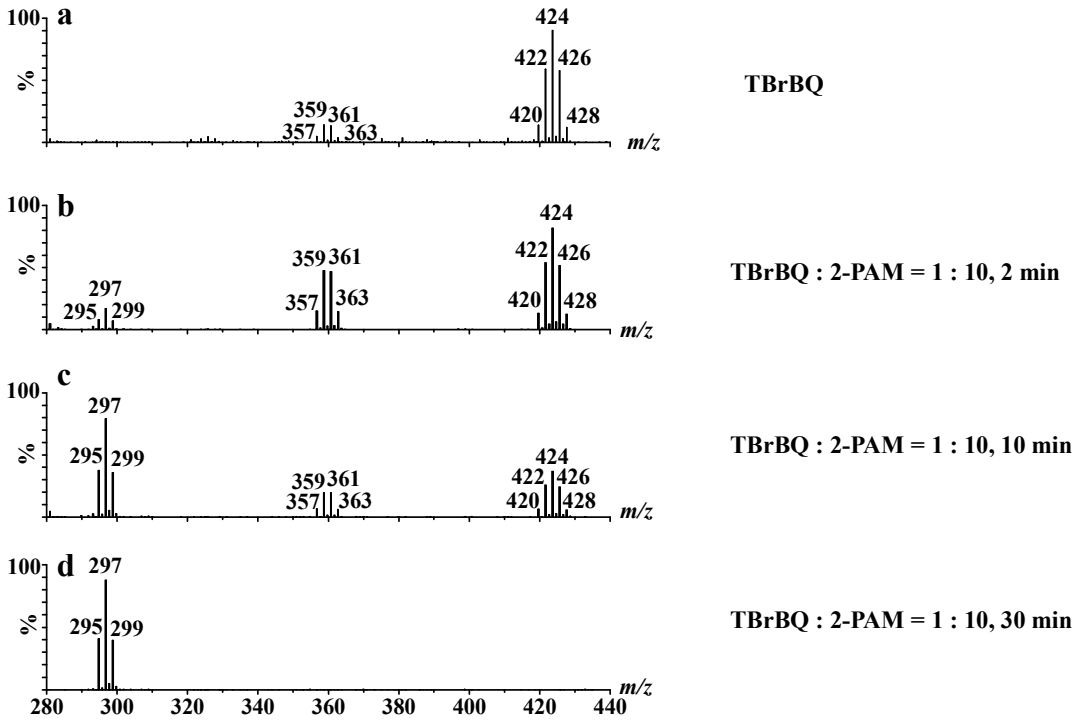


***Figure S2: Mass spectral analysis of the dechlorination and hydroxylation products for TBrBQ.*** ESI-Q-TOF-MS spectra of TBrBQ (a), TBrBQ with 2-PAM at the ratio of 1:10 (b, 2 min; c, 10 min; d, 30 min) in $CH_3COONH_4$ buffer (pH 7.4, 0.1 M) at room temperature. TBrBQ, 0.05 mM.

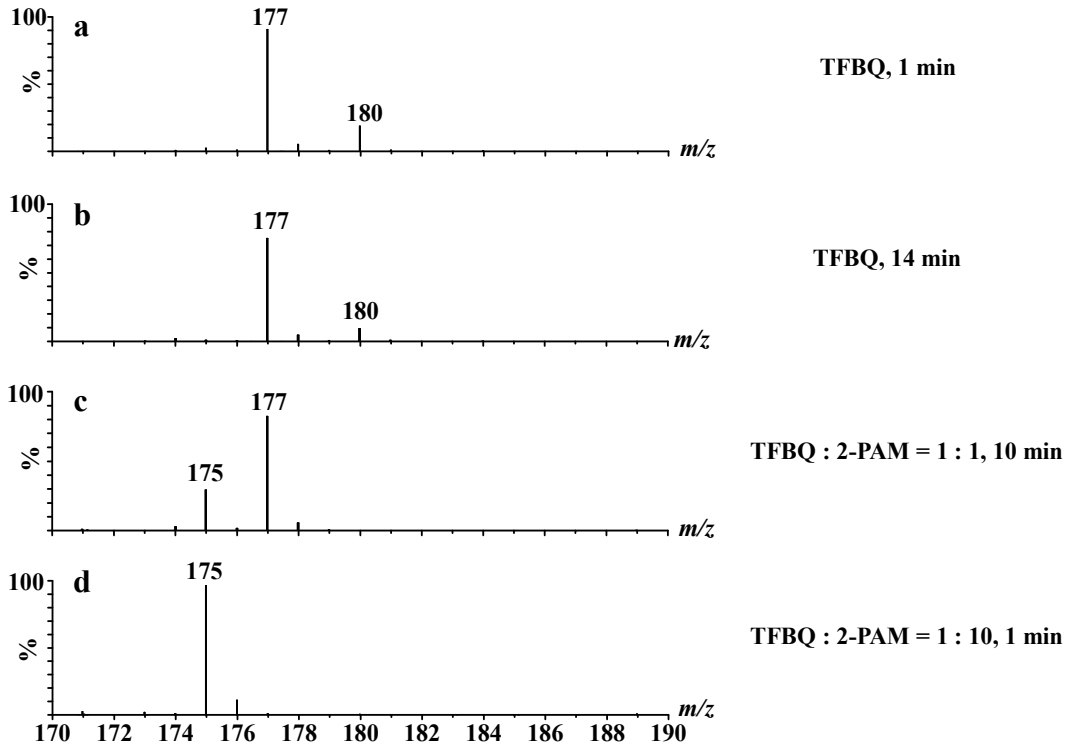


***Figure S3: Mass spectral analysis of the dechlorination and hydroxylation products for TFBQ.*** ESI-Q-TOF-MS spectra of TFBQ (a, b, the hydrolysis rate of TFBQ alone is very fast in $CH_3COONH_4$ buffer), TFBQ with 2-PAM at the ratio of 1:1 and 1:10 (c, 10 min; d, 1 min) in $CH_3COONH_4$ buffer (pH 7.4, 0.1 M) at room temperature. TFBQ, 0.05 mM.

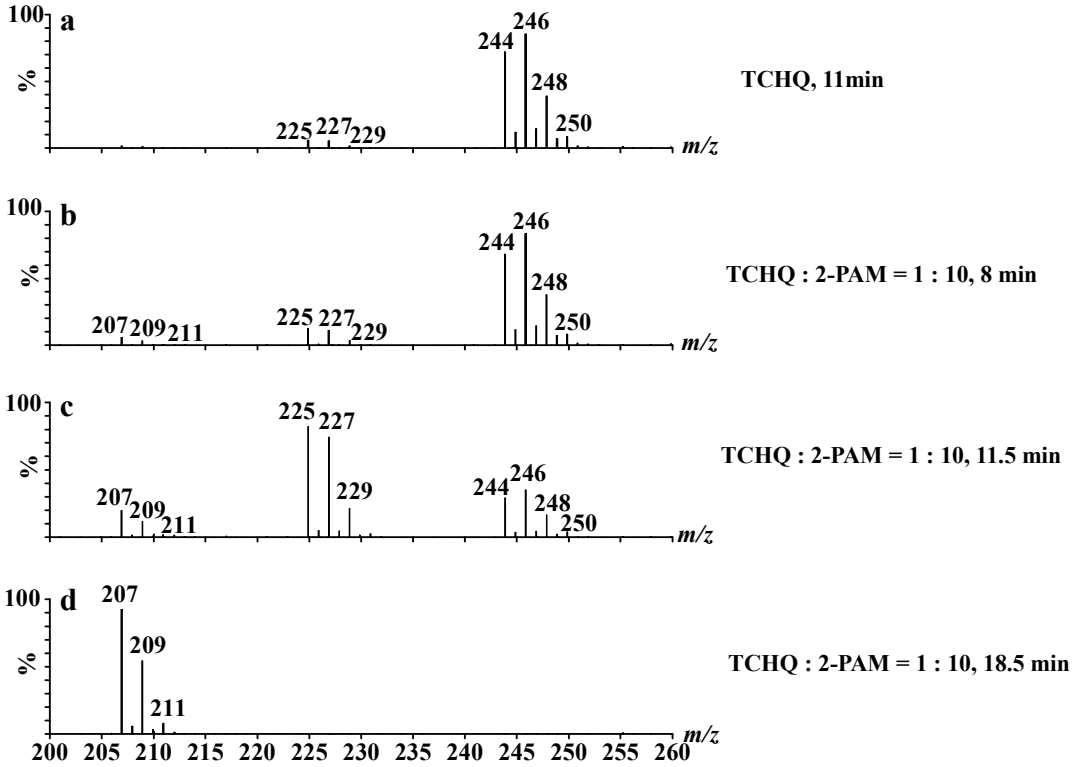


***Figure S4: Mass spectral analysis of the dechlorination and hydroxylation products for TCHQ.*** ESI-Q-TOF-MS spectra of TCHQ (a), TCHQ with 2-PAM at the ratio of 1:10 (b, 8 min; c, 11.5 min; d, 18.5 min) in $CH_3COONH_4$ buffer (pH 7.4, 0.1 M) at room temperature. TCHQ, 0.05 mM.

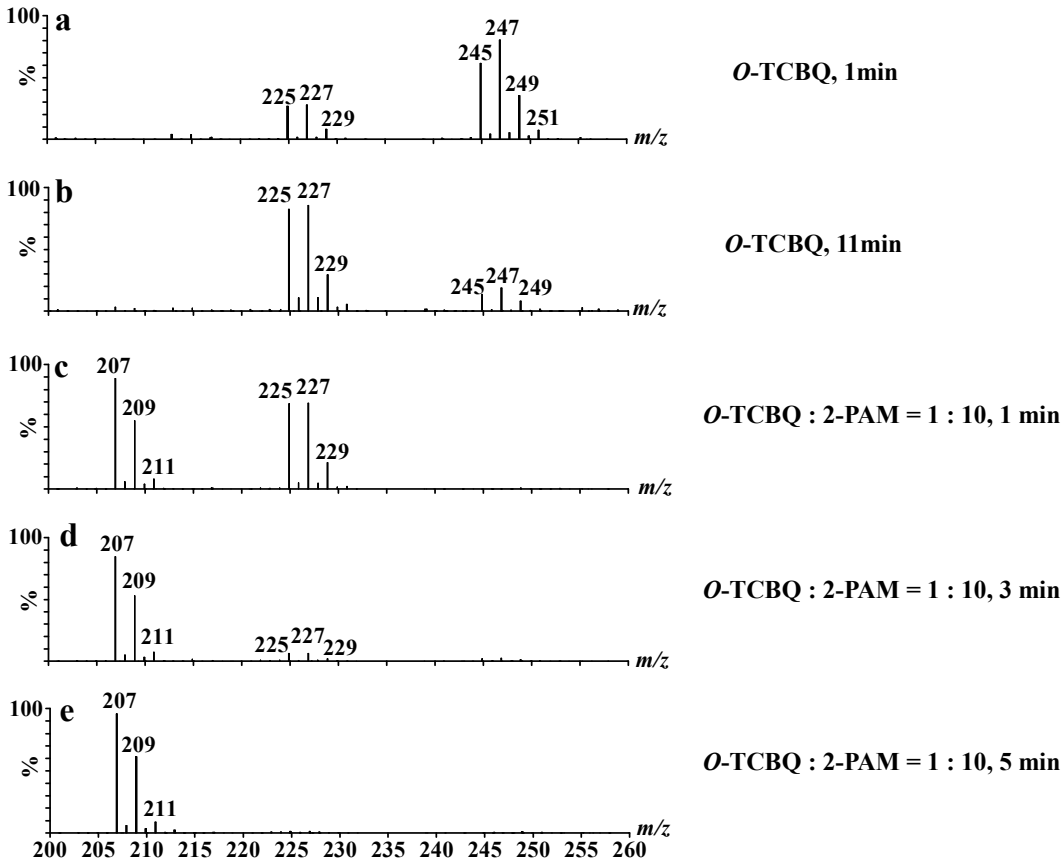


***Figure S5: Mass spectral analysis of the dechlorination and hydroxylation products for O-TCBQ.*** ESI-Q-TOF-MS spectra of *O*-TCBQ (a, b, the hydrolysis rate of *O*-TCBQ alone is very fast in $CH_3COONH_4$ buffer), *O*-TCBQ with 2-PAM at the ratio of 1:10 (c, 1 min; d, 3 min; e, 5 min) in $CH_3COONH_4$ buffer (pH 7.4, 0.1 M) at room temperature. *O*-TCBQ, 0.05 mM

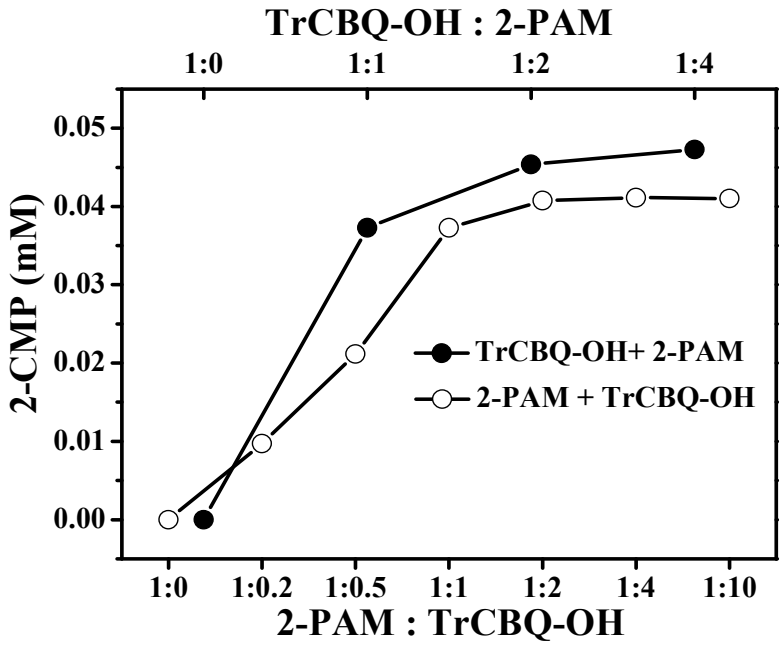


***Figure S6: The yield of 2-cyano-1-methylpyridinium chloride (2-CMP) from the reaction between 2-PAM and TrCBQ-OH.*** All of the reactions were conducted in phosphate buffer (100 mM, pH 7.4) for 36 min at 25℃, and the reaction was initiated by the addition of TrCBQ-OH followed by rapid mixing. 2-PAM, 0.05 mM (2-PAM + TrCBQ-OH); TrCBQ-OH, 0.05 mM (TrCBQ-OH + 2-PAM).

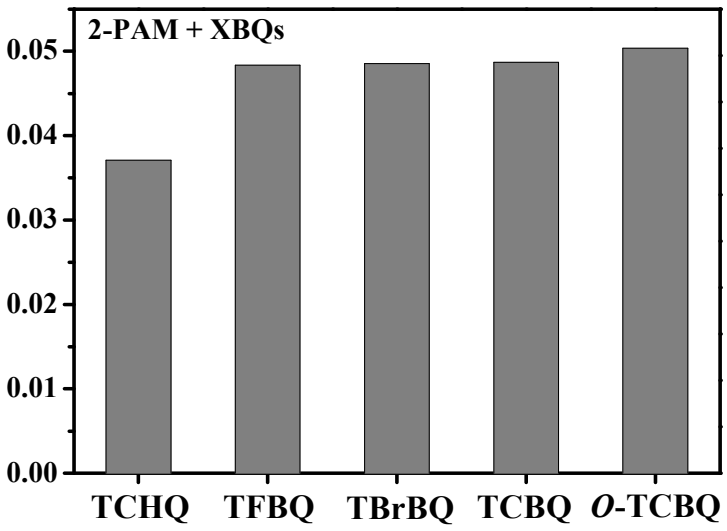


***Figure S7: The yield of 2-cyano-1-methylpyridinium chloride (2-CMP) from the reaction between 2-PAM and different tetrahalogenated quinoid compounds.*** All of the reactions were conducted in phosphate buffer for 36 min (100 mM, pH 7.4) at 25℃, and the reaction was initiated by the addition of tetrahalogenated quinoid compounds (XBQs) followed by rapid mixing. 2-PAM, 0.05 mM; XBQs, 0.5 mM.

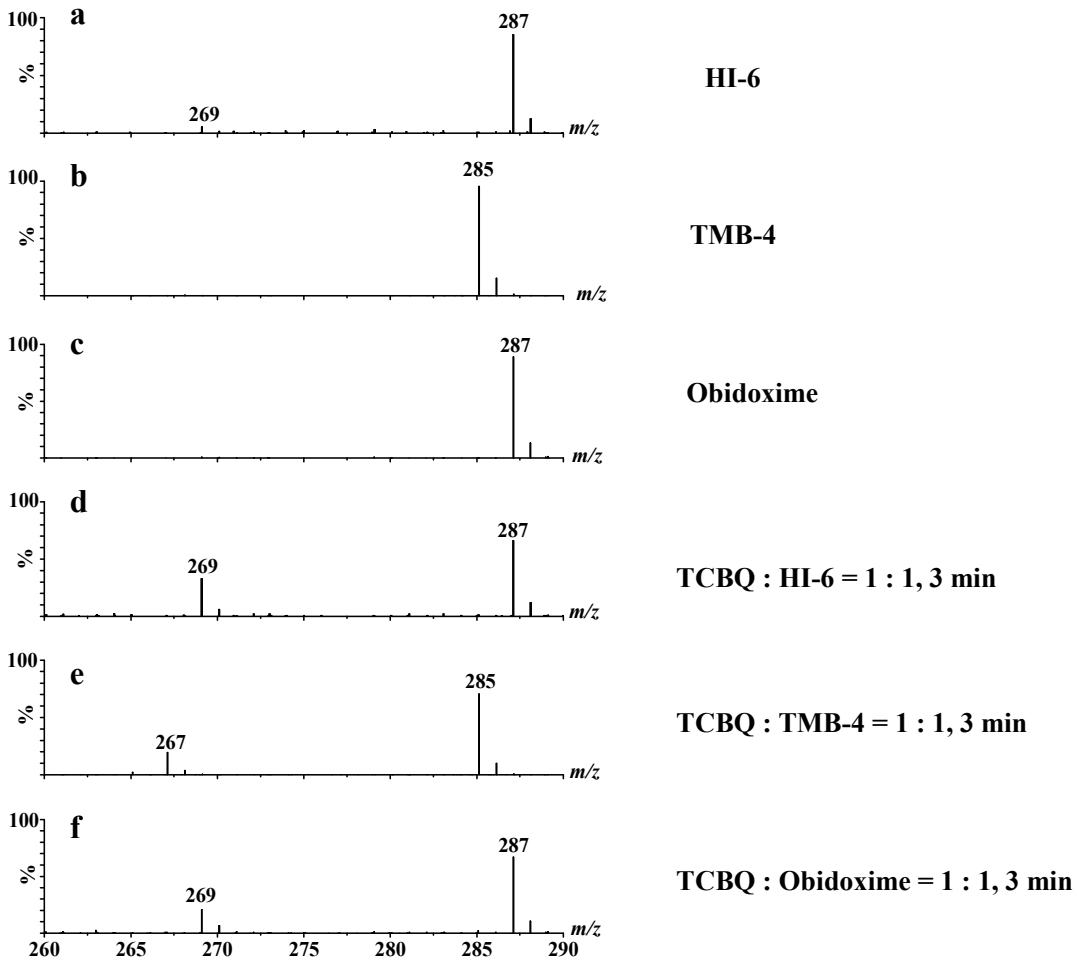


***Figure S8: Mass spectral analysis of the Beckmann fragmentation products of other pyridinium aldoximes (HI-6, TMB-4 and Obidoxime) after reacting with TCBQ.*** ESI-Q-TOF-MS spectra of HI-6 (a), TMB-4 (b), Obidoxime (c), and TCBQ with HI-6 (d), TMB-4 (e), Obidoxime (f) at the ratio of 1:1 in $CH_3COONH_4$ buffer (pH 7.4, 0.1 M) at room temperature, 3min. TCBQ, 0.2 mM.

## II. Protection by other pyridinium aldoximes against TCBQ-induced toxicity in HepG2

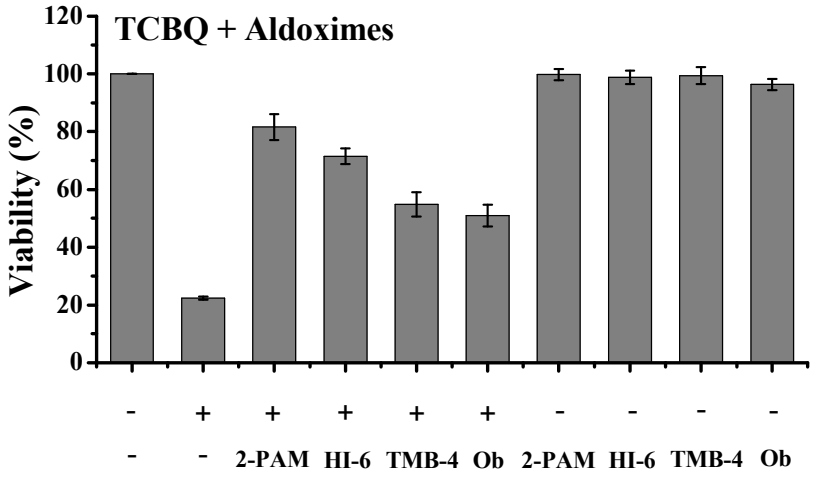


***Figure S9: Protection by other pyridinium aldoximes against TCBQ-induced toxicity in HepG2.*** The experiment was conducted via incubation of HepG2 cells in RPMI 1640 medium at 37℃ for 2h; TCBQ, 0.008 mM; Aldoximes, 0.8 mM. Ob: Obidoxime; Each point represents the mean of three separate experiments with the SD less than 5%.

## III. The reaction conditions to convert aldoximes to corresponding nitriles

***Table S1. The reaction conditions to convert aldoximes to corresponding nitriles***

| Catalyst | Concentration (mol%) | Solvent | Temperature (℃) | Time (h) | Yield (%) |
|---|---|---|---|---|---|
| Cyanuryl Chloride | 100 | DMF | Room Temp. | 4 | 100 [1] |
| Propylphosphonic Anhydride | 15 | THF | 70 | 1-3 | ＞84 [2] |
| Chloral | 50 | None | 120-140 | 2.5-7.5 | ＞67 [2] |
| Chlorosulfonic acid | 3.3 | Toluene | 90 | 0.5 | ≈100 [2] |
| Silphos | 20 | THF | Microwave irradiation | 3-6min | ＞79 [2] |
| Silica-$PCl_3$ | - | MeCN | Room Temp. | 8-10 | ＞87 [2] |
| $FeCl_3$-Montmorillonite K | 40 | Toluene | Reflux | 5-12 | ＞91 [2] |
| Metaboric acid | 3 | None | 140 | 7-58 | ＞62 [2] |
| Diethyl Chlorophosphate | 100 | Toluene | Reflux | 20-120 | ≈90 [2] |
| $Ph_3P$/*N*-Chlorosuccinimide | 120~150/120~150 | $CH_2Cl_2$ | Room Temp. | 0.5 | 75-97 [2] |
| $(Cl_3CO)_2CO$ | 0.3 | DMF/MeCN | Reflux | 1 | ＞72 [2] |
| HCl (gas) | - | - | 70-130 | 5-48 | ＞67 [2] |
| $AlCl_3$/KI | 100/300 | $H_2O$/MeCN | Room Temp./80 | 0.5/6 | 70-96 [2] |

(1) De Luca, L.,Giacomelli, G.,Porcheddu, A. (2002) Beckmann rearrangement of oximes under very mild conditions. *J. Org. Chem.* *67*, 6272-6274.

(2) Chandrasekhar, S. (2014) The Beckmann and related reactions. In *Comprehensive Organic Synthesis II*, Knochel, P.; Molander, G. A., Eds. Elsevier: Vol. 7, pp 770-800.

## IV. Copies of NMR Spectrum

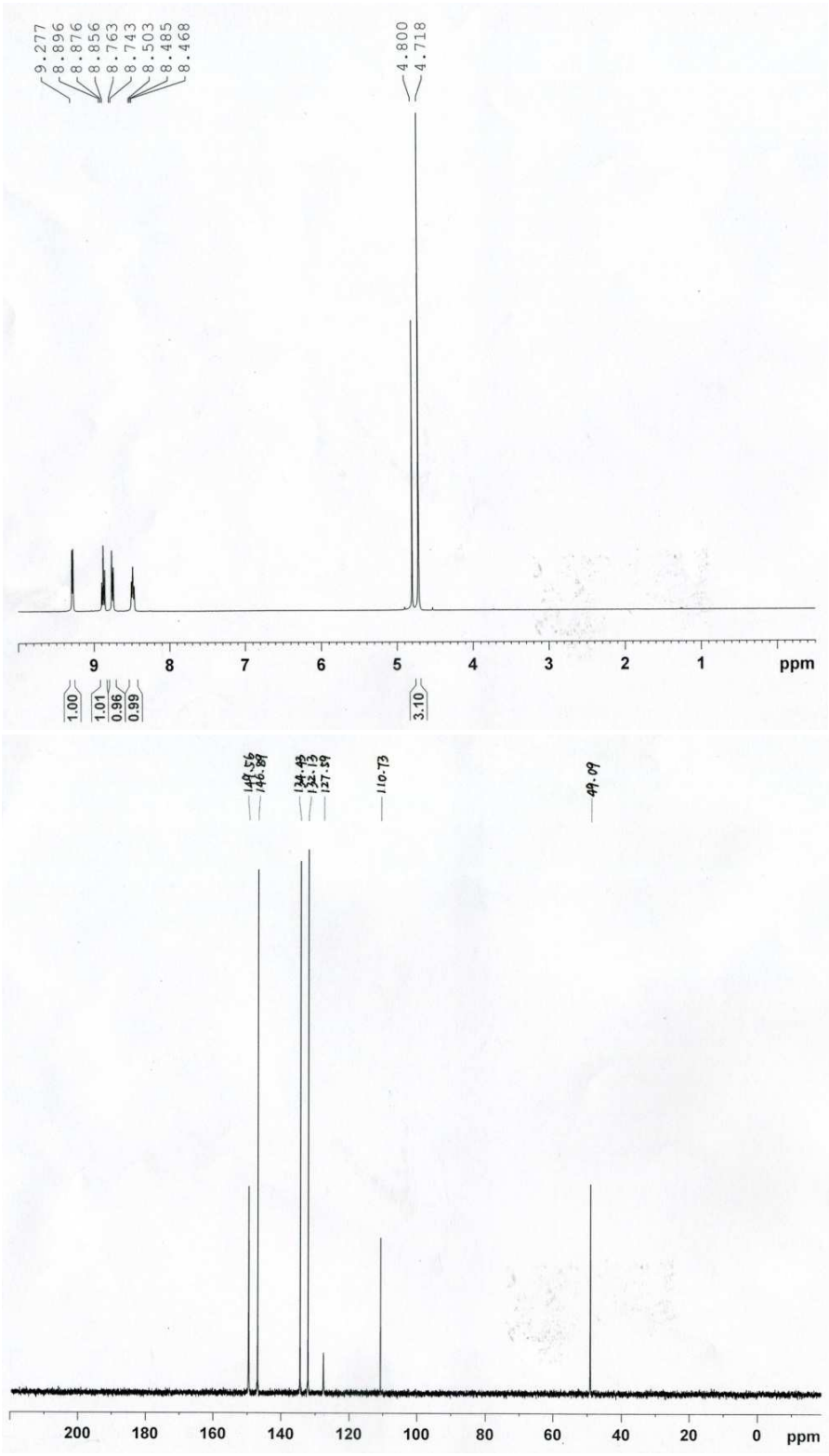


***Figure S10. The $^{1}$H-NMR and $^{13}$C-NMR of 2-CMP in $D_2O$.***

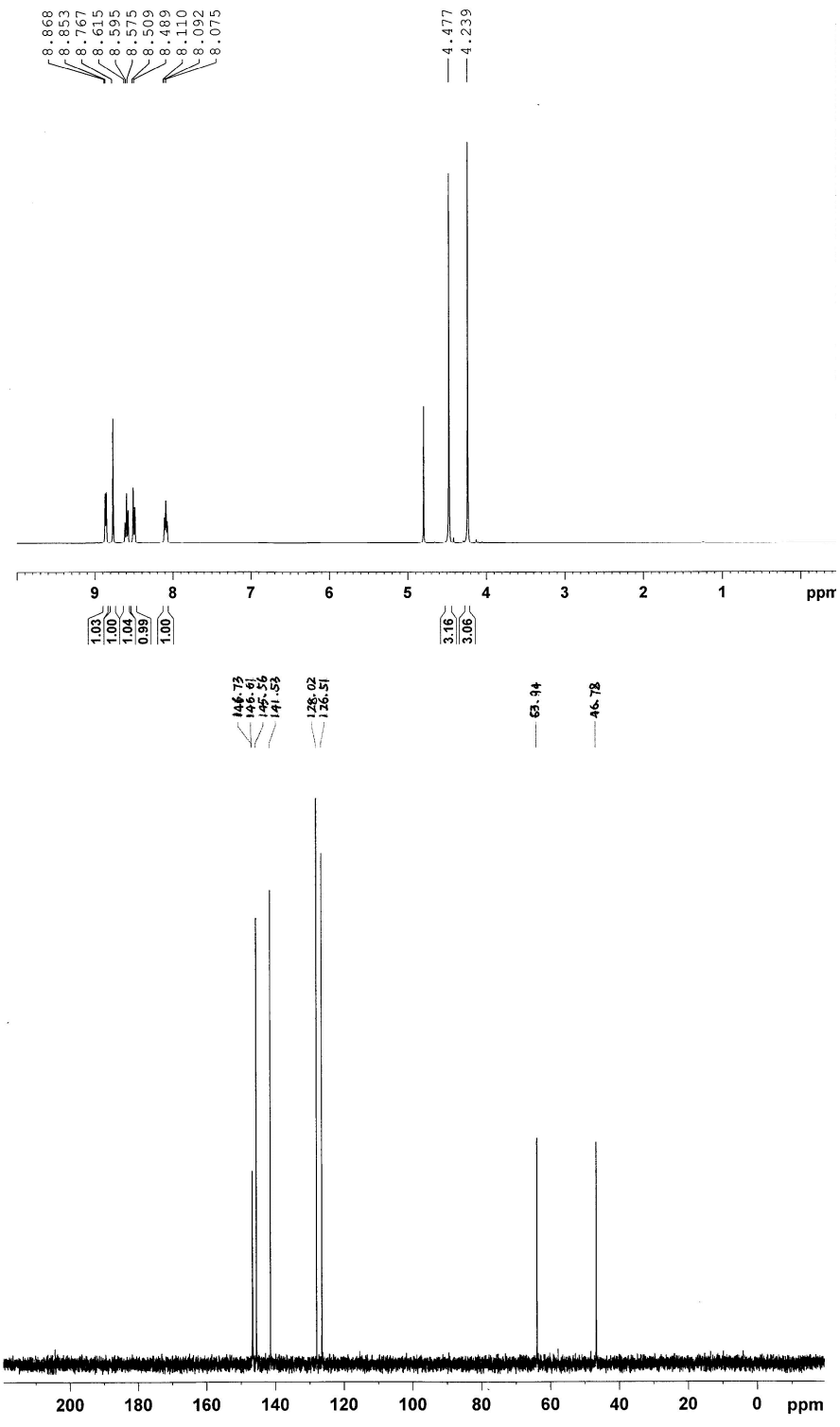


***Figure S11. The $^{1}$H-NMR and $^{13}$C-NMR of O-methyl-2-PAM in $D_2O$.***