Electronic Supplementary Information for

Sulfur, Oxygen, andNitrogen Mustards: Stability and Reactivity

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**Table S1.** Crystallographic data for 4,4-dimethylmorpholinium chloride (A) and 2,2'-oxybis(N,N,N-trimethylethanaminium) dichloride (B).

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**General experimental procedure**

Oxygen mustard, bis(β-chloroethyl) ether (BCEE), and half mustard, 2-chloroethyl ethyl sulfide (CEES) were purchased from Aldrich and used as received. Nitrogen mustards HN2 and HN3 were purchased from Aldrich and received as hydrochloride form, mechlorethamine hydrochloride and tris(2-chloroethyl)amine hydrochloride. The hydrochloride was neutralized by NaOH in water and extracted rapidly with diethyl ether, dried over anhydrous Na$_2$SO$_4$ to give the free amine form. Deuterated solvents CDCl$_3$, CD$_3$CN, DMSO-$d_6$, CD$_3$OD and D$_2$O were purchased from Cambridge Isotope Laboratories, Inc. Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance 400 spectrometer. Chemical shifts of the protons are expressed in ppm and calibrated against TMS as an internal reference or the residue solvent proton signals. Mass spectral data were obtained from the Mass Spectrometry Laboratory at the University of Kansas on a LCT Premier Mass spectrometer.

For X-ray crystallography study, intensity data were collected at 100K using a Bruker APEX II CCD area detector mounted on a Bruker D8 goniometer. Monochromatic Cu K$_\alpha$ radiation ($\lambda = 1.54178$ Å) was provided with Helios multilayer optics and a Bruker MicroStar microfocus rotating anode operating at 45kV and 60mA. The crystallographic data and details of data collection for 4,4-dimethylmorpholinium chloride (A) and 2,2'-oxybis(N,N,N-trimethylethanaminium) dichloride (B) are given in Table S1.
Figure S1. $^1$H NMR changes (400 MHz, rt) of CEES in CD$_3$OD over time.
Figure S2. $^1$H NMR changes (400 MHz, rt) of CEES in D$_2$O over time.
Figure S3. $^1$H NMR changes (400 MHz, rt) of HN2 in DMSO-$d_6$ over time.
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Figure S5. $^1$H NMR changes of HN2 in D$_2$O over time.
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Figure S9. $^1$H NMR monitoring (400 MHz, rt) of the reaction between BCEE and $(\text{CH}_3)_3\text{N}$ in CDCl$_3$ (with ESI-MS data).
**Figure S10.** $^1$H NMR monitoring (400 MHz, rt) of the reaction between CEES and (CH$_3$)$_2$NH in CDCl$_3$. 

< 10% conversion (7 d)
Figure S11. $^1$H NMR monitoring (400 MHz, rt) of the reaction between CEES and (CH$_3$)$_3$N in CDCl$_3$ (with ESI-MS data).
Figure S12. $^1$H NMR monitoring (400 MHz, rt) of the reaction between HN2 and CH$_3$NH$_2$ in CDCl$_3$.

ca. 25% conversion (7 d)
possible main product:
Figure S13. $^1$H NMR monitoring (400 MHz, rt) of the reaction between HN2 and CH$_3$CH$_2$NH$_2$ in CDCl$_3$. 

< 10% conversion (7 d)
Figure S14. $^1$H NMR monitoring (400 MHz, rt) of the reaction between HN2 and (CH$_3$)$_2$NH in CDCl$_3$ (with ESI-MS data).
Figure S15. $^1$H NMR monitoring (400 MHz, rt) of the reaction between HN2 and (CH$_3$CH$_2$)$_2$NH in CDCl$_3$ (with ESI-MS data).

Ca. 20% conversion (7 d)

Main product:

C$_9$H$_{21}$N$_2^+$ (ESI-MS)
Calc. 157.17
Expt. 157.17
Figure S16. $^1$H NMR monitoring (400 MHz, rt) of the reaction between HN2 and (CH$_3$)$_3$N in CDCl$_3$ (with ESI-MS data).
Figure S17. $^1$H NMR monitoring (400 MHz, rt) of the reaction between HN3 and (CH$_3$)$_2$NH in CDCl$_3$ (with ESI-MS data).

c. 50% conversion (7 d)

main product:

C$_8$H$_{18}$ClN$_2^+$ (ESI-MS)
Calc. 177.12
Expt. 177.11
Figure S18. $^1$H NMR monitoring (400 MHz, rt) of the reaction between HN3 and (CH₃CH₂)₂NH in CDCl₃ (with ESI-MS data).
Figure S19. $^1$H NMR monitoring (400 MHz, rt) of the reaction between HN3 and (CH$_3$)$_3$N in CDCl$_3$ (with ESI-MS data).
Figure S20. $^1$H NMR (400 MHz, rt, D$_2$O) of the precipitates isolated from the reaction between BCEE and (CH$_3$)$_2$NH in CDCl$_3$ (with ESI-MS data).

$\text{C}_6\text{H}_{14}\text{NO}^+$ (ESI-MS)
Calc. 116.11
Expt. 116.11
Figure S21. $^1$H NMR (400 MHz, rt, D$_2$O) of the precipitates isolated from the reaction between HN3 and CH$_3$NH$_2$ in CDCl$_3$ (with ESI-MS data).
### Table S1. Crystallographic data for 4,4-dimethylmorpholinium chloride (A) and 2,2’-oxybis(N,N,N-trimethylethanammonium) dichloride (B)

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<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
</tr>
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<tbody>
<tr>
<td>Formula</td>
<td>C₆H₁₄ClNO</td>
<td>C₁₀H₂₈Cl₂N₂O₂</td>
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<tr>
<td>Formula weight</td>
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<td>279.24</td>
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<td>Crystal size (mm³)</td>
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<td>0.13×0.06×0.02</td>
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<tr>
<td>Space group</td>
<td>P2₁2₁2₁</td>
<td>Cc</td>
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<tr>
<td>a (Å)</td>
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<td>21.0466(7)</td>
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<tr>
<td>b (Å)</td>
<td>9.7455(4)</td>
<td>5.8427(2)</td>
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<tr>
<td>c (Å)</td>
<td>9.7543(4)</td>
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<td>90</td>
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<tr>
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<td>γ (°)</td>
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<td>90</td>
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<td>1519.68(9)</td>
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<tr>
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<td>4</td>
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<tr>
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<td>λ (Å)</td>
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<td>F(000)</td>
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<td>3.777</td>
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<td>Abs corr</td>
<td>Multi-scan</td>
<td>Multi-scan</td>
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<tr>
<td>Max, min trans</td>
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<td>1.000, 0.791</td>
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<tr>
<td>θ range (°)</td>
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<td>4.34-69.06</td>
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<tr>
<td>Reflns collected</td>
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<td>4835</td>
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<td>Indep reflns</td>
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<td>2177</td>
</tr>
<tr>
<td>R(int)</td>
<td>0.0223</td>
<td>0.0227</td>
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<tr>
<td>Data/restr/param</td>
<td>1438 / 0 / 140</td>
<td>2177 / 2 / 257</td>
</tr>
</tbody>
</table>

\[ a R_1; \ wR_2 = 0.154; 0.0418 \]
\[ \text{GOF } (F^2) = 1.154 \]
\[ \text{Obsd data [I > 2σ(I)] = 1438} \]
\[ \text{Largest diff. peak and hole (e Å⁻³) = 0.161, -0.135, 0.272, -0.147} \]

\[ a R_f(\text{obsd data}) = \Sigma |F_o| - |F_c| \ / \Sigma |F_o| \]
\[ wR_2(\text{all data}) = \left( \Sigma \left[w(F_o^2 - F_c^2)^2 \right] / \Sigma \left[w(F_o^2)^2 \right] \right)^{1/2} \]