

# Synthesis of 'Nereid', a new phenol-free detergent to replace Triton

## X-100 in virus inactivation

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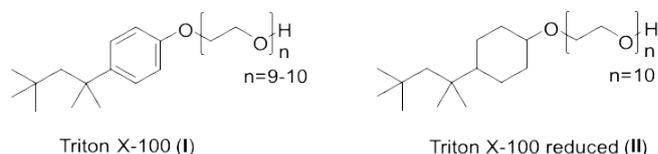
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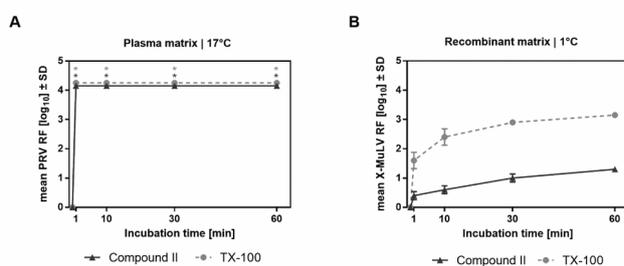
Electronic Supplementary Information (ESI) available: Synthetic procedures and NMR spectra. See

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## Figures and Schemes:

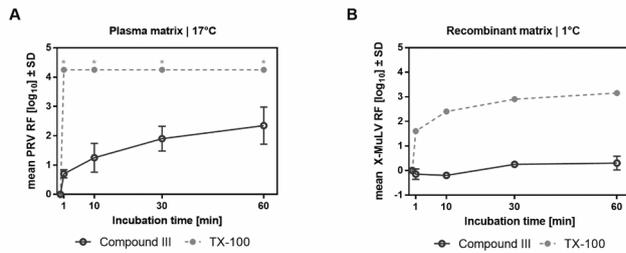


**Figure 1: Structures of TX-100 and TX-100 reduced**

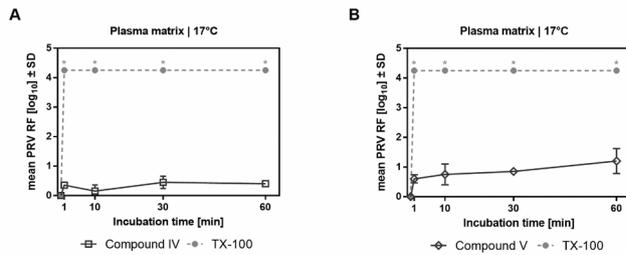


**Figure 2. Virus inactivation by S/D mixes containing TX-100 versus compound II (TX-100 reduced).**

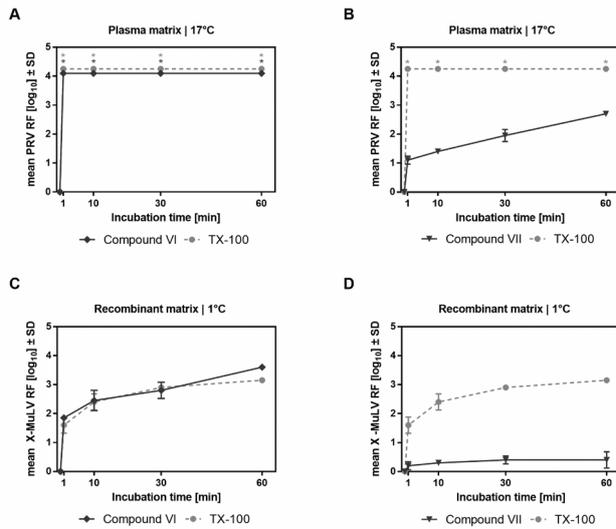
**(A)** Plasma-derived model matrix was spiked with Pseudorabies virus (PRV) before addition of S/D mix consisting of PS80, TNBP and TX-100 or compound II. Duplicate runs were performed at 17°C at a final S/D mix concentration of 5% as specified for manufacturing. **(B)** Recombinant model matrix was spiked with Xenotropic murine leukemia virus (X-MuLV) before addition of S/D mix consisting of PS80, TNBP and TX-100 or compound II. Duplicate runs were performed at 1°C at a final S/D mix concentration of 10% as specified for manufacturing. **(A,B)** Samples were drawn after 1 min, 10 min, 30 min and 60 min; viral loads of these samples were compared to a sample drawn before S/D mix addition to calculate the respective reduction factor (RF). Asterisks indicate viral inactivation below detection limit. SD ... standard deviation (only shown if larger than the height of symbols).



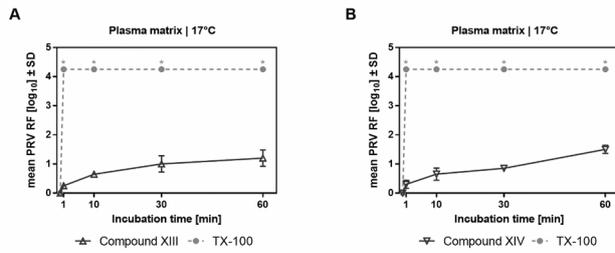
**Figure 3. Virus inactivation by S/D mixes containing novel compound III.** Matrices were spiked with the respective virus before addition of S/D mix (PS80, TNBP, compound III). Samples were drawn 1 min, 10 min, 30 min and 60 min after S/D mix addition; viral loads of these samples were compared to a sample drawn before S/D mix addition to calculate the respective reduction factor (RF). **(A)** Duplicate runs were performed at 17°C using a plasma-derived model matrix and Pseudorabies virus (PRV); the final S/D mix concentrations were 5% of manufacturing. Asterisks indicate viral inactivation below detection limit. **(B)** Duplicate runs were performed at 1°C using a recombinant model matrix and Xenotropic murine leukemia virus (X-MuLV); the final S/D mix concentrations were 10% of manufacturing. SD ... standard deviation (only shown if larger than the height of symbols).



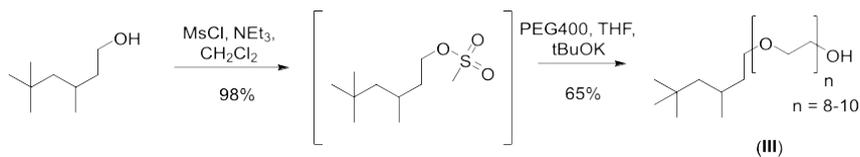
**Figure 4. Virus inactivation by S/D mixes containing novel compounds IV and V.** Duplicate runs were performed at 17°C using a plasma-derived model matrix and Pseudorabies virus (PRV). PS80 and TNBP were combined with (A) compound IV or (B) compound V and added to the virus-spiked matrix to reach a final concentration of 5% as specified for manufacturing. (A,B) Samples were drawn 1 min, 10 min, 30 min and 60 min after S/D mix addition; viral loads of these samples were compared to a sample drawn before S/D mix addition to calculate the respective reduction factor (RF). Asterisks indicate viral inactivation below detection limit. SD ... standard deviation (only shown if larger than the height of symbols).



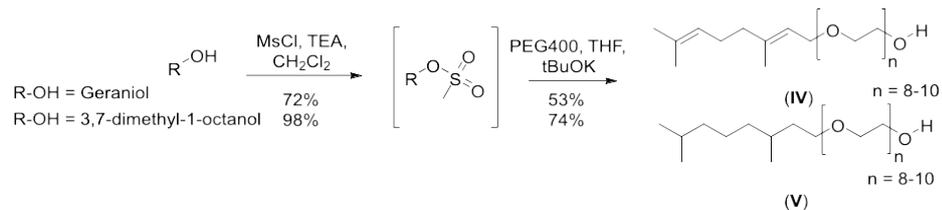
**Figure 5. Virus inactivation by S/D mixes containing novel compounds VI and VII.** Matrices were spiked with the respective virus before addition of S/D mix (PS80, TNBP, compound VI / compound VII). Samples were drawn 1 min, 10 min, 30 min and 60 min after S/D mix addition; viral loads of these samples were compared to a sample drawn before S/D mix addition to calculate the respective reduction factor (RF). (A,B) Duplicate runs were performed at 17°C using a plasma-derived model matrix and Pseudorabies virus (PRV); the final S/D mix concentrations were 5% of manufacturing. Asterisks indicate viral inactivation below detection limit. (C,D) Duplicate runs were performed at 1°C using a recombinant model matrix and Xenotropic murine leukemia virus (X-MuLV); the final S/D mix concentrations were 10% of manufacturing. SD ... standard deviation (only shown if larger than the height of symbols).



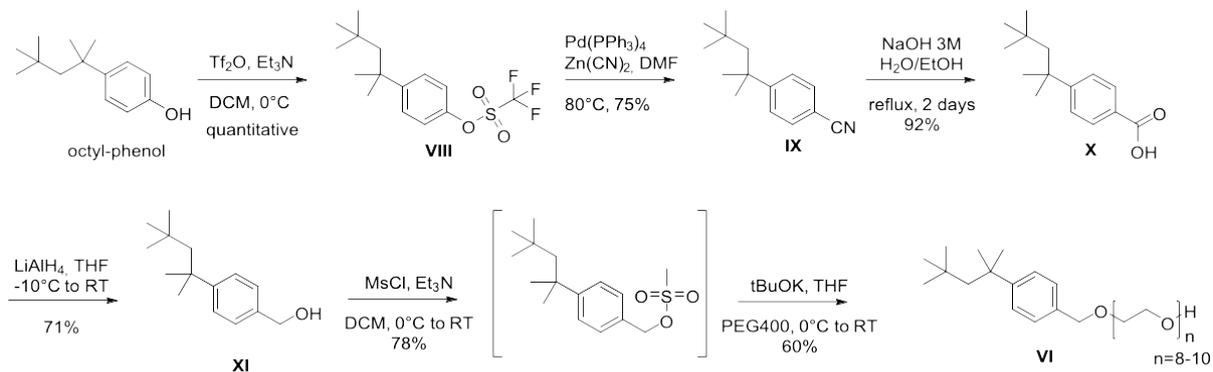
**Figure 6. Virus inactivation by S/D mixes containing novel compounds XIII and XIV.** Duplicate runs were performed at 17°C using a plasma-derived model matrix and Pseudorabies virus (PRV). PS80 and TNBP were combined with (A) compound XIII or (B) compound XIV and added to the virus-spiked matrix to reach a final concentration of 5% as specified for manufacturing. Samples were drawn 1 min, 10 min, 30 min and 60 min after S/D mix addition; viral loads of these samples were compared to a sample drawn before S/D mix addition to calculate the respective reduction factor (RF). Asterisks indicate viral inactivation below detection limit. SD ... standard deviation (only shown if larger than the height of symbols).



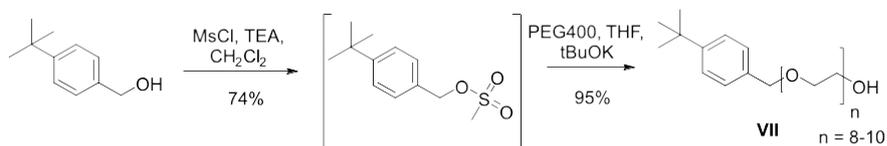
**Scheme 1**



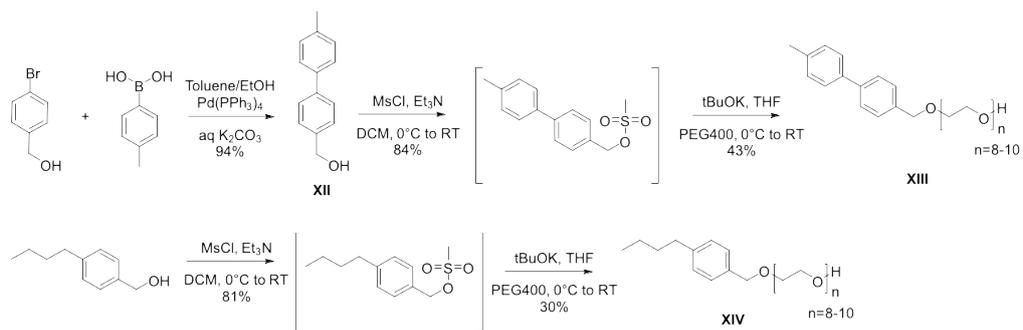
**Scheme 2**



**Scheme 3**

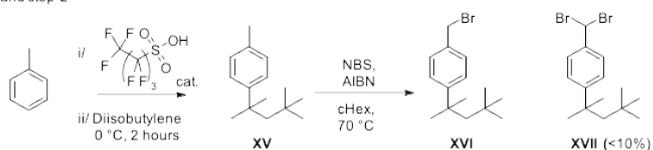


**Scheme 4**

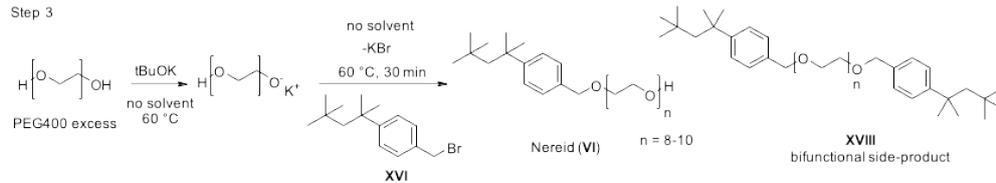


## Scheme 5

Step 1 and step 2



Step 3



## Scheme 6