Supplementary Information

Effect of Ion to Ligand Ratio on the Aqueous to Organic Relative Solubility of a Lanthanide-Ligand Complex

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Table S1. Details on model construction.

Exchanged Molecule	Water Molecule Count	Organic Molecule Count	Additional Components	Equilibrated Box Dimensions (nm)
Ethylbenzene	3500	500 octanol	--	$4.17752 \times 4.17752 \times 13.61871$
	3500	500 hexane	--	$4.07038 \times 4.07038 \times 13.02523$
Formamide	3500	500 octanol	--	$4.17803 \times 4.17803 \times 13.62040$
	3500	500 hexane	--	$4.07259 \times 4.07259 \times 13.03228$
Acetonitrile	3500	500 octanol	--	$4.17581 \times 4.17581 \times 13.61316$
	3500	500 hexane	--	$4.08276 \times 4.08276 \times 13.06482$
Gd^{3+}	3500	500 octanol	3 Cl^-	$4.17535 \times 4.17535 \times 13.61165$
	3500	500 hexane	3 Cl^-	$4.44776 \times 4.44776 \times 10.94147$
HDEHP	4000	500 octanol	1 Na^+	$4.25623 \times 4.25623 \times 14.00299$
	4000	500 hexane	1 Na^+	$4.13736 \times 4.13736 \times 13.61191$
Gd(HDEHP)	4000	500 octanol	2 Cl^-	$4.24756 \times 4.24756 \times 13.97450$
	4000	500 hexane	2 Cl^-	$4.14806 \times 4.14806 \times 13.64711$
Gd(HDEHP)$_2$	4850	575 octanol	1 Cl^-	$4.39440 \times 4.29440 \times 15.38038$
	4850	775 hexane	1 Cl^-	$4.50606 \times 4.50606 \times 15.77123$
Gd(HDEHP)$_3$	4850	575 octanol	--	$4.40599 \times 4.40599 \times 15.42095$
	4850	775 hexane	--	$4.50933 \times 4.50933 \times 15.78266$

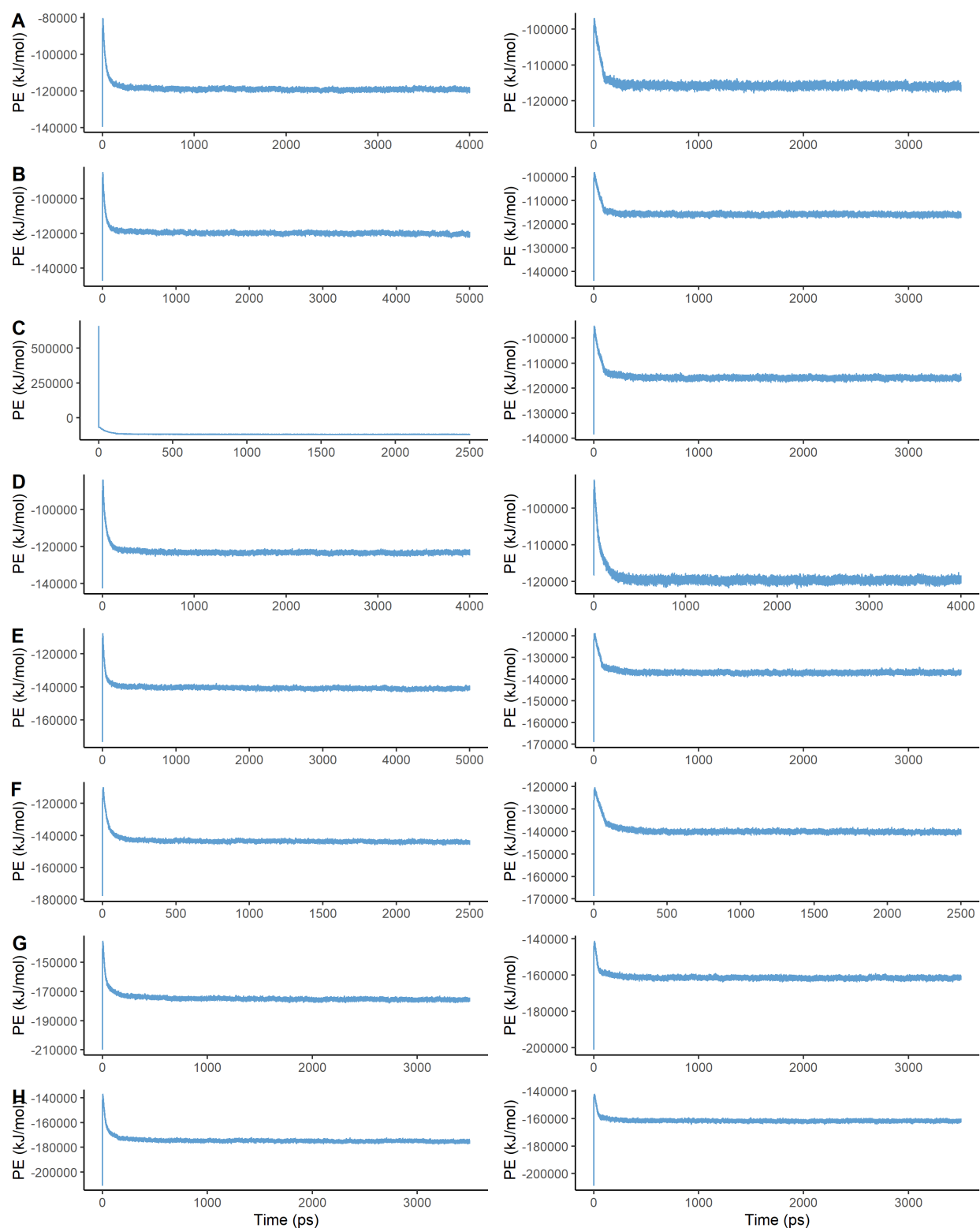DEHP$^-$ gromacs topology file appears at the end of the SI

Figure S1. Plots of the potential energy (PE) of the biphasic system equilibrations of water and either octanol (left column) or hexane (right column) for the simulations of (A) ethylbenzene, (B) formamide, (C) acetonitrile, (D) Gd^{3+} ion, (E) $DEHP^-$ ion, (F) Gd-DEHP 1:1, (G) Gd-DEHP 1:2, and (H) Gd-DEHP 1:3.
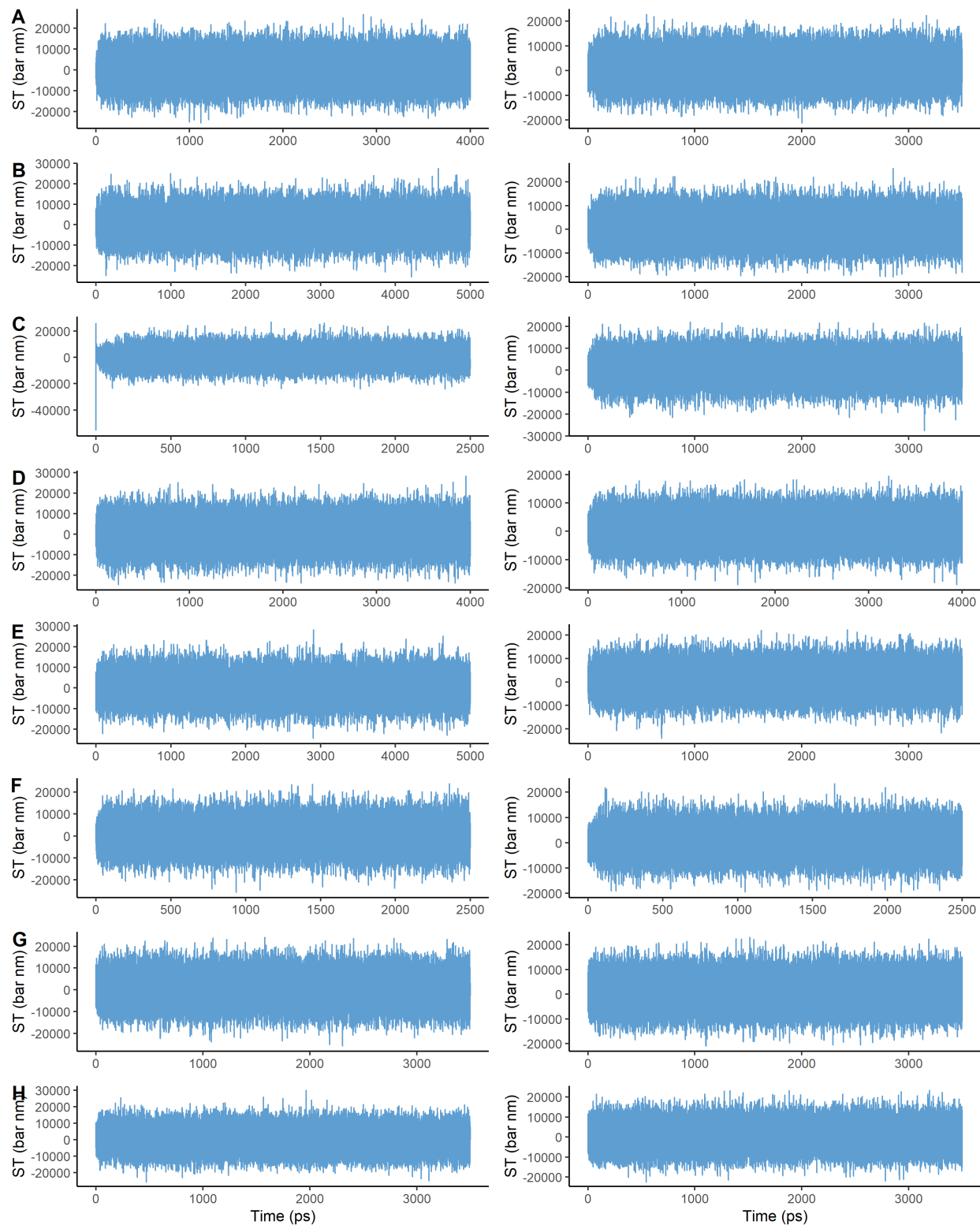
Figure S2. Plots of the surface tension of the biphasic system equilibrations of water and either octanol (left column) or hexane (right column) for the simulations of (A) ethylbenzene, (B) formamide, (C) acetonitrile, (D) Gd^{3+} ion, (E) $DEHP^-$ ion, (F) Gd-DEHP 1:1, (G) Gd-DEHP 1:2, and (H) Gd-DEHP 1:3.
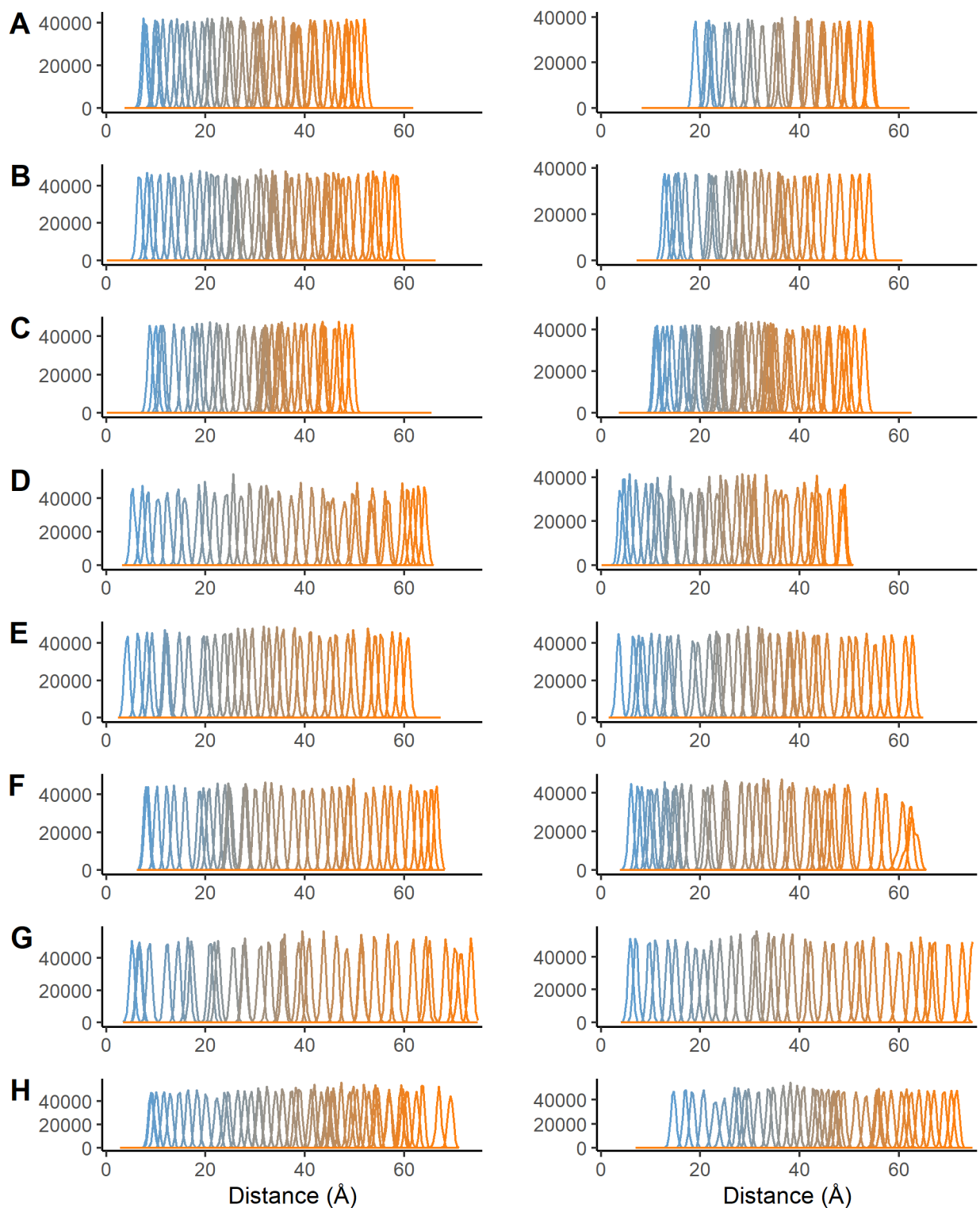
Figure S3. Umbrella sampling windows (Y-axis is sampling count) as the molecules transfer from water to either octanol (left column) or hexane (right column) for (A) ethylbenzene, (B) formamide, (C) acetonitrile, (D) Gd^{3+} ion, (E) $DEHP^-$ ion, (F) Gd-DEHP 1:1, (G) Gd-DEHP 1:2, and (H) Gd-DEHP 1:3.

Figure S4. The potential of mean force as an ethylbenzene molecule transfers from bulk water into (A) octanol or (B) hexane. Background coloring indicates the transition from contact with bulk water (blue) to a mixture (light orange) and to bulk organic (dark orange). Dotted lines indicate statistical upper and lower bounds of the PMF.

Figure S5. The potential of mean force as a formamide molecule transfers from bulk water into (A) octanol or (B) hexane. Background coloring is same as in Figure S1. Dotted lines indicate statistical upper and lower bounds of the PMF.
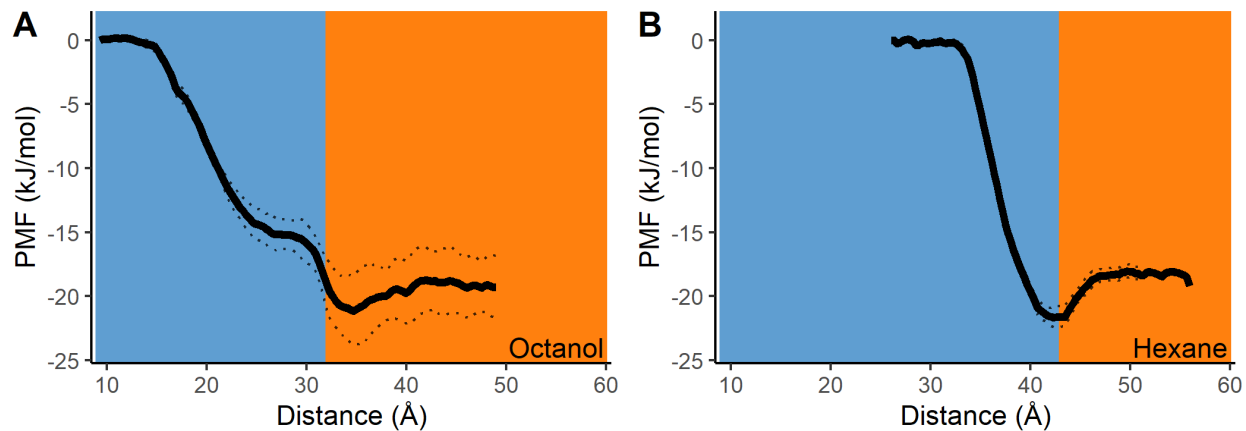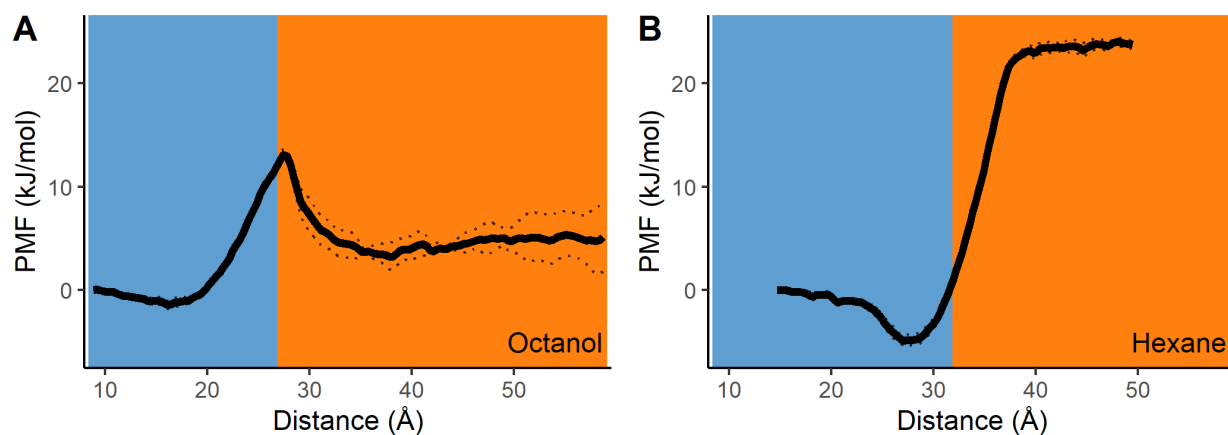
Figure S6. The potential of mean force as an acetonitrile molecule transfers from bulk water into (A) octanol or (B) hexane. Background coloring is same as in Figure S1. Dotted lines indicate statistical upper and lower bounds of the PMF.
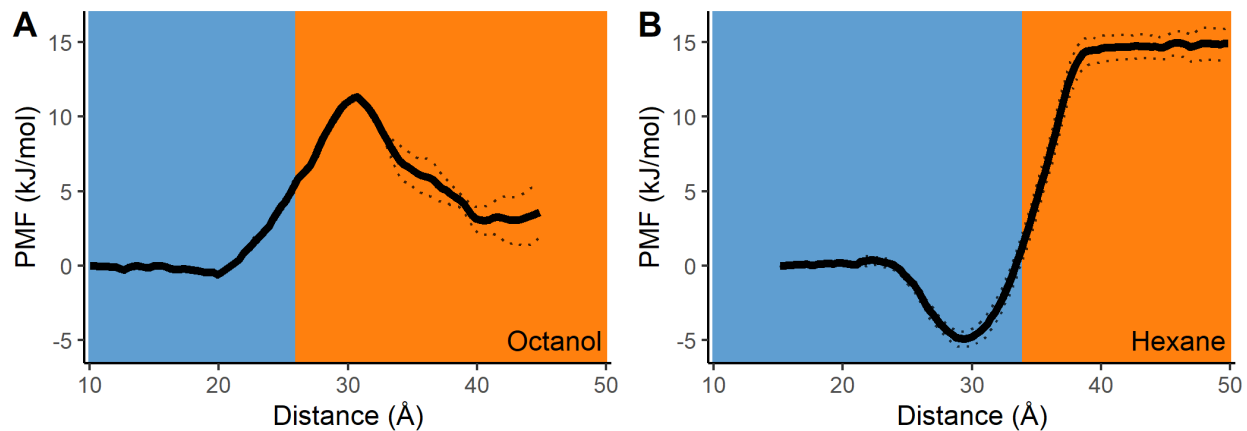
Supplementary information on the unbound Gd³⁺ ion simulations

As the Gd^{3+} ion enters octanol (Figure S7A), the free energy rapidly increases monotonically with no plateauing observed over the length of the simulation. The absence of a plateau in the bulk octanol arises from the limited size of the simulation box and due to the formation of a water finger as the Gd^{3+} hydration complex brings along additional water molecules with it into the organic phase (Figure S7C). As the ion progressed deeper into the bulk octanol, the water finger continued extending and remained intact over the distance covered in this simulation. A water finger also formed when the ion enters the bulk hexane. However, as hexane lacks the hydrophilic head groups of octanol, the volume of the water entering the bulk hexane layer is much greater and thermodynamically more unfavorable (Figure S7B). The observation of water finger formations follows trends seen in previous studies on ion transfer from water into an immiscible liquid.[*]
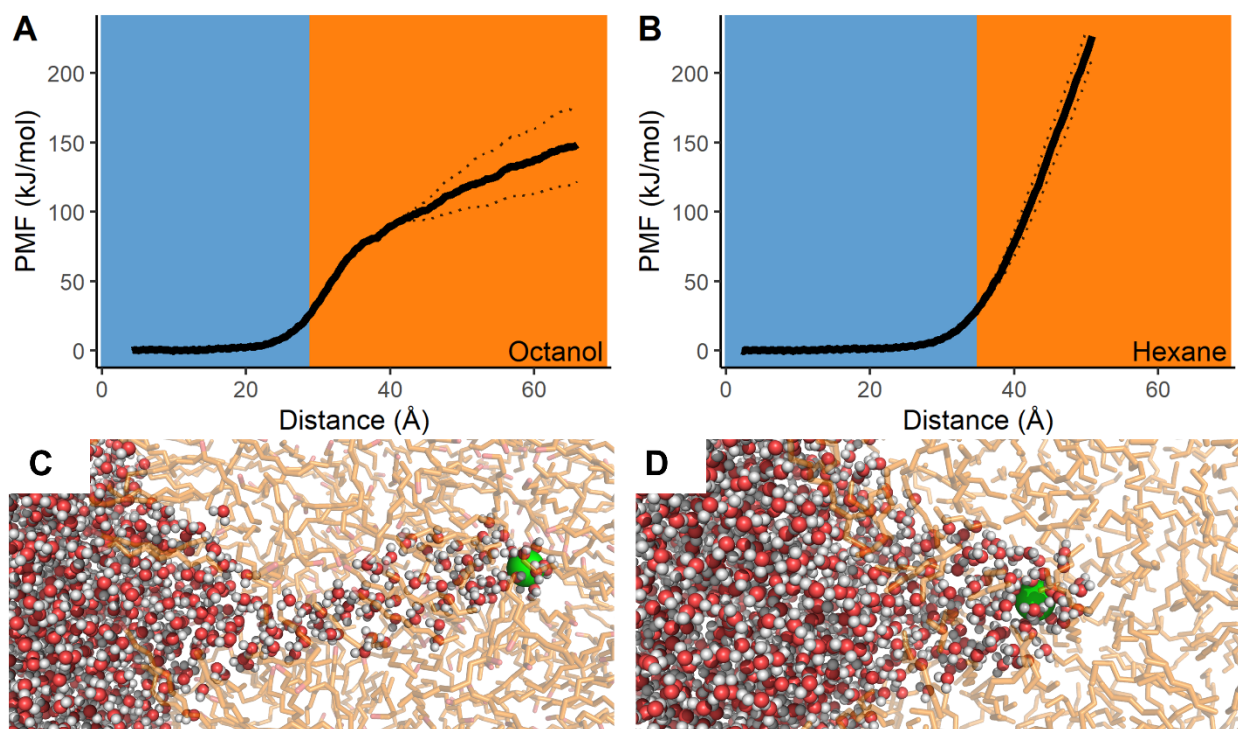
Figure S7. (A, B) Potential of mean force as a Gd^{3+} ion transfers from aqueous to either octanol or hexane layers. Dotted lines indicate statistical upper and lower bounds of the PMF. (C) Water tunnel formed as Gd^{3+} enters bulk octanol. (D) Water tunnel formed as Gd^{3+} enters bulk hexane. Coloring is same as Figure 1 with Gd^{3+} ion shown as a green sphere.

[*] (1) llan Benjamin, *Science*, 1993, **261**, 1558–1560. (2) A. Morita, A. Koizumi and T. Hirano, *J. Chem. Phys.*, 2021, **154**, 080901. (3) N. Kikkawa, L. Wang and A. Morita, *J. Am. Chem. Soc.*, 2015, **137**, 8022–8025. (4) J. J. Karnes and I. Benjamin, *J. Chem. Phys.*, 2016, **145**, 014701.

Supplementary information on the unrestrained DEHP⁻ ion simulations

As additional verification that the DEHP⁻ molecule does readily incorporate into the water-organic interfaces, we conducted additional simulations following the same methodology where an equilibrated system containing the DEHP⁻ molecule positioned within either bulk aqueous or bulk organic layers was simulated for 25ns without any constraints. While the DEHP⁻ molecule readily integrated into the interfacial layer when its starting position was within bulk water or within bulk hexane, it was not able to break past the ordered octanol tails at the octanol-water inface when it was within bulk octanol and so it remained in the octanol layer. This octanol-water simulation was extended to a total time of 200ns without and change; we anticipate that observation of this event without direction would require additional simulation time, but this is beyond the intended purpose of these simulations. The results of the simulations can be quantified by the radial distribution of the DEHP⁻ molecule to nearby solvent molecules (Figure S8). The graphs illustrate the frequent contact between ligand to both water and hexane in the water-hexane simulations as it resides at the interface (Figure S8A) and water and octanol when the ligand begins within bulk water (Figure S8B, right), but there is only frequent contact with octanol molecules when the ligand is initially positioned in the bulk octanol layer (Figure S8B, left).
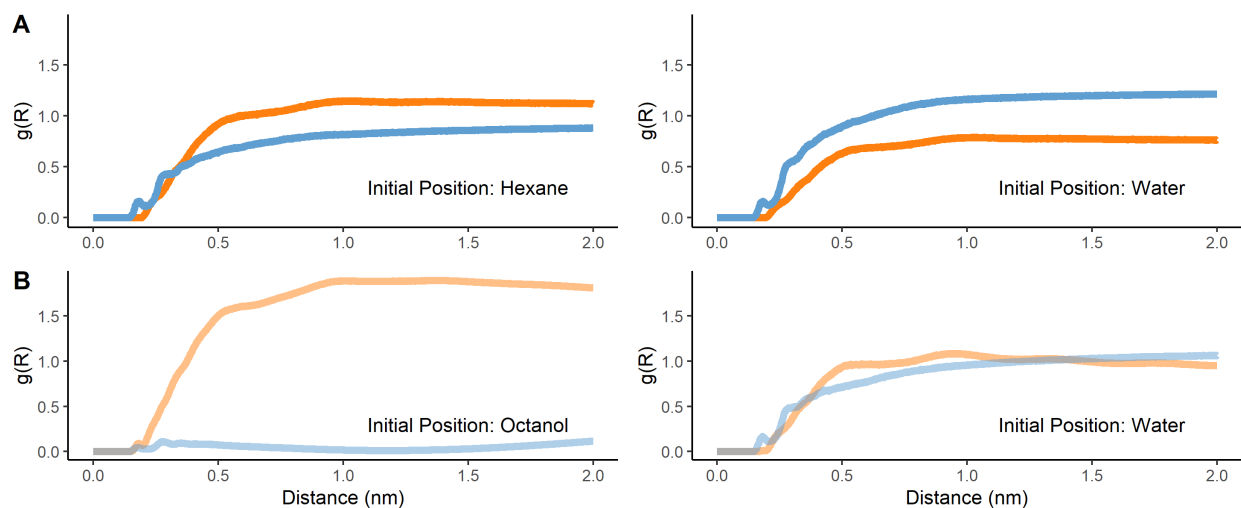
Figure S8. Radial distribution functions of the DEHP⁻ molecule to nearby water (blue) or organic molecules (orange) for (A) the hexane-water and (B) octanol-water systems when the DEHP⁻ molecule begins in bulk organic (left) or aqueous (right) phases.
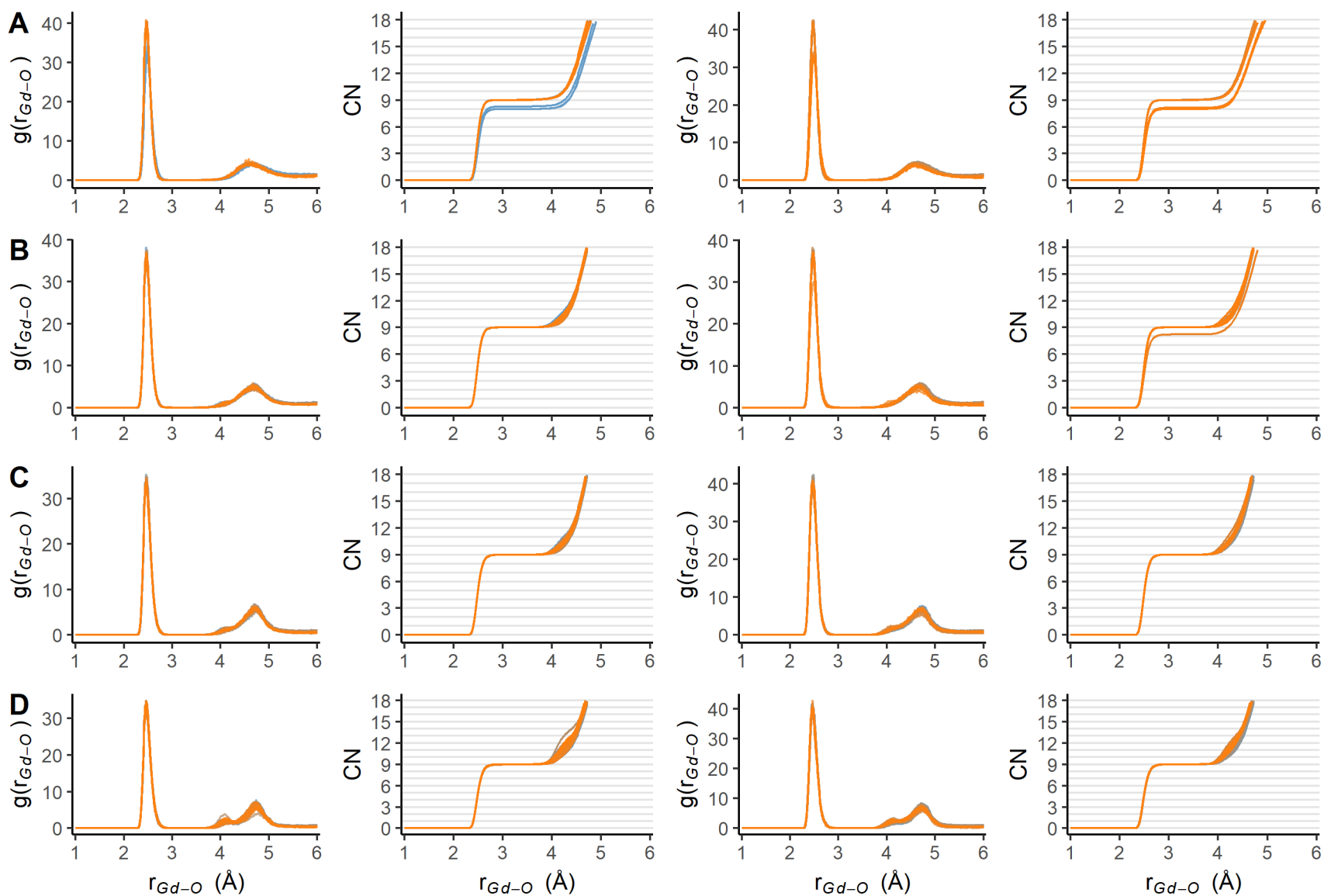
Figure S9. Plots of Gd-O radial distribution functions and coordination numbers (CN) from the umbrella simulations of the transfer of free Gd ion (A) and Gd-DEHP⁻ in 1:1 (B), 1:2 (C) and 1:3 (D) ratios from water to octanol (left columns) or hexane (right)
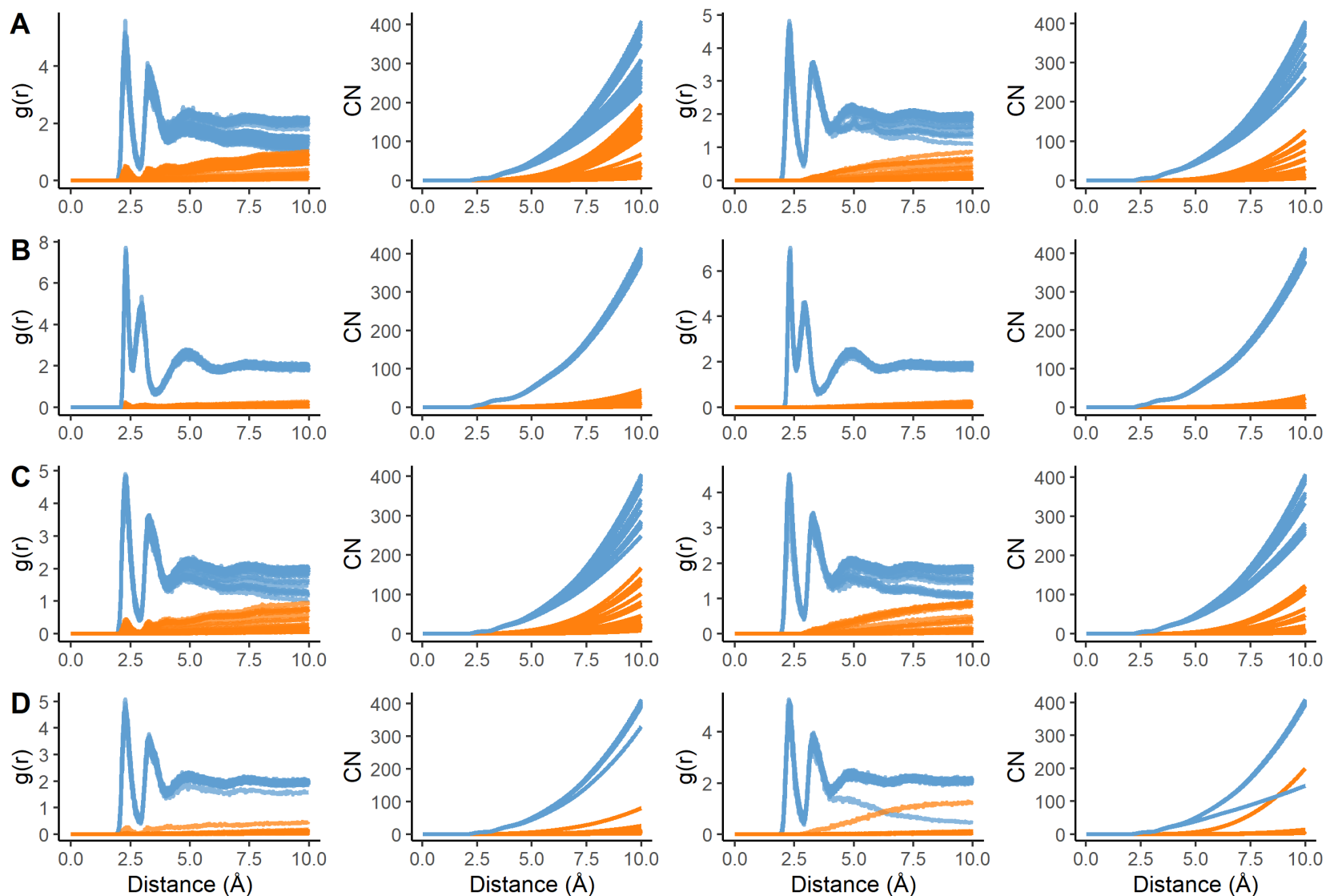
Figure S10. Radial distribution functions and coordination numbers (CN) for the counterions to the center of mass of water (blue) and organic (orange) molecules from the umbrella simulations of the transfer of free Gd ion (A), DEHP⁻ ion (B), and Gd-DEHP⁻ in 1:1 (C), and 1:2 (D) ratios with octanol (left columns) or hexane (right) as the organic solvent.

DEHP structure in GROMACS format

```
Green Red Orange Magenta Azure Cyan Skyblue
   55
    1HDE      O1    1   0.037   0.206  -0.159
    1HDE      P1    2  -0.071   0.195  -0.264
    1HDE      O2    3  -0.182   0.093  -0.250
    1HDE      O3    4  -0.002   0.181  -0.414
    1HDE      O4    5  -0.132   0.346  -0.283
    1HDE      C1    6   0.054   0.054  -0.451
    1HDE      H1    7   0.147   0.038  -0.395
    1HDE      H2    8  -0.015  -0.026  -0.423
    1HDE      C2    9  -0.244   0.366  -0.372
    1HDE      H3   10  -0.218   0.327  -0.471
    1HDE      H4   11  -0.330   0.309  -0.336
    1HDE      C3   12  -0.278   0.515  -0.377
    1HDE      C4   13  -0.159   0.604  -0.422
    1HDE      C5   14  -0.411   0.539  -0.454
    1HDE      H5   15  -0.198   0.705  -0.440
    1HDE      H6   16  -0.091   0.613  -0.336
    1HDE      C6   17  -0.076   0.558  -0.542
    1HDE      H7   18  -0.437   0.645  -0.443
    1HDE      H8   19  -0.490   0.483  -0.402
    1HDE      C7   20  -0.415   0.502  -0.603
    1HDE      H9   21  -0.139   0.547  -0.631
    1HDE     H10   22  -0.032   0.460  -0.522
    1HDE      C8   23   0.038   0.656  -0.575
    1HDE     H11   24  -0.517   0.516  -0.642
    1HDE     H12   25  -0.349   0.565  -0.663
    1HDE     H13   26  -0.388   0.398  -0.621
    1HDE     H14   27   0.101   0.669  -0.485
    1HDE     H15   28  -0.004   0.755  -0.597
    1HDE      C9   29   0.126   0.610  -0.692
    1HDE     H16   30   0.067   0.600  -0.784
    1HDE     H17   31   0.206   0.682  -0.712
    1HDE     H18   32   0.172   0.513  -0.671
    1HDE     C10   33   0.083   0.053  -0.601
    1HDE     C11   34   0.168  -0.070  -0.641
    1HDE     C12   35  -0.043   0.076  -0.688
    1HDE     H19   36   0.199  -0.057  -0.746
    1HDE     H20   37   0.261  -0.067  -0.582
    1HDE     C13   38   0.106  -0.210  -0.625
    1HDE     H21   39  -0.017   0.054  -0.793
    1HDE     H22   40  -0.066   0.184  -0.686
    1HDE     C14   41  -0.171   0.000  -0.650
    1HDE     H23   42   0.020  -0.221  -0.693
    1HDE     H24   43   0.067  -0.223  -0.524
    1HDE     C15   44   0.206  -0.322  -0.655
    1HDE     H25   45  -0.252   0.025  -0.720
    1HDE     H26   46  -0.158  -0.108  -0.652
    1HDE     H27   47  -0.205   0.028  -0.549
    1HDE     H28   48   0.292  -0.313  -0.587
    1HDE     H29   49   0.246  -0.309  -0.757
    1HDE     C16   50   0.146  -0.463  -0.642
    1HDE     H30   51   0.062  -0.476  -0.711
    1HDE     H31   52   0.220  -0.540  -0.664
    1HDE     H32   53   0.108  -0.480  -0.541
    1HDE     H33   54   0.148   0.140  -0.620
    1HDE     H34   55  -0.300   0.544  -0.273
   0.00000   0.00000   0.00000
```

DEHP parameters

```
HDE                     3
[ atoms ]
     1 opls_441    1  HDE   O1        1    -0.867   15.999400
     2 opls_440    1  HDE   P1        2     1.7108  30.973760
     3 opls_441    1  HDE   O2        3    -0.867   15.999400
     4 opls_442    1  HDE   O3        4    -0.8043  15.999400
     5 opls_442    1  HDE   O4        5    -0.8043  15.999400
     6 opls_443    1  HDE   C1        6     0.0546  12.011000
     7 opls_444    1  HDE   H1        7     0.1623   1.008000
     8 opls_444    1  HDE   H2        8     0.1623   1.008000
     9 opls_443    1  HDE   C2        9     0.0546  12.011000
    10 opls_444    1  HDE   H3       10     0.1623   1.008000
    11 opls_444    1  HDE   H4       11     0.1623   1.008000
    12 opls_137    1  HDE   C3       12    -0.1823  12.011000
    13 opls_136    1  HDE   C4       13    -0.312   12.011000
    14 opls_136    1  HDE   C5       14    -0.312   12.011000
    15 opls_140    1  HDE   H5       15     0.1551   1.008000
    16 opls_140    1  HDE   H6       16     0.1551   1.008000
    17 opls_136    1  HDE   C6       17    -0.312   12.011000
    18 opls_140    1  HDE   H7       18     0.1551   1.008000
    19 opls_140    1  HDE   H8       19     0.1551   1.008000
    20 opls_135    1  HDE   C7       20    -0.4965  12.011000
    21 opls_140    1  HDE   H9       21     0.1551   1.008000
    22 opls_140    1  HDE   H10      22     0.1551   1.008000
    23 opls_136    1  HDE   C8       23    -0.312   12.011000
    24 opls_140    1  HDE   H11      24     0.1591   1.008000
    25 opls_140    1  HDE   H12      25     0.1591   1.008000
    26 opls_140    1  HDE   H13      26     0.1591   1.008000
    27 opls_140    1  HDE   H14      27     0.1551   1.008000
    28 opls_140    1  HDE   H15      28     0.1551   1.008000
    29 opls_135    1  HDE   C9       29    -0.4965  12.011000
    30 opls_140    1  HDE   H16      30     0.1591   1.008000
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    32 opls_140    1  HDE   H18      32     0.1591   1.008000
    33 opls_137    1  HDE   C10      33    -0.1823  12.011000
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    37 opls_140    1  HDE   H20      37     0.1551   1.008000
    38 opls_136    1  HDE   C13      38    -0.312   12.011000
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    55 opls_140    1  HDE   H34      55     0.1646   1.008000
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