

Supporting Information

Development of Potent and Selective Inhibitors for Group VIA Calcium-Independent Phospholipase A₂ Guided by Molecular Dynamics and Structure-Activity Relationships

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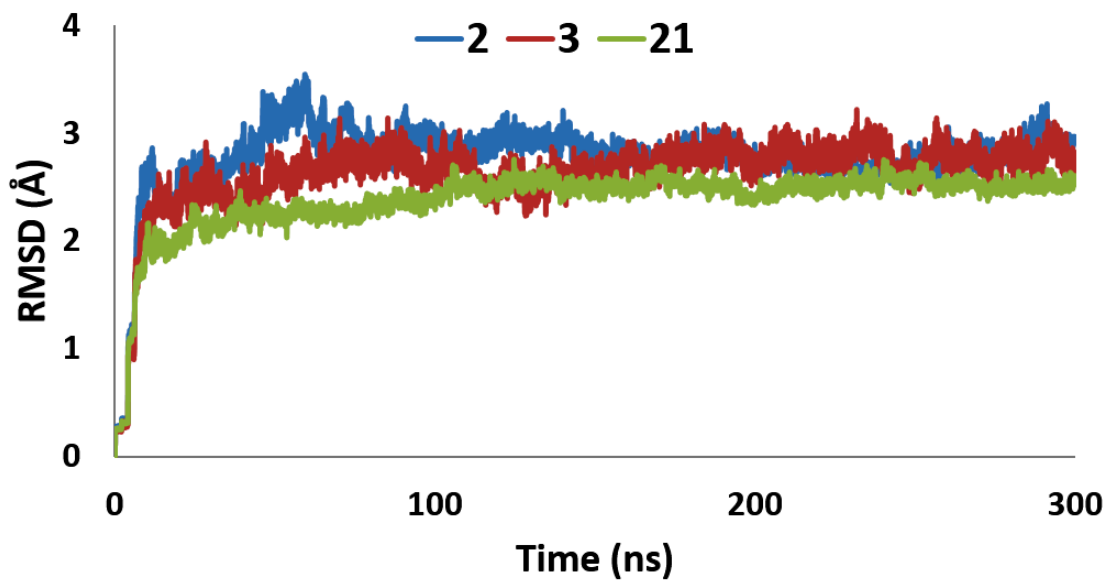


Fig. S1. RMSD of the enzyme backbone atoms over the time course of the MD simulations. Blue and brown curves represent MD simulations on the GVIA iPLA₂-**2** and GVIA iPLA₂-**3** complexes, respectively. The green curve represents a MD simulation on the GIVA cPLA₂-**21** complex.

1. Toppar stream file for compound 2

```
RESI lig      0.000 ! param penalty= 137.000 ; charge penalty= 110.907
GROUP        ! CHARGE  CH_PENALTY
ATOM C1      CG302  0.369 ! 85.312
ATOM C2      CG312  0.521 ! 110.907
ATOM C3      CG205  0.349 ! 82.596
ATOM C4      CG321 -0.140 ! 4.453
ATOM C5      CG321 -0.181 ! 0.600
ATOM C6      CG321 -0.181 ! 0.000
ATOM C7      CG321 -0.184 ! 0.000
ATOM O8      OG2D3 -0.481 ! 5.758
ATOM C9      CG2R61 0.002 ! 0.000
ATOM C10     CG2R61 -0.117 ! 0.000
ATOM C11     CG2R61 -0.110 ! 0.000
ATOM C12     CG2R61 0.219 ! 0.000
ATOM C13     CG2R61 -0.110 ! 0.000
ATOM C14     CG2R61 -0.117 ! 0.000
ATOM O15     OG301 -0.391 ! 0.000
ATOM C16     CG331 -0.100 ! 0.000
ATOM F17     FGA3  -0.142 ! 6.074
ATOM F18     FGA3  -0.142 ! 6.074
ATOM F19     FGA3  -0.142 ! 6.074
ATOM F20     FGA2  -0.186 ! 16.594
ATOM F21     FGA2  -0.186 ! 16.594
ATOM H22     HGA2   0.090 ! 0.600
ATOM H23     HGA2   0.090 ! 0.600
ATOM H24     HGA2   0.090 ! 0.000
ATOM H25     HGA2   0.090 ! 0.000
ATOM H26     HGA2   0.090 ! 0.000
ATOM H27     HGA2   0.090 ! 0.000
ATOM H28     HGA2   0.090 ! 0.000
ATOM H29     HGA2   0.090 ! 0.000
ATOM H30     HGR61  0.115 ! 0.000
ATOM H31     HGR61  0.115 ! 0.000
ATOM H32     HGR61  0.115 ! 0.000
ATOM H33     HGR61  0.115 ! 0.000
ATOM H34     HGA3   0.090 ! 0.000
```

ATOM H35 HGA3 0.090 ! 0.000
ATOM H36 HGA3 0.090 ! 0.000

BOND C9 C14
BOND C9 C10
BOND C9 C7
BOND C7 H29
BOND C7 H28
BOND C7 C6
BOND C6 H27
BOND C6 H26
BOND C6 C5
BOND C5 H25
BOND C5 H24
BOND C5 C4
BOND C4 H23
BOND C4 H22
BOND C4 C3
BOND C3 O8
BOND C3 C2
BOND C2 F21
BOND C2 F20
BOND C2 C1
BOND C1 F19
BOND C1 F18
BOND C1 F17
BOND C10 H30
BOND C10 C11
BOND C11 H31
BOND C11 C12
BOND C12 O15
BOND C12 C13
BOND C13 H32
BOND C13 C14
BOND C14 H33
BOND O15 C16
BOND C16 H36
BOND C16 H35

BOND C16 H34
IMPR C3 C2 C4 O8
END

BONDS

CG205 CG312 330.00 1.5000 ! lig , from CG205 CG321, penalty= 55
CG302 CG312 250.00 1.5200 ! lig , from CG302 CG321, penalty= 55

ANGLES

CG312 CG205 CG321 35.00 115.60 ! lig , from CG321 CG205 CG321, penalty= 12
CG312 CG205 OG2D3 75.00 122.20 ! lig , from CG321 CG205 OG2D3, penalty= 12
CG312 CG302 FGA3 42.00 112.00 30.00 2.35700 ! lig , from CG321 CG302 FGA3,
penalty= 12
CG205 CG312 CG302 60.00 113.80 ! lig , from CG205 CG321 CG321, penalty= 67
CG205 CG312 FGA2 50.00 115.00 30.00 2.35700 ! lig , from CG2R61 CG312
FGA2, penalty= 25
CG302 CG312 FGA2 50.00 112.00 30.00 2.35700 ! lig , from CG331 CG312 FGA2,
penalty= 12.9

DIHEDRALS

CG321 CG205 CG312 CG302 0.7500 1 0.00 ! lig , from CG321 CG205 CG321
CG321, penalty= 67
CG321 CG205 CG312 CG302 0.1800 2 180.00 ! lig , from CG321 CG205 CG321
CG321, penalty= 67
CG321 CG205 CG312 CG302 0.0650 3 0.00 ! lig , from CG321 CG205 CG321
CG321, penalty= 67
CG321 CG205 CG312 CG302 0.0300 6 0.00 ! lig , from CG321 CG205 CG321
CG321, penalty= 67
CG321 CG205 CG312 FGA2 0.7500 1 0.00 ! lig , from CG321 CG205 CG321
CG321, penalty= 98
CG321 CG205 CG312 FGA2 0.1800 2 180.00 ! lig , from CG321 CG205 CG321
CG321, penalty= 98
CG321 CG205 CG312 FGA2 0.0650 3 0.00 ! lig , from CG321 CG205 CG321
CG321, penalty= 98
CG321 CG205 CG312 FGA2 0.0300 6 0.00 ! lig , from CG321 CG205 CG321
CG321, penalty= 98
OG2D3 CG205 CG312 CG302 0.7500 1 180.00 ! lig , from OG2D3 CG205 CG321
CG321, penalty= 67

OG2D3 CG2O5 CG312 CG302 0.1800 2 180.00 ! lig , from OG2D3 CG2O5 CG321
 CG321, penalty= 67
 OG2D3 CG2O5 CG312 CG302 0.0650 3 180.00 ! lig , from OG2D3 CG2O5 CG321
 CG321, penalty= 67
 OG2D3 CG2O5 CG312 CG302 0.0300 6 0.00 ! lig , from OG2D3 CG2O5 CG321
 CG321, penalty= 67
 OG2D3 CG2O5 CG312 FGA2 0.0000 2 0.00 ! lig , from OG2D3 CG2O5 CG311
 OG311, penalty= 89
 CG312 CG2O5 CG321 CG321 0.7500 1 0.00 ! lig , from CG321 CG2O5 CG321
 CG321, penalty= 12
 CG312 CG2O5 CG321 CG321 0.1800 2 180.00 ! lig , from CG321 CG2O5 CG321
 CG321, penalty= 12
 CG312 CG2O5 CG321 CG321 0.0650 3 0.00 ! lig , from CG321 CG2O5 CG321
 CG321, penalty= 12
 CG312 CG2O5 CG321 CG321 0.0300 6 0.00 ! lig , from CG321 CG2O5 CG321
 CG321, penalty= 12
 CG312 CG2O5 CG321 HGA2 0.1000 3 0.00 ! lig , from CG321 CG2O5 CG321
 HGA2, penalty= 12
 FGA3 CG302 CG312 CG2O5 0.2500 3 0.00 ! lig , from FGA3 CG302 CG321 OG311,
 penalty= 137
 FGA3 CG302 CG312 FGA2 0.2500 3 0.00 ! lig , from FGA3 CG302 CG321 OG311,
 penalty= 85

IMPROPERS

CG2O5 CG312 CG321 OG2D3 70.0000 0 0.00 ! lig , from CG2O5 CG321 CG321
 OG2D3, penalty= 5.5

END of Toppar stream file for compound 2

2. Toppar stream file for compound 3

```
RESI lig      0.000 ! param penalty= 98.000 ; charge penalty= 81.690
GROUP        !CHARGE  CH_PENALTY
ATOM C1      CG2R61  0.001 !  0.000
ATOM C2      CG321  -0.184 !  0.000
ATOM C3      CG321  -0.181 !  0.000
ATOM C4      CG321  -0.181 !  0.600
ATOM C5      CG321  -0.140 !  4.453
ATOM C6      CG2O5   0.349 ! 81.690
ATOM C7      CG302   0.422 ! 80.848
ATOM F8      FGA3   -0.110 ! 25.387
ATOM F9      FGA3   -0.110 ! 25.387
ATOM F10     FGA3   -0.110 ! 25.387
ATOM O11     OG2D3  -0.481 !  5.758
ATOM C12     CG2R61 -0.119 !  0.000
ATOM C13     CG2R61  0.009 !  0.000
ATOM C14     CG2R61 -0.116 !  0.000
ATOM C15     CG2R61 -0.116 !  0.000
ATOM C16     CG2R61 -0.116 !  0.000
ATOM C17     CG2R61 -0.116 !  0.000
ATOM C18     CG2R61  0.004 !  0.000
ATOM C19     CG2R61 -0.111 !  0.000
ATOM C20     CG2R61 -0.119 !  0.000
ATOM H21     HGA2   0.090 !  0.000
ATOM H22     HGA2   0.090 !  0.000
ATOM H23     HGA2   0.090 !  0.000
ATOM H24     HGA2   0.090 !  0.000
ATOM H25     HGA2   0.090 !  0.000
ATOM H26     HGA2   0.090 !  0.000
ATOM H27     HGA2   0.090 !  0.600
ATOM H28     HGA2   0.090 !  0.600
ATOM H29     HGR61  0.115 !  0.000
ATOM H30     HGR61  0.115 !  0.000
ATOM H31     HGR61  0.115 !  0.000
ATOM H32     HGR61  0.115 !  0.000
ATOM H33     HGR61  0.115 !  0.000
ATOM H34     HGR61  0.115 !  0.000
```

ATOM H35 HGR61 0.115 ! 0.000

BOND C1 C20
BOND C1 C12
BOND C1 C2
BOND C2 C3
BOND C3 C4
BOND C4 C5
BOND C5 C6
BOND C6 O11
BOND C6 C7
BOND C7 F10
BOND C7 F9
BOND C7 F8
BOND C12 C13
BOND C13 C18
BOND C13 C14
BOND C14 C15
BOND C15 C16
BOND C16 C17
BOND C17 C18
BOND C18 C19
BOND C19 C20
BOND C2 H21
BOND C2 H22
BOND C3 H23
BOND C3 H24
BOND C4 H25
BOND C4 H26
BOND C5 H27
BOND C5 H28
BOND C12 H29
BOND C14 H30
BOND C15 H31
BOND C16 H32
BOND C17 H33
BOND C19 H34
BOND C20 H35

IMPR C6 C7 C5 O11

END

BONDS

CG2O5 CG302 330.00 1.5000 ! lig , from CG2O5 CG321, penalty= 55

ANGLES

CG302 CG2O5 CG321 35.00 115.60 ! lig , from CG321 CG2O5 CG321, penalty= 12

CG302 CG2O5 OG2D3 75.00 122.20 ! lig , from CG321 CG2O5 OG2D3, penalty= 12

CG2O5 CG302 FGA3 50.00 115.00 30.00 2.35700 ! lig , from CG2R61 CG312
FGA2, penalty= 31.1

DIHEDRALS

CG321 CG2O5 CG302 FGA3 0.7500 1 0.00 ! lig , from CG321 CG2O5 CG321
CG321, penalty= 98

CG321 CG2O5 CG302 FGA3 0.1800 2 180.00 ! lig , from CG321 CG2O5 CG321
CG321, penalty= 98

CG321 CG2O5 CG302 FGA3 0.0650 3 0.00 ! lig , from CG321 CG2O5 CG321
CG321, penalty= 98

CG321 CG2O5 CG302 FGA3 0.0300 6 0.00 ! lig , from CG321 CG2O5 CG321
CG321, penalty= 98

OG2D3 CG2O5 CG302 FGA3 0.0000 2 0.00 ! lig , from OG2D3 CG2O5 CG311
OG311, penalty= 89

CG302 CG2O5 CG321 CG321 0.7500 1 0.00 ! lig , from CG321 CG2O5 CG321
CG321, penalty= 12

CG302 CG2O5 CG321 CG321 0.1800 2 180.00 ! lig , from CG321 CG2O5 CG321
CG321, penalty= 12

CG302 CG2O5 CG321 CG321 0.0650 3 0.00 ! lig , from CG321 CG2O5 CG321
CG321, penalty= 12

CG302 CG2O5 CG321 CG321 0.0300 6 0.00 ! lig , from CG321 CG2O5 CG321
CG321, penalty= 12

CG302 CG2O5 CG321 HGA2 0.1000 3 0.00 ! lig , from CG321 CG2O5 CG321
HGA2, penalty= 12

IMPROPERS

CG2O5 CG302 CG321 OG2D3 70.0000 0 0.00 ! lig , from CG2O5 CG321 CG321
OG2D3, penalty= 5.5

END of Toppar stream file for compound 3

3. Toppar stream file for compound 21

```
RESI Lig      0.000 ! param penalty= 98.000 ; charge penalty= 81.874
GROUP        ! CHARGE  CH_PENALTY
ATOM O1      OG2D3 -0.481 !  5.758
ATOM C2      CG2O5  0.346 ! 81.874
ATOM C3      CG302  0.425 ! 80.614
ATOM F4      FGA3  -0.110 ! 25.387
ATOM F5      FGA3  -0.110 ! 25.387
ATOM F6      FGA3  -0.110 ! 25.387
ATOM C7      CG321 -0.140 !  4.453
ATOM H8      HGA2  0.090 !  0.600
ATOM H9      HGA2  0.090 !  0.600
ATOM C10     CG321 -0.181 !  0.600
ATOM H11     HGA2  0.090 !  0.000
ATOM H12     HGA2  0.090 !  0.000
ATOM C13     CG321 -0.181 !  0.000
ATOM H14     HGA2  0.090 !  0.000
ATOM H15     HGA2  0.090 !  0.000
ATOM C16     CG321 -0.182 !  0.000
ATOM C17     CG2R61 -0.002 !  0.000
ATOM C18     CG2R61 -0.117 !  0.000
ATOM H19     HGR61  0.115 !  0.000
ATOM C20     CG2R61 -0.110 !  0.000
ATOM H21     HGR61  0.115 !  0.000
ATOM C22     CG2R67  0.000 !  0.000
ATOM C23     CG2R67  0.000 !  0.000
ATOM C24     CG2R61 -0.115 !  0.000
ATOM H25     HGR61  0.115 !  0.000
ATOM C26     CG2R61 -0.115 !  0.000
ATOM H27     HGR61  0.115 !  0.000
ATOM C28     CG2R61 -0.115 !  0.000
ATOM H29     HGR61  0.115 !  0.000
ATOM C30     CG2R61 -0.115 !  0.000
ATOM H31     HGR61  0.115 !  0.000
ATOM C32     CG2R61 -0.115 !  0.000
ATOM H33     HGR61  0.115 !  0.000
ATOM C34     CG2R61 -0.110 !  0.000
```

ATOM H35 HGR61 0.115 ! 0.000
ATOM C36 CG2R61 -0.117 ! 0.000
ATOM H37 HGR61 0.115 ! 0.000
ATOM H38 HGA2 0.090 ! 0.000
ATOM H39 HGA2 0.090 ! 0.000

BOND C2 O1
BOND C2 C3
BOND C2 C7
BOND C3 F4
BOND C3 F5
BOND C3 F6
BOND C7 H8
BOND C7 H9
BOND C7 C10
BOND C10 H11
BOND C10 H12
BOND C10 C13
BOND C13 H14
BOND C13 H15
BOND C13 C16
BOND C16 C17
BOND C16 H38
BOND C16 H39
BOND C17 C18
BOND C17 C36
BOND C18 H19
BOND C18 C20
BOND C20 H21
BOND C20 C22
BOND C22 C23
BOND C22 C34
BOND C23 C24
BOND C23 C32
BOND C24 H25
BOND C24 C26
BOND C26 H27
BOND C26 C28

BOND C28 H29
BOND C28 C30
BOND C30 H31
BOND C30 C32
BOND C32 H33
BOND C34 H35
BOND C34 C36
BOND C36 H37
IMPR C2 C3 C7 O1
END

BONDS

CG2O5 CG302 330.00 1.5000 ! Lig , from CG2O5 CG321, penalty= 55

ANGLES

CG302 CG2O5 CG321 35.00 115.60 ! Lig , from CG321 CG2O5 CG321, penalty= 12
CG302 CG2O5 OG2D3 75.00 122.20 ! Lig , from CG321 CG2O5 OG2D3, penalty= 12
CG2O5 CG302 FGA3 50.00 115.00 30.00 2.35700 ! Lig , from CG2R61 CG312
FGA2, penalty= 31.1

DIHEDRALS

CG321 CG2O5 CG302 FGA3 0.7500 1 0.00 ! Lig , from CG321 CG2O5 CG321
CG321, penalty= 98
CG321 CG2O5 CG302 FGA3 0.1800 2 180.00 ! Lig , from CG321 CG2O5 CG321
CG321, penalty= 98
CG321 CG2O5 CG302 FGA3 0.0650 3 0.00 ! Lig , from CG321 CG2O5 CG321
CG321, penalty= 98
CG321 CG2O5 CG302 FGA3 0.0300 6 0.00 ! Lig , from CG321 CG2O5 CG321
CG321, penalty= 98
OG2D3 CG2O5 CG302 FGA3 0.0000 2 0.00 ! Lig , from OG2D3 CG2O5 CG311
OG311, penalty= 89
CG302 CG2O5 CG321 CG321 0.7500 1 0.00 ! Lig , from CG321 CG2O5 CG321
CG321, penalty= 12
CG302 CG2O5 CG321 CG321 0.1800 2 180.00 ! Lig , from CG321 CG2O5 CG321
CG321, penalty= 12
CG302 CG2O5 CG321 CG321 0.0650 3 0.00 ! Lig , from CG321 CG2O5 CG321
CG321, penalty= 12

CG302 CG205 CG321 CG321 0.0300 6 0.00 ! Lig , from CG321 CG205 CG321
CG321, penalty= 12
CG302 CG205 CG321 HGA2 0.1000 3 0.00 ! Lig , from CG321 CG205 CG321
HGA2, penalty= 12

IMPROPERS

CG205 CG302 CG321 OG2D3 70.0000 0 0.00 ! Lig , from CG205 CG321 CG321
OG2D3, penalty= 5.5

END of Toppar stream file for compound 21

4. Toppar stream file for compound 32

```
RESI lig      0.000 ! param penalty= 130.000 ; charge penalty= 68.453
GROUP        ! CHARGE  CH_PENALTY
ATOM C1      CG321 -0.179 ! 11.384
ATOM C2      CG321 -0.073 ! 11.655
ATOM S3      SG311 -0.167 ! 15.097
ATOM C4      CG321 -0.110 ! 11.573
ATOM C5      CG205 0.365 ! 68.323
ATOM O6      OG2D3 -0.470 ! 5.357
ATOM C7      CG2R53 0.755 ! 68.453
ATOM N8      NG2R50 -0.444 ! 6.250
ATOM O9      OG2R50 -0.139 ! 42.699
ATOM C10     CG2R53 0.462 ! 65.130
ATOM N11     NG2R50 -0.675 ! 15.811
ATOM C12     CG301 0.120 ! 61.857
ATOM C13     CG331 -0.266 ! 19.297
ATOM C14     CG331 -0.266 ! 19.297
ATOM C15     CG331 -0.266 ! 19.297
ATOM C16     CG2R61 0.219 ! 0.000
ATOM C17     CG2R61 -0.108 ! 0.000
ATOM C18     CG2R61 -0.117 ! 0.000
ATOM C19     CG2R61 -0.005 ! 11.384
ATOM C20     CG2R61 -0.117 ! 0.000
ATOM C21     CG2R61 -0.108 ! 0.000
ATOM O22     OG301 -0.391 ! 0.000
ATOM C23     CG331 -0.100 ! 0.000
ATOM H24     HGR61 0.115 ! 0.000
ATOM H25     HGR61 0.115 ! 0.000
ATOM H26     HGR61 0.115 ! 0.000
ATOM H27     HGR61 0.115 ! 0.000
ATOM H28     HGA2 0.090 ! 0.000
ATOM H29     HGA2 0.090 ! 0.000
ATOM H30     HGA2 0.090 ! 0.000
ATOM H31     HGA2 0.090 ! 0.000
ATOM H32     HGA2 0.090 ! 0.425
ATOM H33     HGA2 0.090 ! 0.425
ATOM H34     HGA3 0.090 ! 1.025
```

ATOM H35	HGA3	0.090 !	1.025
ATOM H36	HGA3	0.090 !	1.025
ATOM H37	HGA3	0.090 !	1.025
ATOM H38	HGA3	0.090 !	1.025
ATOM H39	HGA3	0.090 !	1.025
ATOM H40	HGA3	0.090 !	1.025
ATOM H41	HGA3	0.090 !	1.025
ATOM H42	HGA3	0.090 !	1.025
ATOM H43	HGA3	0.090 !	0.000
ATOM H44	HGA3	0.090 !	0.000
ATOM H45	HGA3	0.090 !	0.000

BOND C2 C1
BOND C1 C19
BOND C1 H28
BOND C1 H29
BOND C2 H30
BOND C2 H31
BOND C4 C5
BOND C4 H32
BOND C4 H33
BOND C5 O6
BOND C5 C7
BOND C7 N8
BOND C7 N11
BOND N8 O9
BOND C10 O9
BOND N11 C10
BOND C10 C12
BOND C12 C13
BOND C12 C14
BOND C12 C15
BOND C13 H34
BOND C13 H35
BOND C13 H36
BOND C14 H37
BOND C14 H38
BOND C14 H39

BOND C15 H40
BOND C15 H41
BOND C15 H42
BOND C17 C16
BOND C21 C16
BOND C16 O22
BOND C18 C17
BOND C17 H24
BOND C19 C18
BOND C18 H25
BOND C19 C20
BOND C20 C21
BOND C20 H26
BOND C21 H27
BOND O22 C23
BOND C23 H43
BOND C23 H44
BOND C23 H45
BOND S3 C4
BOND C2 S3
IMPR C5 C7 C4 O6
END

BONDS

CG2O5 CG2R53 254.00 1.4600 ! lig , from CG2O5 CG2R61, penalty= 45
CG2R53 CG301 229.63 1.5000 ! lig , from CG2R51 CG321, penalty= 40

ANGLES

CG2R53 CG2O5 CG321 20.00 116.50 ! lig , from CG2R61 CG2O5 CG321, penalty= 8.5
CG2R53 CG2O5 OG2D3 70.00 121.30 ! lig , from CG2R61 CG2O5 OG2D3, penalty=
8.5
CG2O5 CG2R53 NG2R50 65.00 127.80 ! lig , from NG2R53 CG2R53 OG2D1, penalty=
75
CG301 CG2R53 NG2R50 45.80 120.00 ! lig , from CG321 CG2R51 NG2R50, penalty=
29.8
CG301 CG2R53 OG2R50 45.80 124.00 ! lig , from CG321 CG2R51 NG2R51, penalty=
74.8
CG2R53 CG301 CG331 58.35 114.00 ! lig , from CG2R51 CG321 CG331, penalty= 14.5

CG2O5 CG321 SG311 65.00 111.82 ! lig , from CG2O4 CG321 CLGA1, penalty= 16.6

DIHEDRALS

CG321 CG2O5 CG2R53 NG2R50 0.2700 2 180.00 ! lig , from CG321 CG2O5 CG2R61
CG2R61, penalty= 130

OG2D3 CG2O5 CG2R53 NG2R50 1.5850 2 180.00 ! lig , from OG2D3 CG2O5 CG2R61
CG2R61, penalty= 130

CG2R53 CG2O5 CG321 SG311 0.1000 1 0.00 ! lig , from OG2D1 CG2O4 CG321
CLGA1, penalty= 92.1

CG2R53 CG2O5 CG321 SG311 1.0000 2 180.00 ! lig , from OG2D1 CG2O4 CG321
CLGA1, penalty= 92.1

CG2R53 CG2O5 CG321 SG311 0.5500 3 180.00 ! lig , from OG2D1 CG2O4 CG321
CLGA1, penalty= 92.1

CG2R53 CG2O5 CG321 HGA2 0.1000 3 0.00 ! lig , from CG2R61 CG2O5 CG321
HGA2, penalty= 8.5

OG2D3 CG2O5 CG321 SG311 0.1000 1 0.00 ! lig , from OG2D1 CG2O4 CG321
CLGA1, penalty= 36.6

OG2D3 CG2O5 CG321 SG311 1.0000 2 180.00 ! lig , from OG2D1 CG2O4 CG321
CLGA1, penalty= 36.6

OG2D3 CG2O5 CG321 SG311 0.5500 3 180.00 ! lig , from OG2D1 CG2O4 CG321
CLGA1, penalty= 36.6

NG2R50 CG2R53 CG301 CG331 0.1900 3 0.00 ! lig , from NG2R50 CG2R51 CG321
CG311, penalty= 41.5

OG2R50 CG2R53 CG301 CG331 0.1900 3 0.00 ! lig , from NG2R51 CG2R51 CG321
CG331, penalty= 85

CG2O5 CG2R53 NG2R50 CG2R53 12.0000 2 180.00 ! lig , from NG2R51 CG2R53
NG2R50 CG2R53, penalty= 92

CG2O5 CG2R53 NG2R50 OG2R50 12.0000 2 180.00 ! lig , from CG2R51 CG2R52
NG2R50 OG2R50, penalty= 84.5

CG301 CG2R53 NG2R50 CG2R53 3.0000 2 180.00 ! lig , from CG321 CG2R51
NG2R50 CG2R53, penalty= 29.8

CG301 CG2R53 OG2R50 NG2R50 9.0000 2 180.00 ! lig , from NG2R50 CG2R53
OG2R50 NG2R50, penalty= 114.5

CG2R53 CG301 CG331 HGA3 0.1600 3 0.00 ! lig , from CG2R51 CG321 CG331
HGA3, penalty= 14.5

CG2R61 CG321 CG321 SG311 0.2000 3 0.00 ! lig , from CG2O1 CG311 CG321
SG311, penalty= 34

CG205 CG321 SG311 CG321 0.2400 1 180.00 ! lig , from CG321 CG321 SG311
CG321, penalty= 71
CG205 CG321 SG311 CG321 0.3700 3 0.00 ! lig , from CG321 CG321 SG311
CG321, penalty= 71

IMPROPERS

CG205 CG2R53 CG321 OG2D3 72.0000 0 0.00 ! lig , from CG205 CG2R61 CG321
OG2D3, penalty= 4.5

END of Toppar stream file for compound 32

5. Toppar stream file for compound 33

```
RESI lig      0.000 ! param penalty= 130.000 ; charge penalty= 68.409
GROUP        ! CHARGE  CH_PENALTY
ATOM C1      CG321 -0.180 !  0.000
ATOM C2      CG321 -0.183 !  0.000
ATOM C3      CG321 -0.181 !  0.470
ATOM C4      CG321 -0.166 !  5.824
ATOM C5      CG205  0.365 ! 67.969
ATOM O6      OG2D3 -0.470 !  5.247
ATOM C7      CG2R53 0.755 ! 68.409
ATOM N8      NG2R50 -0.444 !  6.250
ATOM O9      OG2R50 -0.139 ! 42.699
ATOM C10     CG2R53 0.462 ! 65.130
ATOM N11     NG2R50 -0.675 ! 15.811
ATOM C12     CG301  0.120 ! 61.857
ATOM C13     CG331 -0.266 ! 19.297
ATOM C14     CG331 -0.266 ! 19.297
ATOM C15     CG331 -0.266 ! 19.297
ATOM C16     CG2R61 0.219 !  0.000
ATOM C17     CG2R61 -0.108 !  0.000
ATOM C18     CG2R61 -0.117 !  0.000
ATOM C19     CG2R61 -0.004 !  0.000
ATOM C20     CG2R61 -0.117 !  0.000
ATOM C21     CG2R61 -0.108 !  0.000
ATOM O22     OG301 -0.391 !  0.000
ATOM C23     CG331 -0.100 !  0.000
ATOM H24     HGR61  0.115 !  0.000
ATOM H25     HGR61  0.115 !  0.000
ATOM H26     HGR61  0.115 !  0.000
ATOM H27     HGR61  0.115 !  0.000
ATOM H28     HGA2   0.090 !  0.000
ATOM H29     HGA2   0.090 !  0.000
ATOM H30     HGA2   0.090 !  0.000
ATOM H31     HGA2   0.090 !  0.000
ATOM H32     HGA2   0.090 !  0.000
ATOM H33     HGA2   0.090 !  0.000
ATOM H34     HGA2   0.090 !  0.425
```

ATOM H35	HGA2	0.090 !	0.425
ATOM H36	HGA3	0.090 !	1.025
ATOM H37	HGA3	0.090 !	1.025
ATOM H38	HGA3	0.090 !	1.025
ATOM H39	HGA3	0.090 !	1.025
ATOM H40	HGA3	0.090 !	1.025
ATOM H41	HGA3	0.090 !	1.025
ATOM H42	HGA3	0.090 !	1.025
ATOM H43	HGA3	0.090 !	1.025
ATOM H44	HGA3	0.090 !	1.025
ATOM H45	HGA3	0.090 !	0.000
ATOM H46	HGA3	0.090 !	0.000
ATOM H47	HGA3	0.090 !	0.000

BOND C1 C2
BOND C19 C1
BOND C1 H28
BOND C1 H29
BOND C2 C3
BOND C2 H30
BOND C2 H31
BOND C3 C4
BOND C3 H32
BOND C3 H33
BOND C4 C5
BOND C4 H34
BOND C4 H35
BOND C5 O6
BOND C5 C7
BOND C7 N8
BOND C7 N11
BOND N8 O9
BOND C10 O9
BOND N11 C10
BOND C10 C12
BOND C12 C13
BOND C12 C14
BOND C12 C15

BOND C13 H36
BOND C13 H37
BOND C13 H38
BOND C14 H39
BOND C14 H40
BOND C14 H41
BOND C15 H42
BOND C15 H43
BOND C15 H44
BOND C16 C17
BOND C16 C21
BOND O22 C16
BOND C17 C18
BOND C17 H24
BOND C18 C19
BOND C18 H25
BOND C20 C19
BOND C21 C20
BOND C20 H26
BOND C21 H27
BOND C23 O22
BOND C23 H45
BOND C23 H46
BOND H47 C23
IMPR C5 C7 C4 O6
END

BONDS

CG2O5 CG2R53 254.00 1.4600 ! lig , from CG2O5 CG2R61, penalty= 45
CG2R53 CG301 229.63 1.5000 ! lig , from CG2R51 CG321, penalty= 40

ANGLES

CG2R53 CG2O5 CG321 20.00 116.50 ! lig , from CG2R61 CG2O5 CG321, penalty= 8.5
CG2R53 CG2O5 OG2D3 70.00 121.30 ! lig , from CG2R61 CG2O5 OG2D3, penalty=
8.5
CG2O5 CG2R53 NG2R50 65.00 127.80 ! lig , from NG2R53 CG2R53 OG2D1, penalty=
75

CG301 CG2R53 NG2R50 45.80 120.00 ! lig , from CG321 CG2R51 NG2R50, penalty=
29.8
CG301 CG2R53 OG2R50 45.80 124.00 ! lig , from CG321 CG2R51 NG2R51, penalty=
74.8
CG2R53 CG301 CG331 58.35 114.00 ! lig , from CG2R51 CG321 CG331, penalty= 14.5

DIHEDRALS

CG321 CG2O5 CG2R53 NG2R50 0.2700 2 180.00 ! lig , from CG321 CG2O5 CG2R61
CG2R61, penalty= 130
OG2D3 CG2O5 CG2R53 NG2R50 1.5850 2 180.00 ! lig , from OG2D3 CG2O5 CG2R61
CG2R61, penalty= 130
CG2R53 CG2O5 CG321 CG321 0.4000 1 0.00 ! lig , from CG2R61 CG2O5 CG321
CG331, penalty= 9.4
CG2R53 CG2O5 CG321 CG321 0.1700 2 180.00 ! lig , from CG2R61 CG2O5 CG321
CG331, penalty= 9.4
CG2R53 CG2O5 CG321 CG321 0.1300 3 180.00 ! lig , from CG2R61 CG2O5 CG321
CG331, penalty= 9.4
CG2R53 CG2O5 CG321 CG321 0.1000 6 180.00 ! lig , from CG2R61 CG2O5 CG321
CG331, penalty= 9.4
CG2R53 CG2O5 CG321 HGA2 0.1000 3 0.00 ! lig , from CG2R61 CG2O5 CG321
HGA2, penalty= 8.5
NG2R50 CG2R53 CG301 CG331 0.1900 3 0.00 ! lig , from NG2R50 CG2R51 CG321
CG311, penalty= 41.5
OG2R50 CG2R53 CG301 CG331 0.1900 3 0.00 ! lig , from NG2R51 CG2R51 CG321
CG331, penalty= 85
CG2O5 CG2R53 NG2R50 CG2R53 12.0000 2 180.00 ! lig , from NG2R51 CG2R53
NG2R50 CG2R53, penalty= 92
CG2O5 CG2R53 NG2R50 OG2R50 12.0000 2 180.00 ! lig , from CG2R51 CG2R52
NG2R50 OG2R50, penalty= 84.5
CG301 CG2R53 NG2R50 CG2R53 3.0000 2 180.00 ! lig , from CG321 CG2R51
NG2R50 CG2R53, penalty= 29.8
CG301 CG2R53 OG2R50 NG2R50 9.0000 2 180.00 ! lig , from NG2R50 CG2R53
OG2R50 NG2R50, penalty= 114.5
CG2R53 CG301 CG331 HGA3 0.1600 3 0.00 ! lig , from CG2R51 CG321 CG331
HGA3, penalty= 14.5

IMPROPERS

CG2O5 CG2R53 CG321 OG2D3 72.0000 0 0.00 ! lig , from CG2O5 CG2R61 CG321
OG2D3, penalty= 4.5

END of Toppar stream file for compound 33

