Supporting Information

Conformationally Constrained Analogues of DAG. 25. Exploration of the *sn*-1 and *sn*-2 carbonyl functionality reveals the essential role of the *sn*-1 carbonyl at the lipid interface in the binding of DAG-lactones to protein kinase C

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4-(2-Iodoethyl)-2,6-dimethylheptane (15).

Anal calcd for $C_{11}H_{23}I$: C, 46.82: H, 8.21; I, 44.97. Found: 47.08; H, 8.17; I, 44.71.

(*E*/*Z*)-4-Methoxy-1-({4-[5-methyl-3-(2-methylpropyl)hexylidene]-2-[(phenylmethoxy)methyl](2-2,3,5-trihydrofuryl)}methoxy)benzene (18).

Anal calcd for $C_{31}H_{44}O_4 \cdot 0.6H_2O$: C, 75.75; H, 9.26. Found: C, 75.62; H, 9.02.

(*E*/*Z*)-{4-[5-Methyl-3-(2-methylpropyl)hexylidene]-2-[(phenylmethoxy)methyl]-2-2,3,5-trihydrofuryl}methan-1-ol (19).

Anal. calcd for $C_{24}H_{38}O_3 \cdot 0.1H_2O$: C, 76.59; H, 10.23. Found: C, 76.37; H, 10.31.

(*E*/*Z*)-{2-(Hydroxymethyl)-4-[5-methyl-3-(2-methylpropyl)hexylidene]-2-2,3,5-trihydrofuryl}methyl 2,2-Dimethylpropanoate (8).

Anal calcd for $C_{22}H_{42}O_5 \cdot 0.5H_2O$: C, 69.98; H, 10.94. Found: C, 69.97; H, 10.50.

(*Z*)-5-(Hydroxymethyl)-5-[(4-methoxyphenoxy)methyl]-3-[5-methyl-3-(2-methylpropyl)hexylidene]-4,5-dihydrofuran-2-one (24).

Anal. calcd for $C_{24}H_{36}O_5$: C, 71.26; H, 8.97. Found: C, 70.98; H, 9.04.

(*Z*)-{2-[(4-Methoxyphenoxy)methyl]-4-[5-methyl-3-(2-methylpropyl)hexylidene]-5-oxo-2-2,3-dihydrofuryl}methyl Methylsulfonate (26).

Anal. calcd for $C_{25}H_{86}O_7S$: C, 62.21; H, 7.94. Found: C, 61.97; H, 7.83.

(*Z*)-{2-(Hydroxymethyl)-4-[5-methyl-3-(2-methylpropyl)hexylidene-5-oxo-2-2,3-dihydrofuryl}methyl Methylsulfonate (28).

Anal. calcd for $C_{18}H_{32}O_6S$: C, 57.42; H, 8.57. Found: C, 57.63; H, 8.66.

(*Z*)-5-[(2,2-Dimethylpropoxy)methyl)-5-(hydroxymethyl)-3-[5-methyl-3-(2-methylpropyl)hexylidene]-4,5-dihydrofuran-2-one (10).

Anal. calcd for $C_{22}H_{40}O_4 \bullet 0.8H_2O$: C, 69.00; H, 10.95. Found: C, 68.82; H, 10.28.

(*E*)-5-(Hydroxymethyl)-5-[(4-methoxyphenoxy)methyl]-3-[5-methyl-3-(2-methylpropyl)hexylidene]-4,5-dihydrofuran-2-one (23)

Anal calcd for $C_{24}H_{36}O_5 \bullet 0.2H_2O$: C, 70.62; H, 8.98. Found: C, 70.31; H, 9.03.

(*E*)-{2-[(4-Methoxyphenoxy)methyl]-4-[5-methyl-3-(2-methylpropyl)hexylidene]-5-oxo-2-2,3-dihydrofuryl}methyl Methylsulfonate (25).

Anal. calcd for $C_{25}H_{86}O_7S$: C, 62.21: H, 7.94. Found: C, 62.38; H, 7.77.

(*E*)-{2-(Hydroxymethyl)-4-[5-methyl-3-(2-methylpropyl)hexylidene-5-oxo-2-2,3-dihydrofuryl}methyl methylsulfonate (27).

Anal calcd for $C_{18}H_{32}O_6S$: C, 57.42; H, 8.57. Found: C, 57.23; H, 8.67.

(*E*)-5-[(2,2-Dimethylpropoxy)methyl)-5-(hydroxymethyl)-3-[5-methyl-3-(2-methylpropyl)hexylidene]-4,5-dihydrofuran-2-one (9).

Anal. calcd for $C_{22}H_{40}O_4$: C, 71.70; H, 10.94. Found: C, 71.38; H, 10.93

5-(Hydroxymethyl)-5-[(phenylmethoxy)methyl]-3,4,5-trihydrofuran-2-one (30).

Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 66.37; H, 6.84.

(*E*)-5,5-bis[Phenylmethoxy)methyl]-3-[5-methyl-3-(2-methylpropyl)hexylidene]-4,5-dihydrofuran-2-one (32).

Anal. calcd for $C_{31}H_{42}O_4 \cdot 0.4H_2O$: C, 76.63; H, 8.87. Found: C, 76.30; H, 8.81.

(*Z*)-5,5-bis[Phenylmethoxy)methyl]-3-[5-methyl-3-(2-methylpropyl)hexylidene]-4,5-dihydrofuran-2-one (33).

Anal. calcd for $C_{31}H_{42}O_4 \cdot 0.2H_2O$; C, 76.63; H, 8.87. Found: C, 76.39; H, 8.81.

(*E*)-5,5-bis[(Phenylmethoxy)methyl]-3-[5-methyl-3-(2-methylpropyl)hexylidene]-4,5-dihydrofuran-2-thione (34).

Anal calcd for $C_{31}H_{42}O_3S \cdot 1.1H_2O$: C, 72.36; H, 8.65. Found: C, 72.55; H, 8.27.

(*E*)-{2-(Hydroxymethyl)-4-[5-methyl-3-(2-methylpropyl)hexylidene]-5-thioxo-2-2,3-dihydrofuryl}methyl 2,2-Dimethylpropanoate (11).

Anal. calcd for $C_{22}H_{38}O_4S \cdot 0.33H_2O$: C, 65.31; H, 9.63. Found: C, 65.20; H, 9.34.

(*E*)-5-[(2,2-Dimethyl-1-thioxopropoxy)methyl]-5-(hydroxymethyl)-3-[5-methyl-3-(2-methylpropyl)hexylidene]-4,5-dihydrofuran-2-one (12).

Anal. Calcd for $C_{22}H_{38}O_4S$: C, 66.29; H, 9.61. Found: C, 65.82; H, 9.57.