Supporting information

**A Modular Approach towards Drug delivery Vehicles Using Oxanorbornane-based Non-ionic Amphiphiles**

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† these authors contributed equally
1. Synthetic scheme:

![Scheme 1-SI](image)

Scheme 1-SI. Syntheses of amphiphiles with C<sub>7</sub> and C<sub>13</sub> chain lengths having amino acid units as spacers between head and tail.
2. Experimental procedure & Spectral data:

*General procedure for the preparation of compounds 5a-e, 6a-e (N-acylation):*

To a stirred solution of the amino acid methyl ester (1.0 equiv.) and Et$_3$N (2.2 equiv.) in dry dichloromethane was added the appropriate acid chloride (1.1 equiv.) at 0 °C under N$_2$ atmosphere. The reaction mixture was warmed to room temperature and allowed to stir for 3-4 h. After completion of the reaction, the mixture was washed with water and extracted with dichloromethane. The organic layer was dried using Na$_2$SO$_4$ and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel using 20-30% EtOAc/Hexane. Yields and spectroscopic details of various compounds are given below.

**N-octanoyl Gly-methyl ester (5a):** Yield, 82%; R$_f$ (5% EtOAc/Hexane), 0.62; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 6.02 (bs, 1H), 4.04 (d, 2H, $J = 4.4$ Hz), 3.75 (s, 3H), 2.24 (t, 2H, $J = 7.6$ Hz), 1.70-1.59 (quin, 2H, $J = 6.8$ Hz), 1.35-1.23 (m, 8H), 0.87 (t, 3H, $J = 6.8$ Hz); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 173.5, 170.7, 52.4, 41.3, 36.5, 31.8, 29.1 (2C), 25.7, 22.6, 14.1; IR (KBr): 2927, 2858, 2364, 1752, 1656, 1547, 1446, 1371, 1208, 1033, 707 cm$^{-1}$; HRMS (ESI) exact mass calcd. for C$_{11}$H$_{22}$NO$_3$ (M+H)$^+$ 216.1600, found (M+H)$^+$ 216.1590.

**N-octanoyl Ala-methyl ester (5b):** Yield, 79%; R$_f$ (5% EtOAc/Hexane), 0.62; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 6.08 (bs, 1H), 4.58 (quin, 1H, $J = 7.0$ Hz), 3.73 (s, 3H), 2.18 (t, 2H, $J = 7.5$ Hz), 1.61 (quin, 2H, $J = 7.0$ Hz), 1.38 (d, 3H, $J = 5.6$ Hz), 1.35-1.20 (m, 8H), 0.85 (t, 3H, $J = 6$ Hz); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 173.8, 172.8, 52.5, 48.0, 36.6, 31.8, 29.3, 29.1, 25.7, 22.7, 18.6, 14.1; IR (KBr): 2864, 1744, 1651, 1538, 1453, 1374, 1266, 1204, 1154, 1014, 759 cm$^{-1}$; HRMS (ESI) exact mass calcd. for C$_{12}$H$_{24}$NO$_3$ (M+H)$^+$ 230.1756, found (M+H)$^+$ 230.1746.

**N-octanoyl Phe-methyl ester (5c):** Yield, 86%; R$_f$ (5% EtOAc/Hexane), 0.70; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.32-7.20 (m, 3H), 7.09 (d, 2H, $J = 6.8$ Hz), 5.90 (d, 1H, $J = 7.6$ Hz), 4.9-4.8 (m, 1H), 3.73 (s, 3H), 3.15 (dd, 1H, $J = 14.0$, 6.0 Hz), 3.09 (dd, 1H, $J = 13.6$, 5.6 Hz), 2.17 (t, 2H, $J = 6.8$ Hz), 1.58 (quin, 2H, $J = 7.2$ Hz), 1.32-1.23 (m, 8H), 0.88 (t, 3H, $J = 6.8$ Hz).
Hz; $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 172.8, 172.3, 136.0, 129.4 (2C), 128.7 (2C), 127.2, 53.0, 52.4, 36.7, 31.8, 29.3, 29.1 (2C), 25.7, 22.7, 14.2; IR (KBr): 2927, 2857, 1751, 1746, 1650, 1540, 1446, 1211, 1179, 743, 701, 697, 670 cm$^{-1}$; HRMS (ESI) exact mass calcd. for C$_{18}$H$_{28}$NO$_3$ (M+H)$^+$ 306.2069, found (M+H)$^+$ 306.2079

**N-octanoyl Val-methyl ester (5d):** Yield, 77%; $R_f$ (5% EtOAc/Hexane), 0.66; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 5.96 (bs, 1H), 4.59-4.54 (m, 1H), 3.72 (s, 3H), 2.22 (t, 2H, $J$ = 7.5 Hz), 2.13 (quin, 1H, $J$ = 6.5 Hz), 1.62 (t, 2H, $J$ = 6.5 Hz), 1.32-1.23 (m, 8H), 0.92 (d, 3H, $J$ = 6.5 Hz), 0.88 (d, 3H, $J$ = 6.5 Hz), 0.86 (t, 3H, $J$ = 7.0 Hz); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 173.2, 172.9, 56.9, 52.2, 36.8, 31.8, 31.4, 29.3, 29.1, 25.8, 22.7, 19.0, 17.9, 14.2; IR (KBr): 3590, 3376, 3272, 3063, 2956, 2859, 1745, 1650, 1539, 1460, 1373, 1206, 1153, 1018 cm$^{-1}$; HRMS (ESI) exact mass calcd. for C$_{14}$H$_{28}$NO$_3$ (M+H)$^+$ 258.2069, found (M+H)$^+$ 258.2063.

**N-octanoyl Leu-methyl ester (5e)**

Yield, 89%; $R_f$ (5% EtOAc/Hexane), 0.66; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 5.87 (bs, 1H), 4.63 (sext, 1H, $J$ = 4.5 Hz), 3.71 (s, 3H), 2.19 (t, 2H, $J$ = 7.0 Hz), 1.68-1.58 (m, 4H), 1.51 (quin, 1H, $J$ = 9.0 Hz), 1.34-1.20 (m, 8H), 0.96-0.90 (m, 6H), 0.86 (t, 3H, $J$ = 6.5 Hz); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 173.9, 173.1, 52.4, 50.6, 41.9, 36.7, 31.8, 29.3, 29.1, 25.7, 25.0, 22.9, 22.7, 22.1, 14.2; IR (KBr): 2954, 2861, 2345, 2338, 1747, 1650, 1543, 1457, 1371, 1273, 1207, 1160, 1024, 721, 667 cm$^{-1}$; HRMS (ESI) exact mass calcd. for C$_{15}$H$_{30}$NO$_3$ (M+H)$^+$ 272.2147, found (M+H)$^+$ 272.2154

**N-myristoyl Ala-methyl ester (6a):** Yield, 94%; $R_f$ (5% EtOAc/Hexane), 0.70; $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 6.02 (bs, 1H), 4.60 (quin, 1H, $J$ = 7.0 Hz), 3.74 (s, 3H), 2.19 (t, 2H, $J$ = 7.5 Hz), 1.62 (quin, 2H, $J$ = 7.5 Hz), 1.39 (d, 3H, $J$ = 7.0 Hz), 1.32-1.22 (m, 20H), 0.87 (t, 3H, $J$ = 6.5 Hz); $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 173.9, 172.8, 52.6, 48.0, 36.7, 32.0, 29.8, 29.77 (3C), 29.74, 29.6, 29.5, 29.4, 25.7, 22.8, 18.7, 14.2; IR (KBr): 3053, 2988, 2932, 2923, 2854, 2309, 2301, 1747, 1742, 1736, 1671, 1509, 1439, 1266, 1215, 1166, 897 cm$^{-1}$; HRMS (ESI) exact mass calcd. for C$_{18}$H$_{36}$NO$_3$ (M+H)$^+$ 314.2695, found (M+H)$^+$ 314.2686.
N-myristoyl Phe-methyl ester (6b): Yield, 67%; R_f (5% EtOAc/Hexane), 0.80; ^1H NMR (CDCl_3, 400 MHz): δ 7.32-7.22 (m, 3H), 7.08 (d, 2H, J = 6.8 Hz), 5.86 (bs 1H), 4.90 (q, 1H, J = 5.6 Hz), 3.73 (s, 3H), 3.15 (dd, 1H, J = 14.0 Hz, 6.0 Hz), 3.09 (dd, 1H, J = 14.0 Hz, 6.0 Hz), 2.16 (t, 2H, J = 7.2 Hz), 1.58 (t, 2H, J = 6.8 Hz), 1.32-1.23 (m, 20 H), 0.88 (t, 3H, J = 6.4 Hz); ^13C NMR (CDCl_3, 100 MHz): δ 172.8, 172.3, 136.0, 129.4 (2C), 128.7 (2C), 127.2, 53.0, 52.4, 38.1, 36.7, 32.0, 29.8, 29.78 (3C), 29.75, 29.6, 29.5, 29.3, 25.7, 22.8, 14.2; IR (KBr): 3332, 3055, 2922, 2854, 2325, 1744, 1673, 1645, 1531, 1462, 1454, 1448, 1428, 1267, 745, 675, 659 cm^{-1}; HRMS (ESI) exact mass calcd. for C_{24}H_{40}NO_3 (M+H)^+ 390.2930, found (M+H)^+ 390.2939

N-myristoyl Val-methyl ester (6c): Yield, 87%; R_f (5% EtOAc/Hexane), 0.75; ^1H NMR (CDCl_3, 400 MHz): δ 5.90 (d, 1H, J = 8.0 Hz), 4.58 (dd, 1H, J = 8.8 Hz, 4.8 Hz), 3.74 (s, 3H), 2.23 (t, 2H, J = 7.2 Hz), 2.20-2.10 (m, 1H), 1.67-1.61 (m, 2H), 1.30-1.23 (bs, 20H), 0.95-0.80 (m, 9H); ^13C NMR (CDCl_3, 100 MHz): δ 173.2, 172.9, 56.9, 52.2, 36.9, 32.0, 31.4, 29.8, 29.76 (3C), 29.72, 29.6, 29.5, 29.4, 25.8, 22.8, 19.0, 17.9, 14.2; IR (KBr): 3059, 3054, 2923, 2916, 2850, 1739, 1658, 1522, 1440, 1375, 1266, 1205, 1019, 739 cm^{-1}; HRMS (ESI) exact mass calcd. for C_{20}H_{40}NO_3 (M+H)^+ 342.3008, found (M+H)^+ 342.2996.

N-myristoyl Leu-methyl ester (6d): Yield, 91%; R_f (5% EtOAc/Hexane), 0.75; ^1H NMR (CDCl_3, 400 MHz): δ 5.90 (d, 1H, J = 8.0 Hz), 4.64 (td, 1H, J = 9.0 Hz, 4.0 Hz), 3.71 (s, 3H), 2.19 (t, 2H, J = 8.0 Hz), 1.68-1.58 (m, 4H), 1.51 (q, 1H, J = 9.0 Hz), 1.30-1.20 (m, 20H), 0.92 (t, 6H, J = 3.5 Hz), 0.86 (t, 3H, J = 6.0 Hz); ^13C NMR (CDCl_3, 125 MHz): δ 173.9, 173.1, 52.3, 50.6, 41.9, 36.7, 32.0, 29.8, 29.76 (3C), 29.72, 29.6, 29.5, 29.3, 25.7, 25.0, 22.9, 22.8, 22.1, 14.2; IR (KBr): 3348, 2918, 2852, 2359, 1751, 1644, 1529, 1462, 1375, 1271, 1239, 1201, 1156, 977, 729 cm^{-1}; HRMS (ESI) exact mass calcd. for C_{21}H_{42}NO_3 (M+H)^+ 356.3165, found (M+H)^+ 356.3168.

N-myristoyl Ileu-methyl ester (6e): Yield, 83%; R_f (5% EtOAc/Hexane), 0.80; ^1H NMR (CDCl_3, 400 MHz): δ 5.81 (bs, 1H), 4.65
(td, 1H, J = 8.8 Hz, 5.2 Hz), 3.72 (s, 3H), 2.20(t, 2H, J = 7.6 Hz), 1.68-1.57 (m, 4H), 1.51 (quin, 1H, J = 9.2 Hz), 1.33-1.22 (m, 20H), 0.94 (d, 3H, J = 2.4 Hz), 0.93 (d, 3H, J = 2.8 Hz), 0.87 (t, 3H, J = 6.4 Hz); $^{13}$C NMR (CDCl$_3$, 100 MHz): δ 173.9, 173.1, 52.4, 50.7, 41.9, 36.7, 32.1, 29.8, 29.77, 29.74, 29.6, 29.5, 29.4, 25.7, 25.0, 22.9, 22.8, 22.1, 14.2 (3C); IR (KBr): 3436, 3056, 2928, 2857, 2360, 2313, 1739, 1671, 1511, 1430, 1265, 896, 743 cm$^{-1}$; HRMS (ESI) exact mass calcd. for C$_{21}$H$_{42}$NO$_3$ (M+H)$^+$ 356.3165, found (M+H)$^+$ 356.3178.

**Procedure for the preparation of esters 10a-e, 11a-e:**

Step 1. Preparation of free acids 7a-e, 8a-e: Lithium hydroxide (2 equiv.) was added to a solution of the methyl esters 5a-e/6a-e (1 equiv.) in THF-H$_2$O (3:1) and the mixture was stirred overnight. The solvent was evaporated, diluted with water and washed with ethyl acetate to remove organic impurities. The aqueous layer was then treated with 10% HCl to bring the pH to ~2, extracted with EtOAc twice, the organic layer washed with water and dried over Na$_2$SO$_4$. Evaporation of the solvent under reduced pressure gave C$_7$ and C$_{13}$ N-acylated amino acids in quantitative yield. These acids were then used for esterification with 9.

Step 2. Preparation of esters 10a-e/11a-e, 12a-f: To a stirred solution containing a mixture of N-acyl amino acid 7a-e/8a-e (1 equiv.) and 1-hydroxybenzotriazole (HOBT, 1 equiv.) in dry DCM at 0 °C was added i-Pr$_2$NEt (1.2 equiv.) and 1-ethyl-3-[3-(dimethylamino)propyl]-carbodiimide hydrochloride (EDCI, 1.1 equiv.). The reaction mixture was stirred at 0 °C for 10 min to which the alcohol 9 was added, allowed to stir at 0 °C for 30 min and then at room temperature for 24 h. After completion of the reaction, mixture was diluted with DCM and washed with water (30 mL). The organic layer was dried over anhydrous Na$_2$SO$_4$, filtered, solvent evaporated under reduced pressure, and the residue was purified by chromatography on silica gel column using EtOAc/Hexane to get compounds 10a-e, 11a-e in 65-87% yields. Use of NBoc amino acids in esterification gave the corresponding esters 12a-f (12a R = H; 12b R=CH$_3$; 12c R=CH$_2$Ph; 12d R=CH(CH$_3$)$_2$; 12e R = CH$_2$CH(CH$_3$)$_2$; 12f R=CH(CH$_3$)CH$_2$CH$_3$ with R$_1$ = -OtBu 69-83% yields.

**Compound 10a:** Yield, 65%; R$_f$ (50% EtOAc/Hexane), 0.38; $^1$H NMR (CDCl$_3$, 400 MHz): δ 6.52 (s, 2H), 5.96 (bs, 1H), 5.26 (s, 2H), 4.32 (t, 2H, J = 4.8 Hz), 3.99 (d, 2H, J = 5.2 Hz), 3.77 (t, 2H, J = 5.2 Hz), 2.88 (s, 2H), 2.22 (t,
2H, \( J = 7.6 \) Hz), 1.68-1.59 (m, 2H), 1.35-1.23 (m, 8H), 0.87 (t, 3H, \( J = 6.4 \) Hz); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \( \delta \) 176.2 (2C), 173.4, 169.9, 136.7 (2C), 81.1 (2C), 61.5, 47.6 (2C), 41.4, 37.8, 36.5, 31.8, 29.4, 29.1, 25.7, 22.8, 14.2; IR (KBr): 3434, 3322, 3056, 2957, 2930, 2857, 1752, 1707, 1676, 1518, 1429, 1400, 1375, 1338, 1266, 1193, 1154, 1127, 1022, 992, 917, 896, 878, 854, 739 cm\(^{-1}\); HRMS (ESI) exact mass calcd. for C\(_{20}\)H\(_{28}\)O\(_6\)Na (M+Na\(^+\)) 415.1845, found (M+Na\(^+\)) 415.1834.

**Compound 10b:** Yield, 74%; \( R_f \) (50% EtOAc/Hexane), 0.40; \(^1\)H NMR (CDCl\(_3\), 500 MHz): \( \delta \) 6.51 (s, 2H), 6.02 (d, 1H, \( J = 9.0 \) Hz), 5.26 (s, 2H), 4.56 (quin, 1H, \( J = 9.5 \)) 4.36-4.26 (m, 2H), 3.77 (t, 2H, \( J = 6.5 \) Hz), 2.88 (q, 2H, \( J = 8.0 \) Hz), 2.19 (t, 2H, \( J = 8.5 \) Hz), 1.61 (quin, 2H, \( J = 7.2 \) Hz), 1.35 (d, 3H, \( J = 9.0 \) Hz), 1.28 (t, 8H, \( J = 6.0 \) Hz), 0.87 (t, 3H, \( J = 8.0 \) Hz); \(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \( \delta \) 176.2, 176.1, 172.7, 172.6, 136.6 (2C), 136.2, 129.4 (2C), 128.6 (2C), 81.0 (2C), 61.5, 48.0, 47.55, 37.8, 36.6, 31.8, 29.3, 29.1, 25.6, 22.7, 18.4, 14.1; IR (KBr): 3056, 2985, 2958, 2858, 1777, 1747, 1701, 1671, 1512, 1456, 1427, 1400, 1337, 1310, 1267, 1194, 1155, 1124, 1063, 1023, 917, 895, 879, 855, 751, 704 cm\(^{-1}\); HRMS (ESI) exact mass calcd. for C\(_{21}\)H\(_{31}\)N\(_2\)O\(_6\) (M+H\(^+\)) 407.2182, found (M+H\(^+\)) 407.2187.

**Compound 10c:** Yield, 81%; \( R_f \) (50% EtOAc/Hexane), 0.5; \(^1\)H NMR (CDCl\(_3\), 500 MHz): \( \delta \) 7.30-7.18 (m, 3H), 7.13-7.07 (m, 2H), 6.50 (s, 2H), 5.88 (d, 1H, \( J = 8.0 \) Hz), 5.24 (d, 2H, \( J = 5.0 \) Hz), 4.86 (td, 1H, \( J = 8.0, 6.0 \) Hz), 4.33-4.20 (m, 2H), 3.75 (t, 2H, \( J = 5.5 \) Hz), 3.14 (dd, 1H, \( J = 5.5, 8.0 \) Hz), 3.02 (dd, 1H, \( J = 14, 6.5 \) Hz), 2.84 (d, 2H, \( J = 1.5 \) Hz), 2.60-2.10 (m, 2H), 1.56 (quin, 2H, \( J = 8.0 \) Hz), 1.32-1.20 (m, 8H), 0.86 (t, 3H, \( J = 7.0 \) Hz); \(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \( \delta \) 176.1 (2C), 172.9, 171.2, 136.6 (2C), 136.2, 129.4 (2C), 128.6 (2C), 127.1, 81.0 (2C), 61.6, 53.1, 47.6, 47.58, 37.73, 37.69, 36.6, 31.8, 29.3, 29.1, 25.6, 22.7, 14.2; IR (KBr): 3427, 3055, 2985, 2958, 2929, 2857, 1746, 1704, 1672, 1510, 1454, 1425, 1399, 1337, 1264, 1193, 1155, 1126, 1023, 917, 896, 879, 701 cm\(^{-1}\); HRMS (ESI) exact mass calcd. for C\(_{27}\)H\(_{35}\)N\(_2\)O\(_6\) (M+H\(^+\)) 483.2495, found (M+H\(^+\)) 483.2485.
**Compound 10d:** Yield, 79%; R\(_f\) (50% EtOAc/Hexane), 0.44; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 6.49 (s, 2H), 6.00 (d, 1H, \(J = 8.8\) Hz), 5.22 (s, 2H), 4.51 (dd, 1H, \(J = 8.4\) Hz, 4.8 Hz), 4.31-4.19 (m, 2H), 3.74 (t, 2H, \(J = 2.8\) Hz), 2.84 (s, 2H), 2.20 (t, 2H, \(J = 7.6\) Hz), 2.09 (sext, 1H, \(J = 6.4\) Hz), 1.59 (quin, 2H, \(J = 6.0\) Hz), 1.33-1.18 (m, 8H), 0.88 (d, 3H, \(J = 6.4\) Hz), 0.86-0.80 (m, 6H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 176.1, 176.0, 173.2, 171.6, 136.6, 136.5, 80.9 (2C), 61.3, 56.8, 47.5, 47.4, 37.7, 36.7, 31.7, 136.6, 136.5, 80.9 (2C), 61.3, 56.8, 47.5, 47.4, 37.7, 36.7, 31.7, 31.1, 29.3, 29.0, 25.7, 22.6, 19.0, 17.7, 14.5; IR (KBr): 3055, 2961, 2929, 2857, 2307, 1778, 1746, 1705, 1651, 1524, 1466, 1398, 1337, 1272, 1192, 1151, 1022, 999, 917, 879, 855, 749 cm\(^{-1}\); HRMS (ESI) exact mass calcd. for C\(_{33}\)H\(_{55}\)N\(_2\)O\(_6\) (M+H\(^+\)) 435.2495, found (M+H\(^+\)) 435.2495.

**Compound 10e:** Yield, 82%; R\(_f\) (50% EtOAc/Hexane), 0.46; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 6.51 (s, 2H), 5.82 (d, 1H, \(J = 8.4\) Hz), 5.26 (d, 2H, \(J = 2.8\) Hz), 4.61 (td, 1H, \(J = 8.8, 4.4\) Hz), 4.30-4.26 (m, 2H), 3.76 (t, 2H, \(J = 6.0\) Hz), 2.87 (q, 2H, \(J = 6.4\) Hz), 2.19 (t, 2H, \(J = 7.6\) Hz), 1.66-1.56 (m, 4H), 1.46 (quin, 1H, \(J = 9.2\) Hz), 1.33-1.22 (m, 8H), 0.92 (d, 6H, \(J = 6.0\) Hz), 0.87 (t, 3H, \(J = 6.4\) Hz); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 176.2, 176.1, 173.1, 172.7, 136.7 (2C), 81.0 (2C), 61.4, 50.6, 47.6, 47.5, 41.6, 37.9, 36.7, 31.8, 29.3, 29.1, 25.7, 24.9, 23.0, 22.7, 21.9, 14.2; IR (KBr): 2957, 2929, 2858, 1748, 1704, 1541, 1399, 1336, 1275, 1193, 1154, 1022, 917, 879, 854, 750, 719 cm\(^{-1}\); HRMS (ESI) exact mass calcd. for C\(_{24}\)H\(_{37}\)N\(_2\)O\(_6\) (M+H\(^+\)) 449.5695, found (M+H\(^+\)) 449.5688.

**Compound 11a:** Yield, 79%; R\(_f\) (50% EtOAc/Hexane), 0.50; \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta\) 6.52 (s, 2H), 6.02 (d, 1H, \(J = 7.0\) Hz), 5.26 (d, 2H, \(J = 7.0\) Hz), 4.56 (quin, 1H, \(J = 4.0\) Hz), 4.31 (sext, 2H, \(J = 5.0\) Hz), 3.78 (t, 2H, \(J = 5.0\) Hz), 2.88 (q, 2H, \(J = 6.5\) Hz), 2.19 (tq, 2H, \(J = 7.5\) Hz, 1.6 Hz), 1.62 (sext, 2H, \(J = 6.0\) Hz), 1.35 (d, 3H, \(J = 7.0\) Hz), 1.30-1.23 (m, 20H), 0.88 (t, 3H, \(J = 6.5\) Hz); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 176.1 (2C), 172.8, 172.7, 136.7 (2C), 81.1 (2C), 61.6, 48.1, 47.6, 47.5, 37.9, 36.7, 32.0, 29.8 (3C), 29.6, 29.5 (3C), 29.4, 25.7, 22.8, 18.4, 14.2; IR (KBr): 3431, 3055, 2986, 2926, 2855,
1777, 1746, 1705, 1672, 1426, 1400, 1337, 1264, 1194, 1156, 1022, 917, 896, 879, 855, 749 cm\(^{-1}\); HRMS (ESI) exact mass calcd. for C\(_{27}\)H\(_{43}\)N\(_2\)O\(_6\) (M+H\(^+\)) 491.6504, found (M+H\(^+\)) 491.6491.

**Compound 11b:** Yield, 72%; \(R_f\) (50% EtOAc/Hexane), 0.60; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 7.29-7.20 (m, 3H), 7.09 (d, 2H, \(J = 7.6\) Hz), 6.51 (s, 2H), 5.90 (d, 1H, \(J = 8.0\) Hz), 5.24 (d, 2H, \(J = 4.0\) Hz), 4.86 (q, 1H, \(J = 6.8\) Hz), 4.32-4.20 (m, 2H), 3.75 (t, 2H, \(J = 5.2\) Hz), 3.14 (dd, 1H, \(J = 14.0\) Hz, 5.6 Hz), 3.02 (dd, 1H, \(J = 14.0\) Hz, 6.4 Hz), 2.84 (s, 2H), 2.15 (td, 2H, \(J = 7.2\) Hz, 3.6 Hz), 1.56 (quin, 2H, \(J = 6.4\) Hz), 1.34-1.22 (m, 20H), 0.88 (t, 3H, \(J = 6.0\) Hz); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 176.1 (2C), 172.9, 171.2, 136.7, 136.6, 136.2, 129.5 (2C), 128.6 (2C), 127.1, 81.1 (2C), 61.7, 53.1, 47.6, 37.8, 37.7, 36.6, 32.1, 29.8 (4C), 29.6, 29.5 (3C), 29.4, 25.7, 22.8, 14.2; IR (KBr): 3431, 3055, 2986, 2928, 2855, 1777, 1745, 1707, 1510, 1455, 1424, 1399, 1337, 1265, 1193, 1154, 1126, 1023, 896, 879, 748, 705 cm\(^{-1}\); HRMS (ESI) exact mass calcd. for C\(_{33}\)H\(_{47}\)N\(_2\)O\(_6\) (M+H\(^+\)) 567.3434, found (M+H\(^+\)) 567.3448.

**Compound 11c:** Yield, 78%; \(R_f\) (50% EtOAc/Hexane), 0.50; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 6.51 (s, 2H), 5.95 (d, 1H, \(J = 8.8\) Hz), 5.26 (d, 2H, \(J = 2.4\) Hz), 4.55 (dd, 1H, \(J = 9.2\) Hz, 5.2 Hz), 4.34-4.22 (m, 2H), 3.77 (t, 2H, \(J = 5.2\) Hz), 2.87 (s, 2H), 2.22 (t, 2H, \(J = 7.2\) Hz), 2.17-2.10 (m, 1H), 1.70-1.60 (m, 2H), 1.32-1.23 (m, 20H), 0.91 (d, 3H, \(J = 6.8\) Hz), 0.87 (t, 3H, \(J = 6.4\) Hz), 0.86 (d, 3H, \(J = 6.8\) Hz); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 176.1, 176.0, 173.2, 171.7, 136.7, 136.6, 81.0 (2C), 61.4, 56.9, 47.6, 47.5, 37.8, 36.8, 32.1, 31.3, 29.8, 29.7 (3C), 29.6, 29.5 (2C), 29.4, 25.8, 22.8, 19.2, 17.8, 14.3; IR (KBr): 3565, 3325, 2958, 2925, 2854, 1744, 1705, 1650, 1537, 1466, 1429, 1398, 1336, 1271, 1192, 1152, 1124, 1022, 917, 878, 854, 748, 720 cm\(^{-1}\); HRMS (ESI) exact mass calcd. for C\(_{29}\)H\(_{46}\)N\(_2\)O\(_6\)Na (M+Na\(^+\)) 541.3254, found (M+H\(^+\)) 541.3231.

**Compound 11d:** Yield, 78%; \(R_f\) (50% EtOAc/Hexane), 0.50; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 6.52 (s, 2H), 5.80 (d, 1H, \(J = 8.8\) Hz), 5.26 (d, 2H, \(J = 2.4\) Hz), 4.62 (td, 1H, \(J = 9.2\) Hz, 4.8 Hz),
4.28 (td, 2H, J = 5.2 Hz, 0.8 Hz), 3.77 (t, 2H, J = 5.6 Hz), 2.88 (q, 2H, J = 6.8 Hz), 2.19 (td, 2H, J = 7.6 Hz, 2.0 Hz), 1.65-1.58 (m, 4H), 1.47 (q, 1H, J = 9.2 Hz), 1.32-1.23 (m, 20H), 0.93 (d, 6H, J = 6.0 Hz), 0.88 (t, 3H, J = 6.8 Hz); 13C NMR (CDCl3, 100 MHz): δ 176.2, 176.1, 173.1, 172.7, 136.7 (2C), 81.0 (2C), 61.4, 50.6, 47.6, 47.5, 41.6, 37.9, 36.7, 32.0, 29.8, 29.7 (3C), 29.6, 29.5 (2C), 29.4, 25.7, 25.0, 23.0, 22.8, 21.9, 14.3; IR (KBr): 3312, 3056, 2956, 2925, 2854, 1776, 1746, 1704, 1651, 1399, 1366, 1337, 1275, 1193, 1154, 1125, 1023, 992, 917, 879, 855, 750, 719 cm⁻¹; HRMS (ESI) exact mass calcd. for C30H48N2O6Na (M+Na)⁺ 555.3410, found (M+Na)⁺ 555.3417.

**Compound 11e:** Yield, 87%; Rf (50% EtOAc/Hexane), 0.60; 1H NMR (CDCl3, 400 MHz): δ 6.50 (s, 2H), 6.03 (d, 1H, J = 8.4 Hz), 5.25 (s, 2H), 4.67 (dd, 1H, J = 8.8 Hz, 4.0 Hz), 4.21 (t, 2H, J = 5.2 Hz), 3.74 (t, 2H, J = 5.6 Hz), 2.85 (s, 2H), 2.24 (t, 2H, J = 7.2 Hz), 1.63 (quin, 2H, J = 6.8 Hz), 1.56 (quin, 2H, J = 7.2 Hz), 1.42 (quin, 1H, J = 7.2 Hz), 1.32-1.20 (m, 20H), 0.94 (quin, 3H, J = 4.4 Hz), 0.91 (d, 3H, J = 7.2 Hz), 0.87 (t, 3H, J = 6.8 Hz); 13C NMR (CDCl3, 100 MHz): δ 176.2 (2C), 175.5, 173.7, 136.7 (2C), 81.1 (2C), 60.5, 56.5, 55.3, 47.6 (2C), 38.1, 34.2, 32.0, 29.8, 29.77 (3C), 29.73, 29.6, 29.59, 29.50, 29.38, 29.35, 29.26, 24.8, 22.7, 14.3; IR (KBr): 3365, 2920, 2851, 2361, 2341, 1746, 1718, 1649, 1555, 1541, 1510, 1468, 1397, 1338, 1196, 1153, 1024, 877, 749, 716 cm⁻¹; HRMS (ESI) exact mass calcd. for C30H48N2O6Na (M+Na)⁺ 555.7132, found (M+Na)⁺ 555.7137.

**Compound 12a:** Yield, 78%; Rf (60% EtOAc/Hexane), 0.30; 1H NMR (CDCl3, 400 MHz): δ 6.51 (s, 2H), 5.26 (s, 2H), 5.02 (bs, 1H), 4.30 (t, 2H, J = 5.2 Hz), 3.85 (d, 2H, J = 5.6 Hz), 3.75 (t, 2H, J = 5.6 Hz), 2.87 (s, 2H), 1.43 (s, 9H); 13C NMR (CDCl3, 100 MHz): δ 176.2 (2C), 170.3, 155.8, 136.6 (2C), 81.1 (2C), 80.1, 61.3, 47.6 (2C), 42.4, 37.8, 28.4 (3C); IR (KBr): 3397, 3008, 2980, 2937, 1751, 1699, 1520, 1398, 1368, 1338, 1278, 1191, 1160, 1126, 1058, 1021, 991, 949, 916, 877, 854 cm⁻¹; HRMS (ESI) exact mass calcd. for C17H22N2O7Na (M+Na)⁺ 389.1325, found (M+Na)⁺ 389.1331.
**Compound 12b:** Yield, 75%; $R_f$ (60% EtOAc/Hexane), 0.30; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 6.50 (s, 2H), 5.26 (s, 2H), 5.04 (bs, 1H), 4.29 (t, 2H, $J = 5.6$ Hz), 3.81 (sext, 2H, $J = 5.2$ Hz), 2.86 (d, 2H, $J = 4.0$ Hz), 1.42 (s, 9H), 1.33 (d, 3H, $J = 7.2$ Hz); NH proton did not appear $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 176.1 (2C), 172.9, 155.2, 136.6 (2C), 81.0 (2C), 79.9, 61.4, 49.3, 47.6, 47.5, 37.9, 28.4 (3C), 18.5; IR (KBr): 3438, 3055, 2986, 1777, 1746, 1708, 1651, 1506, 1423, 1399, 1367, 1338, 1265, 1163, 1068, 1023, 916, 896, 880, 855, 745 cm$^{-1}$; HRMS (ESI) exact mass calcd. for C$_{18}$H$_{24}$N$_2$O$_7$Na (M+Na)$^+$ 403.1481, found (M+Na)$^+$ 403.1479.

**Compound 12c:** Yield, 72%; $R_f$ (60% EtOAc/Hexane), 0.48; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.30-7.26 (m, 2H), 7.24-7.17 (m, 1H), 7.13 (d, 2H, $J = 7.2$ Hz), 6.50 (s, 2H), 5.26 (d, 2H, $J = 12.4$ Hz), 4.97 (d, 1H, $J = 8.0$ Hz), 4.94 (d, 1H, $J = 6.0$ Hz), 4.37-4.27 (m, 1H), 4.26-4.18 (m, 1H), 3.83-3.69 (m, 2H), 3.11 (dd, 1H, $J = 13.6$ Hz, 4.8 Hz), 2.96 (dd, 1H, $J = 13.2$ Hz, 6.8 Hz), 2.85 (s, 2H), 1.39 (s, 9H); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 176.1 (2C), 171.6, 155.6, 136.7, 136.6, 136.4, 129.5 (2C), 128.6 (2C), 127.0, 81.1 (2C), 80.0, 61.4, 54.5, 47.6 (2C), 38.2, 37.7, 28.4 (3C); IR (KBr): 3433, 3056, 2983, 2934, 2307, 1777, 1747, 1704, 1505, 1454, 1428, 1397, 1367, 1338, 1264, 1167, 1126, 1080, 1057, 1023, 998, 917, 896, 879, 856, 802 cm$^{-1}$; HRMS (ESI) exact mass calcd. for C$_{24}$H$_{28}$N$_2$O$_7$Na (M+Na)$^+$ 479.1794, found (M+Na)$^+$ 479.1799.

**Compound 12d:** Yield, 69%; $R_f$ (60% EtOAc/Hexane), 0.40; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 6.49 (s, 2H), 5.28 (d, 2H, $J = 4.0$ Hz), 5.04 (d, 1H, $J = 8.8$ Hz), 4.36-4.27 (m, 1H), 4.26-4.14 (m, 2H), 3.81-3.69 (m, 2H), 2.86 (s, 2H), 2.14-1.93 (m, 1H), 1.42 (s, 9H), 0.92 (d, 3H, $J = 6.8$ Hz), 0.84 (d, 3H, $J = 6.8$ Hz); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 176.0 (2C), 171.9, 155.8, 136.6 (2C), 81.06, 81.03, 79.8, 61.1, 58.6, 47.6 (2C), 37.8, 31.1, 28.4 (3C), 19.2, 17.5; IR (KBr): 3446, 3056, 2985, 1753, 1708, 1509, 1428, 1398, 1370, 1266, 1194, 1165, 1023, 896, 878, 741, 706 cm$^{-1}$; HRMS (ESI) exact mass calcd. for C$_{20}$H$_{28}$N$_2$O$_7$Na (M+Na)$^+$ 431.4426, found (M+Na)$^+$ 431.4431.
Compound 12e: Yield, 72%; R_f (60% EtOAc/Hexane), 0.44; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 6.51 (s, 2H), 5.27 (d, 2H, \(J = 3.2\) Hz), 4.89 (d, 1H, \(J = 8.8\) Hz), 4.35-4.20 (m, 3H), 3.76 (quin, 2H, \(J = 6.4\) Hz), 2.87 (d, 2H, \(J = 3.6\) Hz), 1.78-1.50 (m, 3H), 1.42 (s, 9H), 0.92 (d, 6H, \(J = 6.4\) Hz); \(^1\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 176.1 (2C), 173.1, 155.5, 136.7 (2C), 81.0 (2C), 79.9, 61.2, 52.1, 47.6, 47.59, 41.6, 37.9, 28.4 (3C), 24.9, 23.1, 21.8; IR (KBr): 3437, 3056, 2964, 2872, 1776, 1745, 1708, 1651, 1507, 1397, 1368, 1336, 1266, 1162, 1123, 1050, 1023, 879, 748, 705 cm\(^{-1}\); HRMS (ESI) exact mass calcd. for C\(_{21}\)H\(_{30}\)N\(_2\)O\(_7\)Na (M+Na\(^+\)) 445.1951, found (M+Na\(^+\)) 445.1938.

Compound 12f: Yield, 71%; R_f (60% EtOAc/Hexane), 0.44; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 6.47 (s, 2H), 5.23 (d, 2H, \(J = 10.0\) Hz), 5.07 (d, 1H, \(J = 9.2\) Hz), 4.34-4.25 (m, 1H), 4.23-4.13 (m, 2H), 3.78-3.67 (m, 2H), 2.84 (d, 2H, \(J = 2.0\) Hz), 1.39 (s, 9H), 1.35-1.33 (m, 2H), 1.14-1.10 (m, 1H), 0.85 (t, 6H, \(J = 6.0\) Hz); \(^1\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 176.0 (2C), 171.9, 155.6, 136.6, 136.5, 80.97, 80.94, 79.7, 60.9, 57.9, 47.5 (2C), 37.8, 37.7, 28.4 (3C), 24.9, 15.5, 11.7; IR (KBr): 3585, 3564, 3443, 3055, 2983, 2361, 1709, 1505, 1456, 1423, 1397, 1367, 1337, 1266, 1192, 1159, 1023, 742 cm\(^{-1}\); HRMS (ESI) exact mass calcd. for C\(_{21}\)H\(_{30}\)N\(_2\)O\(_7\)Na (M+Na\(^+\)) 445.4696, found (M+Na\(^+\)) 445.4693.

General procedure for the preparation of 1a-e, 2a-e, 3a-f:

To a stirred solution containing a mixture of the oxanorbornene derivative (10a-e/11a-e/12a-f; 1.0 equiv.), N-methyl morpholine N-Oxide (2.4 equiv.) and pyridine (30 \(\mu\)L for 100 mg of the alkene) in \(t\)-BuOH-H\(_2\)O (3:1) was added osmium tetroxide (0.02 M solution in \(t\)-BuOH, 0.01 equiv.) and it was heated at 80 \(^\circ\)C for 7-8 h. After completion of the reaction, the mixture was cooled to room temperature, treated with 15% aq. Na\(_2\)SO\(_3\) solution (1 mL), allowed to stir for 5-10 min. \(t\)-BuOH was then removed under reduced pressure and the mixture was diluted with dichloromethane, dried using sodium sulfate, evaporated under reduced pressure, and the residue was purified by column chromatography on silica gel using EtOAc/DCM/MeOH.
(50:45:5) in a gradient mode to get the products as colorless solids. Yields and spectroscopic
details of various compounds synthesized are given below.

**Compound 1a:** Yield, 92%; R<sub>f</sub> (EtOAc), 0.40; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz): δ 4.61 (s, 2H), 4.43 (bs, 1H), 4.30 (t, 2H, J = 5.5 Hz), 3.94 (s, 2H), 3.92 (s, 2H), 3.75 (t, 2H, J = 5.0 Hz), 3.40 (bs, 1H), 2.83 (s, 2H), 2.21 (t, 2H, J = 7.5 Hz), 1.60 (quin, 2H, J = 7.5 Hz), 1.29-1.23 (m, 8H), 0.86 (t, 3H, J = 7 Hz), -NH proton did not appear; <sup>13</sup>C NMR (CDCl<sub>3</sub>+CD<sub>3</sub>OD, 100 MHz): δ 176.5 (2C), 174.8, 169.8, 83.8 (2C), 72.2 (2C), 60.8, 45.3 (2C), 40.7, 37.7, 35.8, 31.4, 28.9, 28.7, 25.4, 23.2, 13.6; IR (KBr): 3322, 2921, 2850, 1751, 1705, 1642, 1522, 1438, 1405, 1326, 1190, 1119, 998, 879, 849, 828, 813, 769, 733, 653 cm<sup>-1</sup>; HRMS (ESI) exact mass calcd. for C<sub>20</sub>H<sub>31</sub>N<sub>2</sub>O<sub>8</sub> (M+H)<sup>+</sup> 427.2080, found (M+H)<sup>+</sup> 427.2066.

**Compound 1b:** Yield, 96%; R<sub>f</sub> (EtOAc), 0.40; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ 6.15 (d, 1H, J = 7.6 Hz), 4.65 (s, 1H), 4.62 (s, 1H), 4.52 (quin, 1H, J = 7.2 Hz), 4.38-4.33 (m, 1H), 4.26-4.20 (m, 1H), 4.04 (bs, 1H), 4.00-3.92 (m, 3H), 3.83-3.70 (m, 2H), 2.86 (d, 2H, J = 2.4 Hz), 2.22-2.18 (m, 2H), 1.60 (quin, 2H, J = 6.8 Hz), 1.34 (d, 3H, J = 7.2 Hz), 1.30-1.22 (m, 8H), 0.87 (t, 3H, J = 6.0 Hz); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz): δ 176.2 (2C), 173.5, 172.7, 84.3, 84.2, 73.1 (2C), 61.3, 48.0, 45.6, 45.5, 38.2, 36.7, 31.8, 29.3, 29.1, 25.7, 22.7, 18.4, 14.2; IR (KBr): 3442, 3056, 2985, 1709, 1548, 1428, 1267, 897, 755 cm<sup>-1</sup>; HRMS (ESI) exact mass calcd. for C<sub>21</sub>H<sub>33</sub>N<sub>2</sub>O<sub>8</sub> (M+H)<sup>+</sup> 441.2237, found (M+H)<sup>+</sup> 441.2233.

**Compound 1c:** Yield, 91%; R<sub>f</sub> (EtOAc), 0.50; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz): δ 7.30-7.20 (m, 3H), 7.09 (d, 2H, J = 7.5 Hz), 6.00 (bs, 1H), 4.81 (quin, 1H, J = 7.5 Hz), 4.66 (d, 1H, J = 9.0 Hz), 4.61 (s, 1H), 4.42-4.30 (m, 1H), 4.20-4.14 (m, 1H), 4.00-3.92 (m, 2H), 3.81-3.68 (m, 2H), 3.10 (dd, 1H, J = 14 Hz, 5.5 Hz), 2.99 (ddd, 1H, J = 14 Hz, 6.5 Hz, 2 Hz), 2.82 (s, 2H), 2.15 (sext, 2H, J = 7 Hz), 1.57-1.49 (m, 2H), 1.32-1.20 (m, 8H), 0.87 (t, 3H, J = 5.5 Hz), -OH protons did not appear; <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz): δ 176.2, 173.6, 171.2 (2C),
136.0, 129.4 (2C), 128.7 (2C), 127.2, 84.24, 84.20, 73.1, 61.3, 52.9, 45.6, 45.5, 38.0, 37.8, 36.6, 31.8, 29.8, 29.2, 29.1, 25.7, 22.7, 14.2; IR (KBr): 3426, 3057, 2930, 2861, 1780, 1746, 1708, 1663, 1516, 1429, 1337, 1266, 1190, 1115, 1010, 898, 820, 744 cm⁻¹; HRMS (ESI) exact mass calcd. for C_{27}H_{37}N_{2}O_{8} (M+H)^+ 517.2550, found (M+H)^+ 517.2561.

**Compound 1d:** Yield, 89%; R_f (EtOAc), 0.44; ¹H NMR (CDCl₃, 400 MHz): δ 6.04 (d, 1H, J = 8.8 Hz), 4.66 (s, 1H), 4.60 (s, 1H), 4.48-4.41 (m, 2H), 4.14-4.10 (m, 1H), 3.98 (d, 1H, J = 6.0 Hz), 3.94 (d, 1H, J = 5.6 Hz), 3.86-3.79 (m, 1H), 3.75-3.70 (m, 1H), 2.85 (s, 2H), 2.24 (sext, 2H, J = 4 Hz), 2.10 (sext, 1H, J = 6.4 Hz), 1.65-1.55 (m, 2H), 1.35-1.20 (m, 8H), -2 OH protons did not appear; ¹³C NMR (CDCl₃, 100 MHz): δ 176.1 (2C), 174.1, 171.7, 84.3, 84.2, 73.1, 73.0, 60.9, 56.9, 45.6, 45.5, 38.0, 36.9, 31.8, 31.2, 29.8, 29.3, 29.1, 25.8, 22.7, 19.2, 17.7, 14.2; IR (KBr): 3681, 3299, 3056, 2928, 2860, 2360, 2312, 1709, 1518, 1429, 1266, 1193, 1009, 897, 746 cm⁻¹; HRMS (ESI) exact mass calcd. for C_{23}H_{37}N_{2}O_{8} (M+H)^+ 469.2550, found (M+H)^+ 469.2570.

**Compound 1e:** Yield, 95%; R_f (EtOAc), 0.5; ¹H NMR (CDCl₃, 400 MHz): δ 5.95 (d, 1H, J = 8.8 Hz), 4.66 (s, 1H), 4.60 (s, 1H), 4.55 (dt, 1H, J = 9.2 Hz), 4.41-4.35 (m, 1H), 4.19-4.14 (m, 1H), 3.97 (q, 2H, J = 6 Hz), 3.84-3.61 (m, 2H), 2.85 (d, 2H, J = 1.6 Hz), 2.21 (dt, 2H, J = 7.2, 4.0 Hz), 1.65-1.55 (m, 4H), 1.44 (sext, 2H, J = 9.2 Hz), 1.35-1.20 (m, 8H), 0.93 (d, 6H, J = 6.8 Hz), 0.87 (t, 3H, J = 6.5 Hz) -OH proton did not appear; ¹³C NMR (CDCl₃, 100 MHz): δ 176.2 (2C), 173.8, 172.7, 84.3, 84.2, 73.1 (2C), 61.1, 50.6, 45.6, 45.5, 41.6, 38.1, 36.7, 31.8, 29.3, 29.1, 25.7, 25.0, 23.0, 22.7, 21.8, 14.2; IR (KBr): 3659, 3430, 3057, 2930, 2863, 1708, 1519, 1430, 1400, 1335, 1267, 1194, 1111, 1010, 898, 818, 742, 611 cm⁻¹; HRMS (ESI) exact mass calcd. for C_{24}H_{39}N_{2}O_{8} (M+H)^+ 483.2628, found (M+H)^+ 483.2644.

**Compound 2a:** Yield, 91%; R_f (EtOAc), 0.5; ¹H NMR (CDCl₃, 400 MHz): δ 6.26 (d, 1H, J = 8 Hz), 4.55 (d, 2H, J = 6.0 Hz), 4.49-4.41 (m, 1H), 4.29-
4.17 (m, 2H), 3.89 (s, 2H), 3.72-3.68 (m, 2H), 2.79 (d, 2H, \( J = 3.6 \) Hz), 2.13 (td, 2H, \( J = 7.6 \) Hz, 3.2 Hz), 1.53 (quin, 2H, \( J = 7.2 \) Hz), 1.27 (d, 3H, \( J = 7.2 \) Hz), 1.25-1.15 (m, 20H), 0.81 (t, 3H, \( J = 6.8 \) Hz), -2 OH proton did not appear; \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \( \delta \) 176.3 (2C), 173.6, 172.7, 84.1 84.0, 72.8, 61.2 (2C), 47.9, 47.8, 45.6, 45.5, 38.1, 36.6, 32.0, 29.8, 29.7 (2C), 29.6, 29.5 (2C), 29.3, 25.7, 22.8, 18.2, 14.2; IR (KBr): 3313, 2923, 1705, 1532, 1190, 1108, 1012, 514 cm\(^{-1}\); HRMS (ESI) exact mass calcd. for C\(_{27}\)H\(_{44}\)N\(_2\)O\(_8\)Na (M+Na)\(^+\) 547.6468, found (M+Na)\(^+\) 547.6461.

**Compound 2b:** Yield, 94%; \( R_f \) (EtOAc/Hexane), 0.50; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \( \delta \) 7.30-7.20 (m, 3H), 7.08 (d, 2H, \( J = 6.8 \) Hz), 5.98 (d, 1H, \( J = 8.0 \) Hz), 4.84-4.78 (m, 1H), 4.66 (s, 1H), 4.61 (s, 1H), 4.38-4.34 (m, 1H), 4.19-4.14 (m, 1H), 3.95 (q, 2H, \( J = 6.0 \) Hz), 3.82-3.69 (m, 2H), 3.11 (dd, 1H, \( J = 14.0 \) Hz, 6.4 Hz), 2.99 (dd, 1H, \( J = 14.0 \) Hz, 6.4 Hz), 2.82 (s, 2H), 2.20-2.09 (m, 2H), 1.58-1.48 (m, 2H), 1.32-1.18 (m, 20H), 0.87 (t, 3H, \( J = 6.4 \) Hz), -NH, -OH protons did not appear; \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \( \delta \) 176.2 (2C), 173.5, 171.2, 135.9, 129.4 (2C), 128.7 (2C), 127.2, 84.3, 84.2, 73.1, 61.3, 52.9, 45.6, 45.5, 37.9, 37.8, 36.6, 32.0, 29.8 (4C), 29.6, 29.5 (2C), 29.3, 25.7, 22.8, 14.3; IR (KBr): 3365, 3057, 2927, 2856, 1741, 1707, 1518, 1429, 1266, 1191, 1009, 897, 742 cm\(^{-1}\); HRMS (ESI) exact mass calcd. for C\(_{33}\)H\(_{49}\)N\(_2\)O\(_8\) (M+H)\(^+\) 601.7632, found (M+H)\(^+\) 601.7624.

**Compound 2c:** Yield, 93%; \( R_f \) (EtOAc), 0.50; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \( \delta \) 6.03 (d, 1H, \( J = 9.2 \) Hz), 4.68 (s, 1H), 4.60 (s, 1H), 4.50-4.46 (m, 2H), 4.20 (bs, 1H), 4.13-4.01 (m, 1H), 3.98 (d, 1H, \( J = 6.0 \) Hz), 3.93 (d, 1H, \( J = 6.0 \) Hz), 3.88-3.81 (m, 1H), 3.75-3.69 (m, 1H), 2.85 (s, 2H), 2.28-2.20 (m, 2H), 2.14-2.06 (m, 1H), 1.67-1.55 (m, 2H), 1.30-1.23 (m, 20H), 0.91 (d, 3H, \( J = 6.8 \) Hz), 0.87 (t, 3H, \( J = 6.8 \) Hz), 0.85 (d, 3H, \( J = 6.8 \) Hz), -OH protons did not appear; \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \( \delta \) 176.1 (2C), 174.1, 171.7, 84.2 (2C), 73.0 (2C), 60.8, 56.9, 45.6, 45.1, 37.9, 32.0, 31.3, 29.8 (2C), 29.7 (3C), 29.6, 29.5 (2C), 29.4, 25.8, 22.8, 19.2, 17.7, 14.2; IR (KBr): 3305, 3057, 2927, 2856, 1741, 1709, 1547, 1429, 1267, 897, 755 cm\(^{-1}\); HRMS (ESI) exact mass calcd. for C\(_{29}\)H\(_{49}\)N\(_2\)O\(_8\) (M+H)\(^+\) 553.3489, found (M+H)\(^+\) 553.3481.
**Compound 2d:** Yield, 89%; R$_f$ (EtOAc), 0.50; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 5.86 (d, 1H, $J = 8.4$ Hz), 4.70 (s, 1H), 4.60 (s, 1H), 4.59-4.54 (m, 1H), 4.52-4.44 (m, 1H), 4.10 (dt, 1H, $J = 9.6$ Hz, 4.4 Hz), 4.02-3.97 (m, 1H), 3.93 (d, 1H, $J = 6.0$ Hz), 3.92-3.83 (m, 1H), 3.77-3.67 (m, 1H), 2.85 (s, 2H), 2.27-2.16 (m, 2H), 1.66-1.55 (m, 6H), 1.45 (quin, 1H, $J = 9.6$ Hz), 1.31-1.23 (m, 20H), 0.97-0.91 (m, 6H), 0.88 (t, 3H, $J = 6.8$ Hz); -OH proton did not appear; $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 176.3 (2C), 173.9, 172.8, 84.1 (2C), 72.7 (2C), 61.1, 50.6, 50.5, 45.6, 45.5, 41.3, 38.1, 36.5, 32.0, 29.7 (2C), 29.6 (2C), 29.4 (2C), 29.3, 25.7, 24.9, 22.9, 22.7, 21.8, 14.2; IR (KBr): 3430, 3056, 2928, 2858, 1710, 1518, 1429, 1335, 1266, 1194, 1010, 897, 741 cm$^{-1}$; HRMS (ESI) exact mass calcd. for C$_{30}$H$_{51}$N$_2$O$_8$ (M+H)$^+$ 567.3645, found (M+H)$^+$ 567.3625.

**Compound 2e:** Yield, 84%; R$_f$ (EtOAc), 0.50; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 4.49 (s, 2H), 4.10 (bs, 2H), 3.85-3.83 (m, 2H), 3.64 (bs, 2H), 3.27 (bs, 1H), 2.76-2.73 (m, 2H), 2.15 (bs, 2H), 1.60-1.41 (m, 2H), 1.31-1.28 (m, 1H), 1.27-1.12 (m, 25H), 0.88 (bs, 6H), -OH, -NH protons did not appear; $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 176.5 (2C), 174.4, 174.1, 84.0 (2C), 72.5, 60.4, 55.2, 45.5 (2C), 38.3, 37.5, 34.0, 31.9, 29.7, 29.62 (2C), 29.58, 29.5, 29.3, 29.2, 29.1, 26.3, 24.7, 22.7, 15.3, 14.4, 14.0; IR (KBr): 3315, 2953, 2921, 2851, 2474, 2362, 2342, 1737, 1703, 1464, 1434, 1400, 1328, 1193, 1157, 1005, 992, 885, 733 cm$^{-1}$; HRMS (ESI) exact mass calcd. for C$_{30}$H$_{51}$N$_2$O$_8$ (M+H)$^+$ 567.3645, found (M+H)$^+$ 567.3657.

**Compound 3a:** Yield, 89%; R$_f$ (EtOAc), 0.30; $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 5.21 (bs, 1H), 4.66 (s, 2H), 4.30 (bs, 2H), 3.98 (s, 2H), 3.89 (bs, 1H), 3.83 (d, 2H, $J = 4.8$ Hz), 3.76 (bs, 2H), 2.88 (s, 2H), 1.44 (s, 9H); -OH proton did not appear; $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 176.2 (2C), 170.5, 156.1, 84.2 (2C), 80.4, 73.2 (2C), 61.1, 45.5 (2C), 42.3, 38.2, 28.5 (3C); IR (KBr): 3350, 2980, 2929, 1770, 1694, 1528, 1406, 1268, 1165, 1015, 900, 757 cm$^{-1}$; HRMS (ESI) exact mass calcd. for C$_{17}$H$_{24}$N$_2$O$_9$Na (M+Na)$^+$ 423.3763, found (M+Na)$^+$ 423.3772.
**Compound 3b**: Yield, 91%; R_f (EtOAc), 0.30; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 4.59 (s, 2H), 4.27 (t, 2H, J = 4.8 Hz), 4.24-4.14 (m, 1H), 3.91 (s, 2H), 3.78-3.68 (m, 2H), 2.82 (q, 2H, J = 6.8 Hz), 1.40 (s, 9H), 1.30 (d, 3H, J = 7.2 Hz), -NH, -OH protons did not appear; \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 176.4 (2C), 173.1, 155.5, 83.9 (2C), 80.0, 72.7 (2C), 61.1, 49.1, 45.6, 45.5, 38.1, 28.3 (3C), 17.9; IR (KBr): 3510, 3371, 3056, 2980, 2931, 2860, 2595, 2505, 1743, 1696, 1519, 1441, 1343, 1266, 1166, 1109, 1065, 897, 746 cm\(^{-1}\); HRMS (ESI) exact mass calcd. for C\(_{18}\)H\(_{26}\)N\(_2\)O\(_9\)Na (M+Na)\(^+\) 437.4033, found (M+Na)\(^+\) 437.4041

**Compound 3c**: Yield, 93%; R_f (EtOAc), 0.40; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 7.31-7.28 (m, 2H), 7.26-7.18 (m, 1H), 7.15 (d, 2H, J = 7.2 Hz), 5.26 (d, 2H, J = 12.4 Hz), 5.16 (s, 2H), 4.97 (d, 1H, J = 8.0 Hz), 4.94 (d, 1H, J = 6.0 Hz), 4.38-4.28 (m, 1H), 4.29-4.19 (m, 1H), 3.85-3.71 (m, 2H), 3.15 (dd, 1H, J = 13.6, 4.8 Hz), 2.98 (dd, 2H, J = 13.2, 6.8 Hz), 2.88 (s, 2H), 1.42 (s, 9H), -OH proton did not appear; \(^{13}\)C NMR (CDCl\(_3\) + CD\(_3\)OD, 100 MHz): \(\delta\) 176.4 (2C), 171.7, 155.5, 136.2, 129.4, 129.2, 128.5 (2C), 126.9, 83.9 (2C), 80.2, 72.6(2C), 61.1, 54.4, 45.5 (2C), 38.0, 37.8, 28.2 (3C); IR (KBr): 3516, 3371, 2924, 1700, 1519, 1448, 1345, 1239, 1176, 984, 746 cm\(^{-1}\); HRMS (ESI) exact mass calcd. for C\(_{24}\)H\(_{30}\)N\(_2\)O\(_9\)Na (M+Na)\(^+\) 513.5014, found (M+Na)\(^+\) 513.5028.

**Compound 3d**: Yield, 93%; R_f (EtOAc), 0.33; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 5.07 (d, 1H, J = 7.2 Hz), 4.67 (s, 1H), 4.65 (s, 1H), 4.40-4.30 (m, 1H), 4.24-4.10 (m, 2H), 3.98 (d, 2H, J = 2.8 Hz), 3.82-3.70 (m, 2H), 2.86 (s, 2H), 2.12-2.02 (m, 1H), 1.44 (s, 9H), 0.93 (d, 3H, J = 7.2 Hz), 0.85 (d, 3H, J = 6.4 Hz), -OH protons did not appear; \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 175.9 (2C), 172.2, 156.0, 84.3, 84.2, 80.2, 73.3 (2C), 61.0, 58.6, 45.6 (2C), 38.2, 31.1, 28.5 (3C), 19.2, 17.5; IR (KBr): 3437, 3057, 2977, 2929, 2860, 1710, 1508, 1399, 1265, 1166, 1103, 1010, 898, 739 cm\(^{-1}\); HRMS (ESI) exact mass calcd. for C\(_{20}\)H\(_{30}\)N\(_2\)O\(_9\)Na (M+Na)\(^+\) 465.4572, found (M+Na)\(^+\) 465.4572.
**Compound 3e:** Yield, 92%; \( R_f \) (EtOAc), 0.33; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \( \delta \) 5.03-4.93 (m, 1H), 4.66 (s, 2H), 4.65 (s, 1H), 4.37-4.27 (m, 2H), 4.26-4.17 (m, 2H), 3.98 (d, 2H, \( J = 2.8 \) Hz), 3.81-3.70 (m, 2H), 2.86 (q, 2H, \( J = 7.2 \) Hz), 1.67 (sep, 1H, \( J = 6.8 \) Hz), 1.60-1.52 (m, 1H), 1.51-1.44 (m, 1H), 1.43 (s, 9H), 0.93 (d, 6H, \( J = 6.4 \) Hz); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \( \delta \) 176.0 (2C), 173.3, 155.8, 84.2 (2C), 80.2, 73.3, 73.2, 61.1, 52.2, 45.6, 45.5, 41.5, 38.3, 28.5 (3C), 24.9, 23.1, 21.8; IR (KBr): 3364, 2949, 1705, 1634, 1519, 1445, 1397, 1167, 1112, 1012, 899, 727, 600 cm\(^{-1}\); HRMS (ESI) exact mass calcd. for C\(_{21}\)H\(_{32}\)N\(_2\)O\(_9\)Na (M+Na\(^+\)) 479.4842, found (M+Na\(^+\)) 479.4818.

**Compound 3f:** Yield, 97%; \( R_f \) (EtOAc), 0.33; \(^1\)H NMR (CDCl\(_3\), 400 MHz): \( \delta \) 5.10 (d, 1H, \( J = 9.2 \) Hz), 4.64 (s, 2H), 4.40-4.30 (m, 1H), 4.24-4.12 (m, 2H), 3.96 (s, 2H), 3.82-3.69 (m, 2H), 3.43 (bs, 2H), 2.87 (s, 2H), 1.86-1.77 (m, 1H), 1.42 (s, 9H), 1.39-1.30 (m, 1H), 1.19-1.06 (m, 1H), 0.88 (t, 6H, \( J = 7.2 \) Hz); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \( \delta \) 176.1 (2C), 172.2, 155.9, 84.2, 84.1, 80.2, 73.2, 73.1, 60.9, 58.1, 45.6 (2C), 38.1, 37.8, 28.4 (3C), 24.9, 15.6, 11.7; IR (KBr): 3476, 2967, 2930, 1780, 1696, 1527, 1398, 1164, 1111, 1008, 902, 858, 831, 780, 734, 697 cm\(^{-1}\); HRMS (ESI) exact mass calcd. for C\(_{21}\)H\(_{32}\)N\(_2\)O\(_9\)Na (M+Na\(^+\)) 479.4842, found (M+Na\(^+\)) 479.4855.
3. SEM images and DLS analysis results of samples prepared under various conditions:

**Figure SI-1.** DLS histograms of 1b (F), 1c (G), 1d (H) and 1e (I) are shown.

**Figure SI-2.** SEM images of samples of 1c made from acetone solutions of different concentrations A) 0.1 mg/1.5 mL, B) 0.5 mg/1.5 mL, C) 1.0 mg/1.5 mL, D) 1.5 mg/1.5 mL, and E) 2.0 mg/1.5 mL; Samples were prepared by directly drop-casting their acetone solutions on silica substrate. DLS histograms of solutions of 1c at various concentrations: F) 0.5 mg/1.5 ml, G) 1.0 mg/1.5 mL, H) 1.5 mg/1.5 mL, and I) 2.0 mg/1.5 mL.
**Figure SI-3.** SEM images of samples of 1a (A), 1b (B), 1d (C), and 1e (D) prepared by directly drop-casting their methanol solution (1 mg/1.5 mL) on silica substrate. DLS of histogram of 1a (E), 1d (F), and 1e (G) are also shown; image of sample of 1c in MeOH is given in Fig. SI-9.

**Figure SI-4.** SEM images of samples of 3a (A), 3b (B), 3d (C), 3e (D) and 3f (E), prepared by directly drop-casting their acetone solutions (1 mg/1.5 mL) on silica substrate; DLS histograms of samples of 3a (F), 3b (G), 3d (H), 3e (I) and 3f (J) in this solvent (1 mg/1.5 mL) are also shown.
**Figure SI-5.** SEM images of samples of 2a (A), 2b (B), 2c (C) and 2d (D) and 2e (E) prepared by directly drop-casting their acetone solutions (1 mg/1.5 mL) on silica substrate.

**Figure SI-6.** SEM images of samples of 2a (A), 2b (B), 2c (C) and 2e (E) prepared by directly drop-casting their methanol solutions (1 mg/1.5 mL) on silica substrate.

**Figure SI-7.** TEM images of sample of 1d (C&D) prepared by directly drop-casting its acetone solution (1 mg/1.5 mL) on carbon coated copper grid.
4. Critical micellar concentration

Critical micellar concentration (cmc) was calculated by fluorescent probe-based method using pyrene in water. Solutions of 1a-e in water with concentrations ranging from 0.3 mM to 5.0 mM were admixed with 0.125 mM solution (50 µL) of pyrene in methanol in a quartz fluorescence cell and made up to a final volume of 3 mL. After exciting pyrene at 334 nm, its emission at 373 and 384 nm, corresponding to the first and third vibrational bands (I₁, I₃) respectively were noted. From the plots of I₃/I₁ vs. concentration of the lipid (Figure 8), the cmcs were measured.

**Figure SI-8.** Plots of intensity of fluorescence emission I₃/I₁ vs concentration of the lipids A) 1a, B) 1b, C) 1c, D) 1d, E) 1e

**Figure SI-9.** SEM images of samples of 1e from A) MeOH, B) THF, C) CHCl₃ and D) Water; prepared by directly drop-casting their methanol solution (1 mg/1.5 mL) on silica substrate.
5. Results from PXRD analysis:

Table SI-1. Results from PXRD analysis of 1a-e

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6. Composition of Niosomal formulations:

Table SI-2. Composition of different formulations (lipid/methanol = 1 (mg)/1.5 mL)

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<th>amphiphiles</th>
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</table>
7. Niosomal formulations – particle size distribution and morphology:

**Figure SI-10.** SEM images of samples of LCPC (A), NC1a (B), NC1b (C), NC1c (D), NC1d (E) and NC1e (F) prepared by directly drop-casting these formulations on silica substrate. DLS histogram of LCPC (G), NC1a (H), NC1b (I), NC1c (J), NC1d (K) and NC1e (L) in phosphate buffer (Amphiphile: Drug = 1:1:0.5, concentration 1mg of amphiphile/1.5 mL of buffer)

**Figure SI-11.** SEM images of samples of N1a (A), N1b (B), N1c (C), N1d (D) and N1e (E) prepared by directly drop-casting the liposomes without cholesterol, on silica substrate. DLS histogram of N1a (F), N1b (G), N1c (H), N1d (I) and N1e (J) in phosphate buffer (Amphiphile: Drug = 1:1, concentration 1mg of amphiphile/1.5 mL of buffer).
8. CryoTEM Images of 1c

![CryoTEM Images of 1c](image1)

**Figure SI-12.** A. Cryo TEM image of Amphiphile 1c in water after thin film hydration method. B. Cryo TEM image of Amphiphile 1c alone entrapped with Ibuprofen in water. C. Cryo TEM image of NC1c in water

9. Drug loading and drug release studies:

$\lambda_{\text{max}}$ of Ibuprofen was determined in phosphate buffer at pH 7.2 and was found to be 223 nm. To make the calibration curve, different concentrations (5 to 30µg/mL) of this drug in phosphate buffer (pH 7.2) were prepared and their absorbances at 223 nm were measured using a UV spectrophotometer. The absorbance was plotted against concentration (µg/ml) to obtain the standard graph which is given below.

![Calibration Curve of Ibuprofen](image2)

**Figure SI-13.** Calibration Curve of Ibuprofen in phosphate buffer of pH 7.2

*Drug encapsulation efficiency:* Ibuprofen-loaded vesicles were separated from un-entrapped drug by centrifuging at 10,000 rpm at 4°C for 2 hr. The supernatant was taken and diluted three
times with phosphate buffer of pH 7.2. The concentration of Ibuprofen in the solution (supernatant) was determined by a UV spectrophotometer by noting the absorption at 223 nm. The absorbance was then converted to concentration/mL using standard calibration curve. The percentage of drug encapsulated was then calculated using the following equation:
Encapsulation efficiency = (Drug \text{encapsulated} / \text{Total drug}) \times 100

Table 3-SI. Drug encapsulation efficiency of various formulations (in triplicate)

<table>
<thead>
<tr>
<th>Name</th>
<th>Trial 1</th>
<th>Trial 2</th>
<th>Trial 3</th>
<th>Mean encapsulation efficiency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LCPC</td>
<td>78.9</td>
<td>78.8</td>
<td>78.2</td>
<td>78.6±0.3</td>
</tr>
<tr>
<td>NC1a</td>
<td>49.1</td>
<td>49.6</td>
<td>48.1</td>
<td>48.9±0.8</td>
</tr>
<tr>
<td>NC1b</td>
<td>57.3</td>
<td>56.5</td>
<td>56.6</td>
<td>56.8±0.4</td>
</tr>
<tr>
<td>NC1c</td>
<td>66.2</td>
<td>65.7</td>
<td>66.2</td>
<td>66.1±0.3</td>
</tr>
<tr>
<td>NC1d</td>
<td>65.8</td>
<td>64.9</td>
<td>65.4</td>
<td>65.4±0.4</td>
</tr>
<tr>
<td>NC1e</td>
<td>65.7</td>
<td>64.7</td>
<td>64.8</td>
<td>65.1±0.6</td>
</tr>
<tr>
<td>N1a</td>
<td>32.9</td>
<td>32.7</td>
<td>32.6</td>
<td>32.8±0.2</td>
</tr>
<tr>
<td>N1b</td>
<td>31.1</td>
<td>32.9</td>
<td>31.9</td>
<td>31.9±0.9</td>
</tr>
<tr>
<td>N1c</td>
<td>31.9</td>
<td>33.4</td>
<td>32.4</td>
<td>32.6±0.7</td>
</tr>
<tr>
<td>N1d</td>
<td>27.0</td>
<td>26.7</td>
<td>26.4</td>
<td>26.7±0.3</td>
</tr>
<tr>
<td>N1e</td>
<td>33.1</td>
<td>32.7</td>
<td>41.2</td>
<td>35.7±0.8</td>
</tr>
</tbody>
</table>
**Table 4-SI.** Results from drug-release studies (procedure discussed in the main text).

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Drug release (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LCPC</td>
</tr>
<tr>
<td>0</td>
<td>0.9±0.4</td>
</tr>
<tr>
<td>1</td>
<td>6.6±3.6</td>
</tr>
<tr>
<td>2</td>
<td>9.8±0.2</td>
</tr>
<tr>
<td>3</td>
<td>13.2±0.8</td>
</tr>
<tr>
<td>4</td>
<td>16.8±0.3</td>
</tr>
<tr>
<td>5</td>
<td>19.7±0.6</td>
</tr>
<tr>
<td>6</td>
<td>22.3±0.9</td>
</tr>
<tr>
<td>8</td>
<td>27.3±0.4</td>
</tr>
<tr>
<td>10</td>
<td>30.8±0.5</td>
</tr>
<tr>
<td>12</td>
<td>33.2±0.0</td>
</tr>
<tr>
<td>24</td>
<td><strong>49.6±0.8</strong></td>
</tr>
</tbody>
</table>
**Loading Content**: Niosomes were prepared by thin film hydration method. Towards this, the lipid (1a-e) alone or in combination with cholesterol and Ibuprofen in 1:0.5:1 ratio was dissolved in methanol. Solvent was then removed by rotary evaporation under reduced pressure to get a thin film which was subsequently hydrated using phosphate buffer (pH 7.2). The resulting suspension was sonicated and then extruded through 1000 nm filters to get more-or-less uniformly-sized niosomes. 1 mL of suspension was centrifuged and the supernatant containing unentrapped drug was removed. To the resulting pellet, 0.5% solution of TritonX-100 was added and diluted to 1ml using phosphate buffer (pH 7.2). The solution was again centrifuged and supernatant was assessed to get the loading content by UV-Vis spectrophotometer. The absorbance was converted to concentration per mL using standard calibration curve. The percentage of drug encapsulated in the original aggregate was calculated by the following equation.

\[
\text{Loading content} = \frac{\text{Drug loaded}}{\text{Total drug}} \times 100
\]

**Table 5-S1.** Loading contents of different formulations

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>Percent loading content</th>
<th>Formulation code</th>
<th>Percent loading content</th>
</tr>
</thead>
<tbody>
<tr>
<td>NC1a</td>
<td>19.6566 ± 0.0096</td>
<td>N1a</td>
<td>10.3456 ± 0.0456</td>
</tr>
<tr>
<td>NC1b</td>
<td>27.6683 ± 0.0263</td>
<td>N1b</td>
<td>19.0654 ± 0.0345</td>
</tr>
<tr>
<td>NC1c</td>
<td>43.4216 ± 0.0223</td>
<td>N1c</td>
<td>30.0567 ± 0.1123</td>
</tr>
<tr>
<td>NC1d</td>
<td>37.31 ± 0.0456</td>
<td>N1d</td>
<td>21.0678 ± 0.0243</td>
</tr>
<tr>
<td>NC1e</td>
<td>34.5283 ± 0.0210</td>
<td>N1e</td>
<td>20.0341 ± 0.8765</td>
</tr>
</tbody>
</table>
**Stability Studies:**

The suspensions of aggregates (NC1a-NC1e) prepared through the procedure given above (under loading content) were stored at 4°C for 12 days and the loading content was calculated again to know their stability, especially to see whether there is any leakage of drug from the aggregates.

**Table 6-SI.** Variation in loading content on storage

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>Percent loading efficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>NC1a</td>
<td>18.3909±0.7227</td>
</tr>
<tr>
<td>NC1b</td>
<td>23.6090±1.4072</td>
</tr>
<tr>
<td>NC1c</td>
<td>41.3636±0.9608</td>
</tr>
<tr>
<td>NC1d</td>
<td>33.2181±0.3818</td>
</tr>
<tr>
<td>NC1e</td>
<td>26.5363±0.6883</td>
</tr>
</tbody>
</table>

**Figure SI-14.** (A) SEM images of samples of NC1c, (B) NC1c after adding Triton X 100,(C) NC1c after storing for 12 days in phosphate buffer
10. $^1\text{H}$ & $^{13}\text{C}$ NMR spectra of various compounds:

$^1\text{H}$ NMR spectrum of compound 5a

$^{13}\text{C}$ NMR spectrum of compound 5a
$^1$H NMR spectrum of compound 5b

$^{13}$C NMR spectrum of compound 5b
\[ \text{H NMR spectrum of compound 5c} \]

\[ \text{C NMR spectrum of compound 5c} \]
$^{1}$H NMR spectrum of compound 5d

$^{13}$C NMR spectrum of compound 5d
\[\text{H NMR spectrum of compound 5e}\]

\[\text{13C NMR spectrum of compound 5e}\]
$^1$H NMR spectrum of compound 6a

$^{13}$C NMR spectrum of compound 6a
**H NMR spectrum of compound 6b**

**C NMR spectrum of compound 6b**
\( \text{\^1H NMR spectrum of compound } 6c \)

\( \text{\^13C NMR spectrum of compound } 6c \)
\[ \text{H NMR spectrum of compound 6d} \]

\[ \text{^13C NMR spectrum of compound 6d} \]
$^1$H NMR spectrum of compound 6e

$^{13}$C NMR spectrum of compound 6e
$\text{C}_7\text{H}_5\text{N}\text{O}_2$
$^1$H NMR spectrum of compound 7b

$^{13}$C NMR spectrum of compound 7b
**1H NMR spectrum of compound 7d**

**13C NMR spectrum of compound 7d**
$\text{H NMR spectrum of compound } 7\text{e}$

$\text{C NMR spectrum of compound } 7\text{e}$
H NMR spectrum of compound 8a

C NMR spectrum of compound 8a
H NMR spectrum of compound 8b

C NMR spectrum of compound 8b

13C NMR spectrum of compound 8b
$^{1}H$ NMR spectrum of compound 8c

$^{13}C$ NMR spectrum of compound 8c
1H NMR spectrum of compound 8d

13C NMR spectrum of compound 8d
H NMR spectrum of compound 8e

C NMR spectrum of compound 8e
\[ \text{H NMR spectrum of compound 10a} \]

\[ \text{C NMR spectrum of compound 10a} \]
$^1$H NMR spectrum of compound 10b

$^{13}$C NMR spectrum of compound 10b
H NMR spectrum of compound 7.

C NMR spectrum of compound 7.

1H NMR spectrum of compound 10c

13C NMR spectrum of compound 10c
$^1$H NMR spectrum of compound 10d

$^{13}$C NMR spectrum of compound 10d
$^1$H NMR spectrum of compound 10e

$^{13}$C NMR spectrum of compound 10e
$^1$H NMR spectrum of compound 11a

$^{13}$C NMR spectrum of compound 11a
$^{1}H$ NMR spectrum of compound 11b

$^{13}C$ NMR spectrum of compound 11b
$^1$H NMR spectrum of compound 11c

$^{13}$C NMR spectrum of compound 11c
$^1\text{H NMR spectrum of compound 11d}$

$^{13}\text{C NMR spectrum of compound 11d}$
\textbf{H NMR spectrum of compound 11e}

\textbf{C NMR spectrum of compound 11e}

\textbf{13C NMR spectrum of compound 11e}
$^1$H NMR spectrum of compound 12a

$^{13}$C NMR spectrum of compound 12a
\( ^1 \text{H NMR spectrum of compound 12b} \)

\( ^{13} \text{C NMR spectrum of compound 12b} \)
$^{1}$H NMR spectrum of compound 12c

$^{13}$C NMR spectrum of compound 12c
$^1$H NMR spectrum of compound 12d

$^{13}$C NMR spectrum of compound 12d
$^1$H NMR spectrum of compound 12e

$^13$C NMR spectrum of compound 12e
$^1$H NMR spectrum of compound 12f

$^{13}$C NMR spectrum of compound 12f
$^1$H NMR spectrum of compound 1a

$^{13}$C NMR spectrum of compound 1a
H NMR spectrum of compound 1b

\[ \text{\textsuperscript{1}H NMR spectrum of compound 1b} \]

\[ \text{\textsuperscript{13}C NMR spectrum of compound 1b} \]
\( ^1H \) NMR spectrum of compound 1c

\( ^{13}C \) NMR spectrum of compound 1c
H NMR spectrum of compound 1d

\[ \text{C NMR spectrum of compound 1d} \]
$^1$H NMR spectrum of compound 1e

$^{13}$C NMR spectrum of compound 1e
H NMR spectrum of compound 7a.

C NMR spectrum of compound 1a.

1H NMR spectrum of compound 2a

13C NMR spectrum of compound 2a
H NMR spectrum of compound 2b

C NMR spectrum of compound 2b
$^1$H NMR spectrum of compound 2c

$^{13}$C NMR spectrum of compound 2c
\(^1\text{H} \text{NMR spectrum of compound } 2d\)

\(^{13}\text{C} \text{NMR spectrum of compound } 2d\)
$^1$H NMR spectrum of compound 2e

$^{13}$C NMR spectrum of compound 2e
$^1$H NMR spectrum of compound 3a

$^{13}$C NMR spectrum of compound 3a
\(^{1}\)H NMR spectrum of compound 3b

\(^{13}\)C NMR spectrum of compound 3b
$^1$H NMR spectrum of compound 3d

$^{13}$C NMR spectrum of compound 3d
$^1$H NMR spectrum of compound 3e

$^{13}$C NMR spectrum of compound 3e
\( ^1H \) NMR spectrum of compound 3f

\( ^13C \) NMR spectrum of compound 3f
$^{13}$C NMR spectrum of compound 3c
Evidence of H-bonded association in a mixture of Ibuprofen and 1c in CDCl₃

**¹H NMR spectrum of Ibuprofen**

**¹H NMR of compound 1c**
Upfield shifting of aromatic signals on addition of ibuprofen to its CDCl$_3$ solution

Downfield shift NH signal in 1c on addition of ibuprofen
Upfield shifting carboxyl carbon in Ibuprofen and down-field shifting of amide carbonyl in 1c in their mixture in CDCl₃