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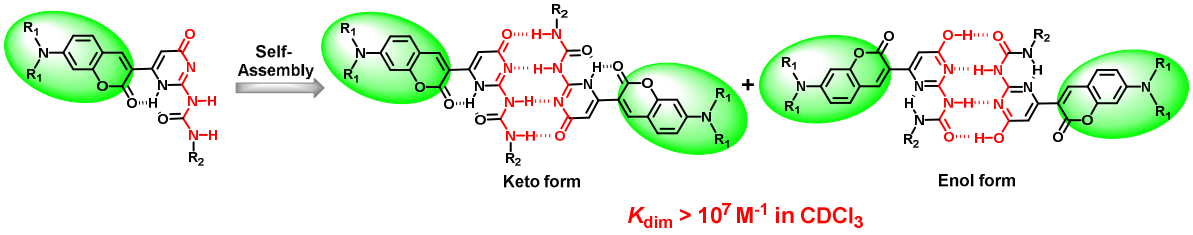
Coumarin-appended Stable Fluorescent Self-complementary Quadruple Hydrogen-bonded Molecular Duplexes

Sanjeev Kheria,[†] Suresh Rayavarapu,[†] Amol S. Kotmale,[§] Dinesh R. Shinde,[§]

Rajesh G. Gonnade,[‡] and Gangadhar J. Sanjayan[*,†]

[†]Organic Chemistry Division, [§]Central NMR Facility, [‡]Centre for Materials Characterization, CSIR-National Chemical Laboratory (CSIR-NCL), Dr. Homi Bhabha Road, Pune 411008, India. E-mail: gj.sanjayan@ncl.res.in

ABSTRACT



This article reports coumarin-conjugated self-assembling system adorned with valuable features such as high duplex stability and a built-in fluorophore, which would augment its application potential. This system forms highly stable molecular duplex in non-polar solvent (K_{dim} > 1.9 x 10^7 M^{-1} in $CDCl_3$). Due to the fluorescent property of coumarin, these new structural motif may find potential application in material chemistry and supramolecular chemistry.

INTRODUCTION

Supramolecular chemistry[1] has attracted considerable interest in recent years, owing to its wide application potential in chemical biology, nanotechnology, and material science.[2] A real-life example of hydrogen bonding is the double helix structure of DNA, where two complementary strands are intertwined by means of hydrogen bonds and π-π stacking in a

self-assembly process. Inspired by Nature's use of DNA base pairs like purines and pyrimidines, organic chemists have designed synthetic hydrogen bonding motif that can self-assemble to form supramolecular architectures.[3] Among the various hydrogen bonded duplexes, quadruple hydrogen bonded dimers have been widely explored, studied and attained significant importance due to their simplicity in design and synthetic accessibility.[4a] Due to its high dimerization constant (K_{dim} > 10^7 M^{-1}) and facile synthetic accessibility, Meijer's ureidopyrimidone[4] (UPy) system has emerged as a promising building block having widespread applications in diverse areas such as material chemistry, catalysis and supramolecular polymers (Figure 1a).[5] High duplex stability is also exhibited by deazapterin-based self-assembling system, which is somewhat closely related to Meijer's system (Figure 1b).[6] It is noteworthy that self-assembly of heterocycle-based UPy systems are often associated with tautomerization, and as a result, the protamers (*keto* and *enol* forms) generate different structures, both in the solution- and in the solid-state.[4a]

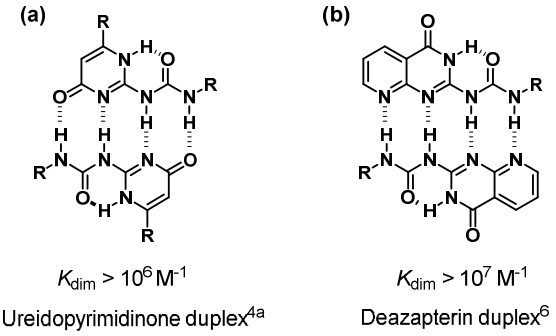


Figure 1. AADD-type self-assembling systems forming highly stable duplexes.

The modified coumarin-appended UPy system reported herein actually exists as dimers of pyrimidinone and pyrimidinol tautomeric forms, stabilized by linear array of four hydrogen bonds (Figure 2). The dimers are arranged *via* **AADD** as well as **DADA** arrays of self-complementary type hydrogen bonding. In addition, there is also pre-organisation *via* S(6)-type intramolecular hydrogen bond in both the dimers to further enhance their stability

significantly. To the best of our knowledge, this is the first report of an UPy wherein coumarin moiety is fused on the backbone. As coumarin moiety itself is fluorescent, the resulting self-assembling systems **1** exhibit strong fluorescent properties.

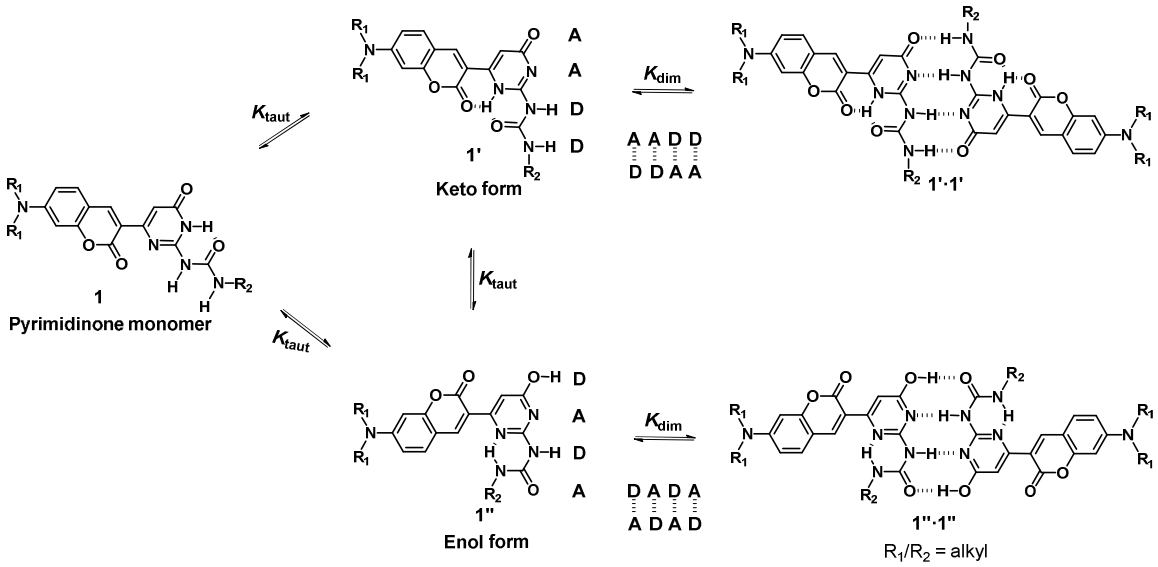
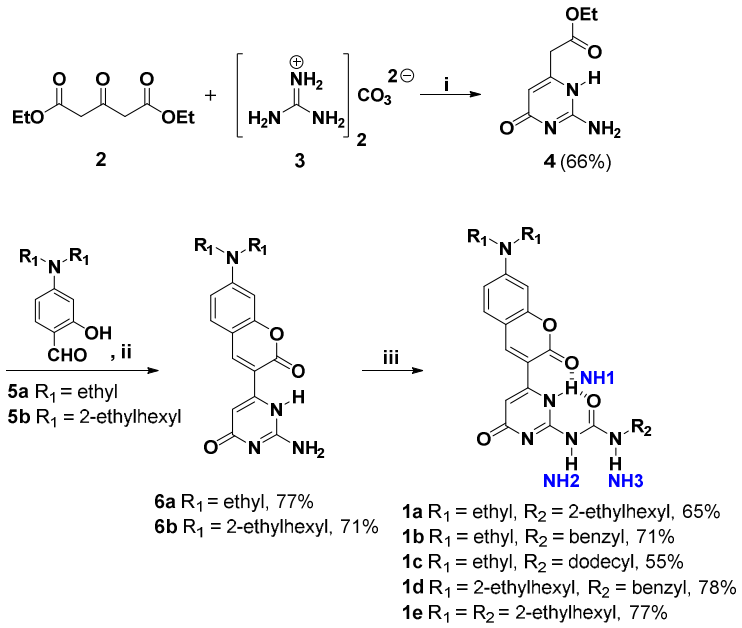


Figure 2. Equilibria between tautomeric forms and between monomer and dimer of self-assembling system **1** reported herein.

RESULTS AND DISCUSSION

Coumarin-appended fluorescent self-assembling motif **1** could be synthesised in a straightforward synthetic route as depicted in scheme 1. Diethyl 1,3-acetonedicarboxylate on reacting with guanidine carbonate gave ethyl isocytosine-6-acetate **4**,[7] which on condensation with 4-(dialkylamino) salicylaldehyde **5a**,**b** furnished the amine **6a**,**b**. Finally, the amine **6a**,**b** on reacting with different isocyanates under heating condition in pyridine resulted in the formation of self-assembling systems **1a-e** in good yields (Scheme 1).

Scheme 1. Synthesis of compounds 1[a]



[a]Reagents and conditions: (i) EtOH, reflux, 24 h; (ii) piperidine (cat), EtOH, reflux, 10 h; (iii) R_2NCO, pyridine, 100 °C, 10 h.

The duplex formation by **1a** and **1d** were investigated, as representative examples, by ^{1}H NMR experiments. In their ^{1}H NMR spectrum in $CDCl_3$, **1a** and **1d** showed two sets of signals. One set of major N-H signals at 14.24, 11.79, 9.95 ppm and 14.23, 11.90, 10.73 ppm were assigned to the pyrimidinone tautomers of **1a** and **1d**, respectively. A second set of minor signals at 13.54, 11.22, 9.81 ppm and 13.39, 11.41, 10.36 ppm were assigned to the pyrimidinol tautomers of **1a** and **1d**, respectively, with a relative abundance of ~ 20%. The relative amounts of the pyrimidinone and pyrimidinol tautomers were determined based on the relative integrating intensity of the benzylic proton signal of **1d**. The significant downfield shift of NHs of **1a** and **1d** were indicative of strong intermolecular hydrogen bonding interactions involving the urea NH protons. Furthermore, the far downfield shift of NH signals of **1a** and **1d** at 14.24 and 14.23 ppm, respectively, clearly suggested the strong involvement of intramolecular bifurcated H-bonding.

The dimerization of **1d** was investigated by ^{1}H NMR dilution experiments (Supporting Information, Figure S16). When a $CDCl_3$ solution of **1d** was diluted from 100 mM to 10 μM, no detectable changes were observed in the chemical shift values of all the NH protons. This showed that dimerization of **1d** persisted at a lower concentration in $CDCl_3$ with high K_{dim} value. Conservatively assuming more than 95% dimer formation at the lowest concentration studied (10 μM), the K_{dim} of compound **1d** was estimated to be at a lower limit of 1.9×10^7 M^{-1} in $CDCl_3$.

The dimerization of **1d** in various DMSO-d_6/$CDCl_3$ mixtures was studied in order to further support self-assembly by increasing the polarity of the solvent. The K_{dim} values of **1d**·**1d** was determined quantitatively in the range from 5% to 20% DMSO-d_6/$CDCl_3$ (v/v) mixtures by ^{1}H NMR dilution experiments. In 5% and 10% DMSO-d_6/$CDCl_3$ mixtures, we observed negligible chemical shift changes of urea protons. Therefore, K_{dim} values were estimated to be at a lower limit of 10^5 M^{-1} for **1d** under this condition. These findings proved that the duplexes are quite stable in mixture of solvents even though DMSO is a strongly competitive solvent for hydrogen bonded complexes. Nonlinear regression analysis[8] of the chemical shift gave the dimerization constant K_{dim} value of 7.4 M^{-1} for **1d** in 20% DMSO-d_6/$CDCl_3$ mixture.

The stability of molecular duplexes was further studied by variable temperature ^{1}H NMR studies (ranging from 223-323 K). Signals of NH2 (-0.60 ppb K^{-1} for **1a** and -0.23 ppb K^{-1} for **1d**) and NH3 (-2.40 ppb K^{-1} for **1a** and -2.35 ppb K^{-1} for **1d**) showed temperature coefficients suggestive of their strong involvement in intermolecular hydrogen bonds when compared to NH1 which is involved in intramolecular S(6)-type hydrogen bonds (-3.20 ppb K^{-1} for **1a** and -2.94 ppb K^{-1} for **1d**). These values also indicate the high stability of the molecular duplexes (Supporting Information, Figure S1 and S3).

The self-assembling systems **1** exhibited fluorescence due to the presence of the coumarin moiety on the backbone of the UPy self-assembling systems. Therefore, the duplex stability of **1d**·**1d** was also investigated, as a representative example, by fluorescence spectroscopic methods, in addition to NMR methods (*vide supra*). By using a fluorescence spectroscopic method, as reported previously by the Meijer group,[4b] the dimerization constant of **1d** was determined. Concentration-dependent changes in the intensities of **1d** at 497 nm appeared in the range of 10^{-10} M to 10^{-7} M in chloroform. Nonlinear regression analysis[8a] of the fluorescence data gave a dimerization constant K_{dim} value of (2.18 ± 1.81) x 10^{8} M^{-1} for **1d** (Supporting Information, Figure S20 and S21).

The duplex formation was further investigated *via* solution-state NMR and HRMS-ESI studies. Two-dimensional ^{15}N HSQC NMR studies in $CDCl_3$ confirmed that **1a** and **1d** exist in two tautomeric forms, **A** and **B** in solution. The major tautomer is pyrimidinone tautomer, **A** with **AADD**-type self-complementary H-bonding arrays whereas the minor tautomer is pyrimidinol tautomer, **B** having **DADA**-type self-complementary H-bonding arrays in solution (Figure 3). In addition, HRMS-ESI mass spectra showed molecular ion peaks (963.5451 for [**1a**·**1a** + H]$^+$, calcd 963.5444) and (1255.7642 for [**1d**·**1d** + H]$^+$, calcd 1255.7640), corresponding to the presence of the duplex (Supporting Information, page S6 and S18).

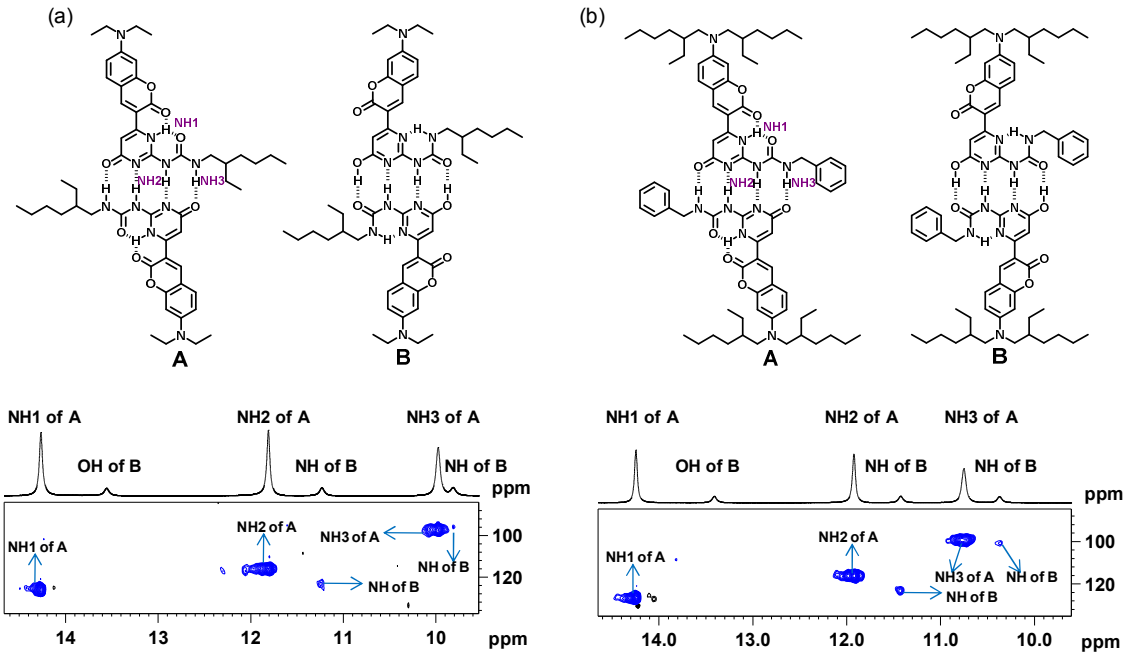


Figure 3. 2D ^{15}N HSQC spectra of **1a** (a) and **1d** (b) ($CDCl_3$, 500 MHz, 298 K).

After several trials of crystallization in a variety of solvents, slow evaporation from CH_2Cl_2 solvent resulted in the formation of crystals of **1a** as pyrimidinol dimers (Figure 4).[9] X-ray crystallography studies unambiguously revealed the formation of hydrogen bonded molecular duplex. From the X-ray structure, it is amply clear that the C-C bond connecting UPy and the coumarin ring is rotated, as a result, the homodimer is arranged in **DADA** sequence. The duplex is held together by four C(4)-type intermolecular hydrogen bonds between the self-complementary **DADA**-type linear hydrogen-bonding arrays, which is further stabilized by an intramolecular N-H•••N hydrogen bond (bond distance is 2.006 Å). The outer O-H•••O hydrogen bonds are slightly shorter than the inner N-H•••N bonds, as seen in Meijer's ureidopyrimidone.[4a] The hydrogen bond distances of O-H•••O is 1.747 Å and N-H•••N is 2.141 Å. The bond angles of O-H•••O is 162° and N-H•••N is 168°. Thus, there is 0.394 Å difference between the outer O-H•••O and the inner N-H•••N bonds.

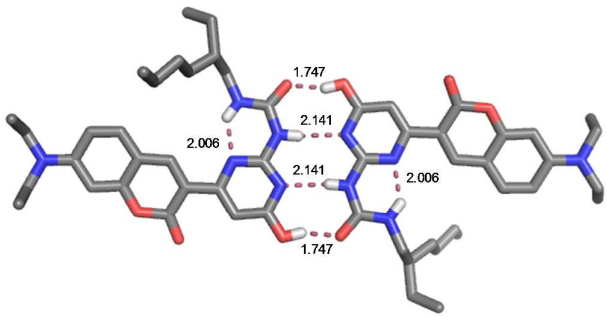


Figure. 4. Single-crystal X-ray structure of dimer **1a**.[9] Hydrogen bonding is highlighted in dashes (salmon colored), above which hydrogen bond distances (O-H•••O and N-H•••N) are displayed in Å. All hydrogens, other than those at the hydrogen-bonding sites, have been removed for clarity.

CONCLUSION

In summary, based on the results obtained from extensive NMR studies, we could unambiguously confirm that the modified coumarin-appended ureidopyrimidone-based self-complementary quadruple hydrogen-bonded systems show high K_{dim} value ($K_{dim} > 10^7$ M^{-1} in $CDCl_3$). Advantageously, using this strategy, we could also design a novel quadruple hydrogen bonding system tethered with a fluorophore, which could augment its application potential in supramolecular chemistry. We believe that this new structural motif having high stability may have potential applications in the field of supramolecular chemistry as well as in making OPV devices.

EXPERIMENTAL SECTION

General methods

Unless otherwise stated, all the chemicals and reagents were obtained commercially. Compound **4** was synthesized as per the reported procedure.[7] Dry solvents were prepared by the standard procedures. Analytical Thin Layer Chromatography was done on precoated silica gel plates (Kieselgel $60F_{254}$, Merck). Column chromatographic purifications were done with 100-200 mesh silica gel. NMR spectra were recorded in $CDCl_3$ on AV 200 MHz, AV

400 MHz, AV 500 MHz and AV 700 MHz Bruker NMR spectrometers. All chemical shifts are reported in δ ppm downfield to TMS and peak multiplicities are referred to as singlet (s), doublet (d), quartet (q), broad singlet (bs), and multiplet (m). The titration studies were done in $CDCl_3$. Elemental analyses were performed on an Elmentar-Vario-EL (Heraeus Company Ltd., Germany). IR spectra were recorded in $CHCl_3$ using Shimadzu FTIR-8400 spectrophotometer. Melting points were determined on a Buchi Melting Point B-540. HRMS measurements were carried out using ESI method and ion-trap mass analyzer.

2-Amino-6-(7-(diethylamino)-2-oxo-2H-chromen-3-yl)pyrimidin-4(1H)-one (6a)

To a solution containing 4-(diethylamino) salicylaldehyde (**5a**) (0.980 g, 5.076 mmol, 1 equiv.), compound **4** (1 g, 5.076 mmol, 1 equiv.), in 20 ml of absolute EtOH, piperidine (catalytic) amount was added and the reaction mixture was refluxed for 10 h. The reaction mixture was cooled to room temperature, and the resulting precipitate was filtered, washed thoroughly with chilled EtOH and dried under vacuum gave the desired compound **6a** (1.3 g, 77%) as a yellow solid. mp: > 295 ^{o}C; IR ($CHCl_3$) ν (cm^{-1}): 3344, 3154, 2977, 1709, 1671, 1583, 1462, 1261, 1134, 776; ^{1}H NMR (200 MHz, DMSO-d_6) δ: 10.75 (bs, 1H), 8.69 (s, 1H), 7.53-7.49 (d, J = 8.97 Hz, 1H), 6.75-6.74 (m, 1H), 6.69 (s, 1H), 6.55 (s, 1H), 6.48 (bs, 2H), 3.50-3.43 (m, 4H), 1.16-1.09 (t, J = 6.82 Hz, 6H); ^{13}C NMR (50 MHz, DMSO-d_6) δ: 163.4, 159.5, 157.2, 156.5, 154.6, 151.6, 143.7, 130.7, 114.0, 109.6, 107.7, 100.4, 95.8, 44.2, 12.3; HRMS (ESI) calculated $[M+H]^+$ for $C_{17}H_{19}O_3N_4$: 327.1447, found 327.1452.

1-(6-(7-(Diethylamino)-2-oxo-2H-chromen-3-yl)-4-oxo-1,4-dihydropyrimidin-2-yl)-3-(2-ethylhexyl)urea (1a)

To a solution of **6a** (0.2 g, 0.613 mmol, 1 equiv.) in dry pyridine (5 ml), 2-ethylhexyl isocyanate (0.214 ml, 1.226 mmol, 2 equiv.) was added and the reaction mixture was allowed to stir at 100 ^{o}C for 10 h. The resulting suspension was evaporated to dryness and column

chromatographic purification (eluent: 10% MeOH/ DCM, R_f: 0.4) of the residue yielded **1a** (0.191 g, 65%) as a yellow solid. mp: 244-246 ^oC; IR ($CHCl_3$) ν (cm^{-1}): 3747, 3208, 3082, 2921, 1722, 1664, 1593, 1450, 1389, 1258, 1151, 788; ^1H NMR (400 MHz, $CDCl_3$) δ: 14.24 (s, 1H) (major protomer, 80%), 13.54 (s, 1H) (minor protomer, 20%), 11.79 (s, 1H) (major protomer, 80%), 11.22 (s, 1H) (minor protomer, 20%), 9.95 (s, 1H) (major protomer, 80%), 9.81 (s, 1H) (minor protomer, 20%), 8.29 (s, 1H) (minor protomer, 20%), 8.00 (s, 1H) (major protomer, 80%), 7.38-7.36 (d, J = 9.05 Hz, 1H), 6.66-6.63 (dd, J = 9.05 Hz, J = 2.20 Hz, 1H), 6.49 (m, 1H), 6.43 (s, 1H), 3.49-3.44 (q, J = 7.09 Hz, 4H), 3.31-3.20 (m, 2H), 1.48-1.36 (m, 1H), 1.32 (m, 6H), 1.27-1.23 (m, 8H), 0.93-0.81 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.8, 159.9, 157.1, 156.1, 154.3, 152.6, 145.5, 143.1, 142.6, 130.6, 130.1, 109.9, 109.4, 108.2, 108.0, 103.0, 96.7, 45.1, 45.0, 43.4, 39.5, 38.9, 31.0, 30.7, 28.8, 28.7, 24.2, 23.9, 23.1, 22.9, 14.1, 14.0, 12.4, 10.8, 10.6; HRMS (ESI) calculated $[M+H]^+$ for $C_{26}H_{36}O_4N_5$: 482.2757, found 482.2762, 963.5451 $[2M+H]^+$.

1-Benzyl-3-(6-(7-(diethylamino)-2-oxo-2H-chromen-3-yl)-4-oxo-1,4-dihydropyrimidin-2-yl)urea (1b)

Following the same procedure for synthesis of compound **1a** and using benzyl isocyanate, **1b** was synthesized. Purification was effected by column chromatography (eluent: 10% MeOH/ DCM, R_f: 0.5) to yield **1b** (0.2 g, 71%) as a yellow fluffy solid. mp: 268-270 ^oC; IR ($CHCl_3$) ν (cm^{-1}): 3206, 3130, 2974, 1722, 1666, 1582, 1453, 1259, 854; ^1H NMR (400 MHz, DMSO-d_6) δ: 11.60 (s, 1H), 9.88 (s, 1H), 8.52 (s, 1H), 7.76 (s, 1H), 7.38-7.34 (m, 5H), 7.28- 7.25 (m, 1H), 6.97 (s, 1H), 6.73-6.70 (dd, J = 8.8 Hz, J = 1.22 Hz, 1H), 6.52 (s, 1H), 4.41-4.39 (d, J = 5.62 Hz, 2H), 3.45 (m, 4H), 1.14-1.11 (t, J = 6.85 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 159.4, 156.6, 154.8, 151.9, 144.0, 138.9, 130.9, 128.5, 127.2, 127.1, 112.8, 109.8, 107.7, 95.8, 44.3, 42.8, 12.3; HRMS (ESI) calculated $[M+H]^+$ for $C_{25}H_{26}O_4N_5$: 460.1974, found 460.1979, 919.3886 $[2M+H]^+$.

1-(6-(7-(Diethylamino)-2-oxo-2H-chromen-3-yl)-4-oxo-1,4-dihydropyrimidin-2-yl)-3-dodecylurea (1c)

Following the same procedure for synthesis of compound **1a** and using dodecyl isocyanate, **1c** was synthesized. Purification was effected by column chromatography (eluent: 10% MeOH/ DCM, R_f: 0.5) to yield **1c** (0.181 g, 55%) as a yellow solid. mp: 240-242 ^oC; IR ($CHCl_3$) ν (cm^{-1}): 3747, 3284, 3118, 2919, 2849, 1711, 1647, 1565, 1415, 1194, 775; ^1H NMR (400 MHz, $CDCl_3$) δ: 14.30 (s, 1H) (major protomer, 80%), 13.50 (s, 1H) (minor protomer, 20%), 11.72 (s, 1H) (major protomer, 80%), 11.29 (s, 1H) (minor protomer, 20%), 10.08 (s, 1H) (major protomer, 80%), 9.92 (s, 1H) (minor protomer, 20%), 8.31 (s, 1H) (minor protomer, 20%), 8.01 (s, 1H) (major protomer, 80%), 7.38-7.37 (m, 1H), 6.66-6.64 (m, 1H), 6.50 (s, 1H), 6.43 (s, 1H), 3.55-3.40 (m, 4H), 3.38-3.24 (m, 2H), 1.80- 1.64 (m, 2H), 1.25-1.10 (m, 24H), 0.87 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.0, 159.9, 157.2, 156.0, 154.3, 152.6, 145.6, 142.6, 130.6, 109.9, 108.3, 108.1, 102.9, 96.8, 45.1, 45.0, 40.1, 31.9, 29.6, 29.3, 27.0, 22.6, 14.1, 12.4; HRMS (ESI) calculated $[M+H]^+$ for $C_{30}H_{44}O_4N_5$: 538.3386, found 538.3388, 1075.6703 $[2M+H]^+$.

3-(Bis(2-ethylhexyl)amino)phenol (9)[10]

To a solution of 3-aminophenol (2 g, 18.326 mmol, 1 equiv.) in 20 ml of dry DMF, $NaHCO_3$ (6.15 g, 73.307 mmol, 4 equiv.) was added, followed by drop wise addition of 2-ethylhexylbromide (13.03 ml, 73.307 mmol, 4 equiv.) and the reaction mixture was heated at 100 °C for 12 h. The reaction mixture was cooled to room temperature, ethyl acetate and water were added. The combined ethyl acetate layer was washed sequentially with water and brine solution. The organic layer was then dried over Na_2SO_4, filtered and the solvent was stripped off under reduced pressure. Purification by column chromatography (eluent: 20% AcOEt/ pet. ether, R_f: 0.6) afforded **9** (3.41 g, 56%) as a liquid compound. IR ($CHCl_3$) ν (cm^-

[1]): 3341, 2956, 2925, 1738, 1617, 1577, 1242, 1169, 751; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.05-7.01 (t, *J* = 8.31 Hz, 1H), 6.27-6.25 (dd, *J* = 8.31 Hz, *J* = 1.96 Hz, 1H), 6.15 (s, 1H), 6.10-6.08 (dd, *J* = 7.82 Hz, *J* = 1.71 Hz, 1H), 4.64 (s, 1H), 3.25-3.11 (m, 4H), 1.81-1.79 (m, 2H), 1.40-1.26 (m, 16H), 0.92-0.86 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 156.4, 150.0, 129.7, 105.7, 102.0, 99.5, 56.3, 36.7, 30.6, 28.6, 23.9, 23.2, 14.0, 10.6; HRMS (ESI) calculated $[M+H]^+$ for $C_{22}H_{40}ON$: 334.3104, found 334.3104.

4-(Bis(2-ethylhexyl)amino)-2-hydroxybenzaldehyde (5b)[10]

Vilsmeier reagent was prepared by drop wise addition of phosphorous oxychloride (0.307 ml, 3.303 mmol, 1.1 equiv.) to anhydrous DMF (0.92 ml, 12.012 mmol, 4 equiv.) at 0 °C, and the mixture was stirred for 5 min at the same temperature and then for 30 min at room temperature. Compound **9** (1 g, 3.003 mmol, 1 equiv.) in 2 ml of DMF was added to the Vilsmeier reagent drop wise and the mixture was heated at 70 °C for 6 h. Then the mixture was cooled, poured into ice water and basicified with NaOH until pH 6 was reached. The product was extracted with diethyl ether and the organic layer was washed sequentially with water and brine solution. Ether layer was then dried over Na_2SO_4, filtered and the solvent was stripped off under reduced pressure. Purification by column chromatography (eluent: 10% AcOEt/ pet. ether, R_f: 0.5) afforded **5b** (0.791 g, 73%) as a liquid compound. IR ($CHCl_3$) *v* (cm^{-1}): 2957, 2926, 2744, 1727, 1629, 1558, 1459, 1225, 1133, 784; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 11.61(s, 1H), 9.49 (s, 1H), 7.26-7.24 (d, *J* = 8.80 Hz, 1H), 6.29-6.26 (dd, *J* = 8.80 Hz, *J* = 2.20 Hz, 1H), 6.08-6.07 (d, *J* = 2.20 Hz, 1H), 3.35-3.22 (m, 4H), 1.84-1.81 (m, 2H), 1.36-1.27 (m, 16H), 0.92-0.88 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.8, 164.0, 154.8, 134.9, 111.3, 105.3, 97.8, 56.3, 37.1, 30.5, 28.5, 23.8, 23.0, 14.0, 10.6; HRMS (ESI) calculated $[M+H]^+$ for $C_{23}H_{40}O_2N$: 362.3052, found 362.3054.

2-amino-6-(7-(bis(2-ethylhexyl)amino)-2-oxo-2H-chromen-3-yl)pyrimidin-4(1H)-one (6b)

Following the same procedure for synthesis of compound **6a** and using 4-[bis(2-ethylhexyl)amino]-2-hydroxybenzaldehyde (**5b**), **6b** was synthesized. Purification was effected by column chromatography (eluent: 10% MeOH/ DCM, R_f: 0.4) to yield **6b** (0.971 g, 71%) as a yellow solid. mp: 198-200 ^oC; IR ($CHCl_3$) ν (cm^{-1}): 3308, 2955, 2921, 1722, 1650, 1572, 1453, 1215, 893; ^1H NMR (400 MHz, $CDCl_3$) δ: 12.47 (s, 1H), 8.70 (s, 1H), 7.39-7.37 (d, J = 9.16 Hz, 1H), 7.11 (s, 1H), 6.62-6.60 (d, J = 8.55 Hz, 1H), 6.47 (s, 1H), 6.19 (s, 2H), 3.36-3.25 (m, 4H), 1.83 (m, 2H), 1.33-1.28 (m, 16H), 0.91-0.88 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.8, 156.8, 154.7, 152.7, 144.2, 130.3, 110.5, 108.6, 100.9, 97.6, 56.5, 37.0, 30.4, 28.5, 23.7, 23.1, 14.0, 10.6; HRMS (ESI) calculated $[M+H]^+$ for $C_{29}H_{43}O_3N_4$: 495.3331, found 495.3330.

1-Benzyl-3-(6-(7-(bis(2-ethylhexyl)amino)-2-oxo-2H-chromen-3-yl)-4-oxo-1,4-dihydropyrimidin-2-yl)urea (1d)

Following the same procedure for synthesis of compound **1a** and using amine **6b** and benzyl isocyanate, **1d** was synthesized. Purification was effected by column chromatography (eluent: 10% MeOH/ DCM, R_f: 0.5) to yield **1d** (0.198 g, 78%) as a fluffy yellow solid. mp: 146-148 ^oC; IR ($CHCl_3$) ν (cm^{-1}): 3746, 3218, 3131, 2957, 1727, 1666, 1586, 1453, 1235, 741; ^1H NMR (700 MHz, $CDCl_3$) δ: 14.23 (s, 1H) (major protomer, 80%), 13.39 (s, 1H) (minor protomer, 20%), 11.90 (s, 1H) (major protomer, 80%), 11.41 (s, 1H) (minor protomer, 20%), 10.73 (s, 1H) (major protomer, 80%), 10.36 (s, 1H) (minor protomer, 20%), 7.99 (s, 1H), 7.43-7.42 (d, J = 7.74 Hz, 2H), 7.36-7.35 (d, J = 9.03 Hz, 1H), 7.32-7.30 (t, J = 7.74 Hz, 2H), 7.23-7.21 (t, J = 7.31 Hz, 1H), 6.67-6.65 (dd, J = 9.03 Hz, J = 1.94 Hz, 1H), 6.49 (s, 1H), 6.41 (s, 1H), 4.70 (bs, 2H) (minor protomer, 20%), 4.55-4.54 (d, J = 5.81 Hz, 2H) (major

protomer, 80%), 3.39-3.29 (m, 4H), 1.83-1.82 (m, 2H), 1.39-1.28 (m, 16H), 0.93-0.90 (m, 12H); ^{13}C NMR (175 MHz, $CDCl_3$) δ: 172.9, 160.0, 159.9, 156.9, 156.7, 156.1, 154.2, 153.2, 152.5, 145.6, 142.6, 139.1, 138.5, 130.3, 128.7, 128.3, 127.7, 127.6, 127.3, 126.8, 114.3, 110.9, 110.1, 108.1, 108.0, 103.1, 97.8, 97.5, 56.5, 56.4, 44.0, 43.3, 37.0, 36.9, 30.4, 28.5, 23.8, 23.0, 14.0, 13.9, 10.6; HRMS (ESI) calculated $[M+H]^+$ for $C_{37}H_{50}O_4N_5$: 628.3855, found 628.3857, 1255.7642 $[2M+H]^+$.

1-(6-(7-(Bis(2-ethylhexyl)amino)-2-oxo-2H-chromen-3-yl)-4-oxo-1,4-dihydropyrimidin-2-yl)-3-(2-ethylhexyl)urea (1e)

Following the same procedure for synthesis of compound **1a** and using amine **6b** and 2-ethylhexyl isocyanate, **1e** was synthesized. Purification was effected by column chromatography (eluent: 10% MeOH/ DCM, R_f: 0.5) to yield **1e** (0.202 g, 77%) as a fluffy yellow compound. mp: 66-68 ^{o}C; IR ($CHCl_3$) ν (cm^{-1}): 3747, 3131, 3109, 2955, 1723, 1696, 1502, 1270, 1177, 665; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 14.25 (s, 1H) (major protomer, 80%), 13.54 (s, 1H) (minor protomer, 20%), 11.82 (s, 1H) (major protomer, 80%), 11.26 (s, 1H) (minor protomer, 20%), 9.93 (s, 1H) (major protomer, 80%), 9.83 (s, 1H) (minor protomer, 20%), 8.29 (s, 1H) (minor protomer, 20%), 8.01 (s, 1H) (major protomer, 80%), 7.37-7.35 (m, 1H), 6.66-6.64 (d, J = 7.93 Hz, 1H), 6.50 (s, 1H), 6.45 (s, 1H), 3.40-3.29 (m, 4H), 3.27-3.26 (m, 2H), 1.83 (m, 2H), 1.65 (m, 1H), 1.47-1.29 (m, 24H), 0.93-0.89 (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.8, 159.9, 156.9, 156.1, 154.3, 153.2, 145.5, 142.6, 130.2, 110.8, 108.5, 108.1, 103.1, 97.8, 56.5, 43.4, 39.0, 37.0, 30.7, 30.5, 28.7, 28.5, 24.0, 23.8, 23.0, 14.1, 14.0, 10.6; HRMS (ESI) calculated $[M+H]^+$ for $C_{38}H_{60}O_4N_5$: 650.4626, found 650.4640, 1299.9207 $[2M+H]^+$.

ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for all new compounds, studies on the self-assembly of **1a** and **1d** and single-crystal X-ray data of **1a**. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

* gj.sanjayan@ncl.res.in

Notes

The authors declare no competing financial interest.

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