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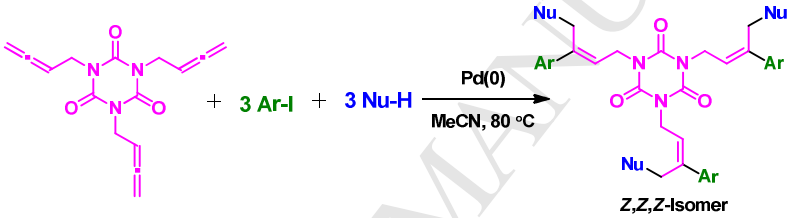

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ABSTRACT

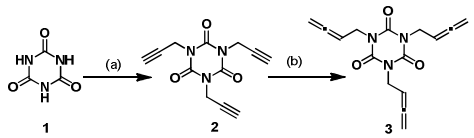
We report the spatially controlled, protecting group free, catalytic assembly of a library of nineteen 7-component cascade products generated from a novel planar trisallenyl 1,3,5-triazinane-2,4,6-trione core in combination with aryl iodides and amines with excellent regio and good stereoselectivity for *Z,Z,Z*-isomers.

1. Introduction

A wide variety of central core compounds that promote attachment, assembly and spatial distribution of multiple attendant molecules have been developed which generate moderate to large superstructures with tuneable properties or multiple recognition sites. The initial core compound may be planar and/or non-planar and possess intrinsic recognition sites.[1a-g] Typical examples for the former are the long known planar benzene-1,3,5-tricarboxamides and porphyrins.[1c] More recently dendrimers[1d] and adamantanes have attracted considerable attention. The latter can display a fixed orthogonal spatial disposition of four reactive arms and we recently used this to achieve 3- and 9-component Pd(0) catalysed cascade assembly of allenes, aryl iodides and *N*-nucleophiles with concomitant installation of one to four trisubstituted *Z*-alkene functionalities.[2a] Aditionally we have engineered novel tridirectional exploration of biochemical space built from 5-component cascades of heterocyclic bisallenes.[2b]

2. Results and discussion

The success of these latter cascades, which are protecting ~~group free~~, prompted us to develop the synthesis and application of the hitherto unknown, trisallene **3** via Scheme 1. The intermediate trisalkyne **2** crystallised as colourless plates from 1:1 v/v $CHCl_3$/MeOH and displayed the expected planar central core (Fig 1). The trisallene **3**, which to our knowledge has not been reported before, was prepared from **2** by a modified Crabbe reaction[3a-c] and obtained as a pale yellow viscous oil.



(a) propargyl bromide, K_2CO_3, DMF, 50 °C, 16 h (58%)
(b) dicyclohexyl amine, CuI, $(CH_2O)_n$, dioxane, reflux 3 h (60%).

Scheme 1. Synthesis of 1,3,5-tri(buta-2,3-dien-1-yl)1,3,5-triazinane-2,4,6-trione **3**.

Related cores have been reported previously[4a,b] but their participation in protecting group free multicomponent catalytic cascade processes is unexplored although the road is signposted by the elegant and extensive studies referred to in references[1a-g,2] spanning nanotechnology, polymer processing and biomedical applications. For example compounds which deliver multiple

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targets often exhibit superior efficacy against complex diseases.[1e-g] A recent review by Weerapana et al summarized the importance and versatility of the related 1,3,5-triazine scaffolds as a source of diverse molecular libraries.[5]

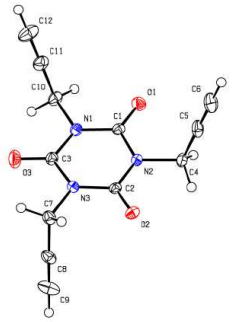


Figure 1. X-ray crystal structure of trisalkyne **2**.

A series of aryl iodides and primary and secondary amines was selected for evaluation of the trisallene **3** (Chart 1). In comparison with our 9-component adamantyl cascade where the cascade process involves populating four distinctly different non-competitive areas of space[2] the planar nature of the trisallene is potentially more significantly compromised by buttressing effects (Scheme 2). The conditions, catalyst, solvent and temperature employed are noted in Scheme 2.

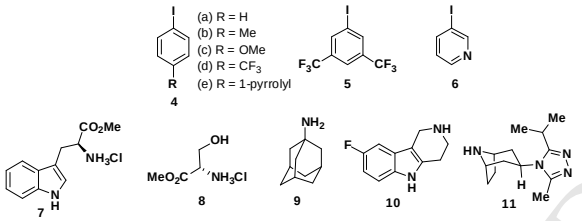
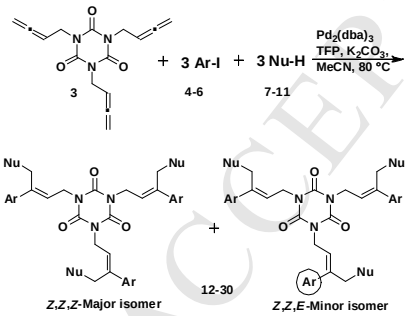


Chart 1. Aryl iodides and amines used in 7-component cascades.



Scheme 2. Seven component cascades. TFP = tri(2-furylphosphine)

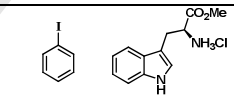
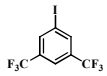
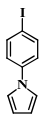
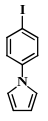
Initially, we investigated the cascades with the pharmaceutically important α-amino acid esters (*S*)-tryptophan **7** and (*S*)-serine **8**. The former reacted with iodobenzene in acetonitrile at 80 °C over 6 h in the presence of $Pd_2(dba)_3$ (7.5 mol%) and TFP (30 mol%) to give the *Z,Z,Z*-cascade product **12** in 74% yield (Table 1, entry 1). Repeating the reaction with reduced amount of $Pd_2(dba)_3$ (2.5 mol%) and TFP (10 mol%) over 18 h gave an improved yield of **12** (82%). The significant reduction in the amount of $Pd_2(dba)_3$ and TFP prompted us to use the slower process for the amino acid ester cascades of **7** and **8** (Table 1, entries 1-6). In all cases only trace amounts of the corresponding *Z,Z,E*-isomer were detected. Additionally, the presence of iodides with *para*- or *meta*- electron withdrawing groups was not deleterious and the aliphatic hydroxyl group of **8** (Table 1, entry 6) was not competitive.

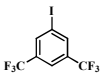
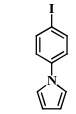
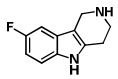
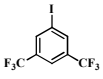
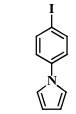
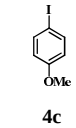
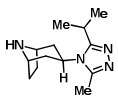
Next, we evaluated an analogous cascade series involving 1-aminoadamantane **9** which continues to attract multiple applications in drug discovery.[6a-g] In this case, we employed the higher loading faster reacting catalyst combination of $Pd_2(dba)_3$ (7.5 mol%) and TFP (30 mol%) at 80 °C. Reaction times ranged from 1.5 to 2.5 h and product yields ranged from 57-91% whilst isomer ratios were typically 87:13 of *Z,Z,Z*- versus *Z,Z,E*- (Table 1, entries 7-13). In the case of entry 11, involving the 4-trifluoromethyliodobenzene, the selectivity was lower although the yield of the mixed isomers was high.

A third series (Table 1, entries 14-18) employing 8-fluoro-2,3,4,4a,5,9b-hexahydro-1*H*-pyrido[4,3-*b*]indole **10** as nucleophile produced products with *Z,Z,Z*- to *Z,Z,E*- ratios of 87-13 apart from entry 18 which was lower.

The final cascade (Table 1, entry 19) employed the sterically demanding bridged ring 3-(3-isopropyl-5-methyl-4*H*-1,2,4-triazol-4-yl)-8-azabicyclo[3.2.1]-octane **11** together with high loading catalyst combination at 80 °C. As expected, this was the least selective cascade generating a 62:38 mixture of *Z,Z,Z*- and *Z,Z,E*-isomers.

Table 1. Seven component cascade selectivity.

Entry	Ar-I	Nu-H	Time (h)	Product	*Z,Z,Z*: *Z,Z,E*[a]	Yield (%)[b]
1	 **4a**	**7**	6	**12**	>99:1	74[c]
			18			82[d]
2	 **4c**	**7**	24	**13**	>99:1	73[d]
3	 **4d**	**7**	19	**14**	>99:1	79[d]
4	 **5**	**7**	19	**15**	>99:1	79[d]
5	 **4e**	**7**	21	**16**	>99:1	60[d]
6	 **4e**	**8**	20	**17**	>99:1	60[d]

7	 **4c**	 **9**	2	**18**	87:13	72[c]
8	 **4a**	**9**	2	**19**	87:13	63[c]
9	 **5**	**9**	2.5	**20**	87:13	57[c]
10	 **4b**	**9**	2	**21**	87:13	72[c]
11	 **4d**	**9**	1.5	**22**	76:24	91[c]
12	 **6**	**9**	2	**23**	87:13	66[c]
13	 **4e**	**9**	2	**24**	n.d[e]	85[c]
14	 **4a**	 **10**	2	**25**	87:13	82[c]
15	 **5**	**10**	2.5	**26**	87:13	64[c]
16	 **4e**	**10**	2	**27**	87:13	73[c]
17	 **6**	**10**	2	**28**	86:14	70[c]
18	 **4c**	**10**	2	**29**	79:21[f]	78[c]
19	 **6**	 **11**	3	**30**	62:38	69[c]

[a]Isomeric ratio was determined by ^{1}H-NMR of the crude material.
[b]Isolated yield after column chromatography.
[c]Allene (1 equiv), aryl iodide (3.6 equiv), nucleophile (3.6 equiv), $Pd_2(dba)_3$ (7.5 mol%), TFP (30 mol%), K_2CO_3 (9 equiv), MeCN (5 mL/ mmol) at 80 °C.
[d]$Pd_2(dba)_3$ (2.5 mol%), TFP (10 mol%) and K_2CO_3 (6 equiv) was used.
[e]Isomeric ratio was determined after column chromatography (One single isomer).
[f]Isomeric ratio was determined after column chromatography.

3. Conclusion

In conclusion, we have demonstrated that the hitherto unknown planar 1,3,5-tri(buta-2,3-dien-1-yl)-1,3,5-triazinane-2,4,6-trione **3** participates in seven component palladium catalyzed stereoselective cascade reactions with a combination of aryl/heteroaryl iodides and primary and secondary amines, including α-amino acid esters. The latter are highly selective for Z,Z,Z-isomers. Thus, the novel planar 1,3,5-triazinane-2,4,6-trione provides a compact planar core particularly suitable for cascades employing amino acid ester nucleophiles.

4. Experimental section

The crystallographic data for the trisalkyne **2** has been deposited with the Cambridge Crystallographic Data Center as CCDC 996268. Thin layer chromatography (TLC) was carried out on aluminium plates pre-coated with silica gel 60 F254 (Merck), and were visualised using ultraviolet light and/or aqueous $KMnO_4/I_2$. Flash column chromatography employed silica gel 60 (Merck, 230-400 mesh). Melting points were determined on a Reichert hot-stage microscope and are uncorrected. Microanalyses were performed on a Carlo Erba 1108 elemental analyser and optical rotations were measured on a Polartronic H 532 (Schmidt + Haensch) instrument. Infrared spectra were recorded on a Perkin-Elmer Spectrum FT-IR spectrometer either as thin films on sodium chloride discs or as solids using a golden gate apparatus. The former were created by dissolving the compound in $CHCl_3$ and transfering the solution to a sodium chloride disc and allowing the solvent to evaporate. Proton nuclear magnetic resonance spectra were recorded on 500 MHz Avance and 300 MHz DPX300 Bruker instruments. Chemical shifts (δ) are reported in parts per million relative to tetramethylsilane (δ = 0.00) and coupling constants are given in hertz (Hz). The following abbreviations are used: s = singlet, br = broad, d = doublet, dd = doublet of doublets, ddd = doublet of double doublets, dt = doublet of triplets, m = multiplet, t = triplet, td = triplet of doublets. ^{13}C-NMR spectra were recorded at 125 MHz Avance and 75 MHz DPX300 Bruker instruments and chemical shifts are reported in parts per million (ppm). ^{1}H-NMR peak assignments are mainly based on DEPT135, COSY, HMQC and HMBC spectral data. Accurate masses were obtained using a Bruker Daltonics micrOTOF spectrometer. The m/z data mentioned in the case of 7-component cascade products are the result of two runs: one using the auto sampler technique and the other by injecting the sample directly into the machine using a syringe pump. All compounds are named according to the IUPAC system using the ACD/ILAB (ACD/IUPAC v.12.0 programme) web service (http:/www.acdlabs.com). Microwave reactions employed the CEM Discovery Explorer SP. Cyanuric acid (Aldrich, 98%), propargyl bromide (Alfa aesar, 80% wt/wt in toluene) and acetonitrile (VWR, BDH) are commercially available and were used as received.

*4.1. 1,3,5-Tri(prop-2-yn-1-yl)-1,3,5-triazinane-2,4,6-trione (**2**).*

Cyanuric acid **1** (5.0 g, 38.76 mmol) and K_2CO_3 (20.86 g, 151.16 mmol) were added to a mixture of DMF (90 mL), and propargyl bromide (15.5 mL, 139.50 mmol) at room temperature

and the mixture was heated and stirred at 50 °C for 24 h. The solution was then cooled, filtered and the filtrate evaporated. The resultant residue was dissolved in $CHCl_3$ (200 mL) and washed with 10% NH_4Cl solution (3 × 100 mL) and finally with water (100 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the filtrate evaporated under vacuum. The resulted solid was crystallised from 1:1 v/v MeOH/$CHCl_3$ to give the pure trisalkyne 2 (4.5 g, 48%) as colourless plates, mp 164-166 °C; δ_H (300 MHz, $CDCl_3$); 4.70 (6H, d, *J* 2.4, 3 × CH_2), 2.31 (3H, t, *J* 2.4, 3 × CH); δ_C (500 MHz, $CDCl_3$); 147.3, 76.7, 72.7, 32.6; δ_C (75 MHz, $CDCl_3$); 147.2, 76.6, 72.4, 32.5; Anal. Calcd for $C_{12}H_9N_3O_3$: C, 59.26; H, 3.73; N, 17.28. Found: C, 59.30; H, 3.60; N, 17.40; υ_{max}/cm^{-1} (film); 3277, 3011, 2128, 1693, 1461, 1414, 1356, 1310; *m/z* (ESI^+) 266.1 (100%, MNa^+); (Found MNa^+, 266.0540. $C_{12}H_9N_3NaO_3$ requires 266.0536).

*4.2. 1,3,5-Tri(buta-2,3-dien-1-yl)-1,3,5-triazinane-2,4,6-trione (**3**).*

A mixture of trisalkyne **2** (1.0 g, 4.2 mmol), paraformaldehyde (0.92 g, 30.7 mmol), dicyclohexylamine (4.4 mL, 22.1 mmol) and CuI (1.17 g, 6.15 mmol) in dry dioxane (6 mL) was refluxed for 3 h then cooled, filtered and the filtrate evaporated under vacuum. The residue was dissolved in EtOAc (100 mL) and the organic layer washed with 10% ammonium hydroxide solution (2 × 60 mL), water (60 mL) and 3 M HCl (2 × 30 mL) (during extraction some yellow precipitate of dicyclohexylamine hydrochloride was formed between two phase). The water layer was extracted again with EtOAc (2 × 30 mL). All the organic layers combined, filtered to remove yellow precipitate and the precipitate washed two times with EtOAc (2 × 10 mL). The organic layer was dried over anhydrous $MgSO_4$ and the residue was purified by flash column chromatography eluting with 90:10 v/v hexane/EtOAc to give the pure trisallene **3** (0.68, 59%) as a pale yellow viscous oil; δ_H (300 MHz, $CDCl_3$); 5.26 (3H, m, 3 × CH), 4.85 (6H, dt, *J* 2.9 and 6.4, 3 × CH_2), 4.50 (6H, dt, *J* 2.9 and 6.4, 3 × CH_2); δ_C (75 MHz, $CDCl_3$); 208.9, 148.3, 85.5, 77.6, 41.1; υ_{max}/cm^{-1} (film); 3384, 3066, 2991, 2959, 1957, 1685, 1458, 1361, 1317; Anal. Calcd for $C_{15}H_{15}N_3O_3$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.20; H, 5.40; N, 14.60; *m/z* (ESI^+) 308.1 (100%, MNa^+); (Found MNa^+, 308.1003. $C_{15}H_{15}N_3NaO_3$ requires 308.1006).

4.3. General Procedure A: Pd catalysed 7-component cascades.

A mixture of trisallene **3** (0.25 mmol), aryl/heteroaryl iodides (0.90 mmol), nucleophiles (0.90 mmol), $Pd_2(dba)_3$ (7.5 mol%), TFP (tri-(2-furyl)phosphine) (30 mol%), and K_2CO_3 (2.25 mmol) in MeCN (5 mL) was stirred and heated at 80 °C (oil bath temperature) until the starting material was completely consumed as monitored by tlc (see Table 1). The mixture was cooled and solvent removed under vacuo. The residue was dissolved in $CHCl_3$ (25 mL) and extracted with H_2O (20 mL) three times. The organic layer was dried over anhydrous $MgSO_4$ and evaporated under rotatory evaporator to give the crude product which purified by flash chromatography.

4.4. General Procedure B: Pd catalysed 7-component cascades.

A mixture of trisallene **3** (0.25 mmol), aryl/hetereoaryl iodides (0.90 mmol), nucleophiles (0.90 mmol), $Pd_2(dba)_3$ (2.5 mol%), TFP (tri-(2-furyl)phosphine) (10 mol%), and K_2CO_3 (1.5 mmol) in MeCN (5 mL) was stirred and heated at 80 °C (oil bath temperature) until the starting material was completely consumed as monitored by tlc (see Table 1). The mixture was worked up as mentioned in general procedure A.

*4.5. Trimethyl (2S,2'S,2''S)-2,2',2''-[(2,4,6-trioxo-1,3,5-triazinane-1,3,5-triyl)tris{[(2Z)-2-phenylbut-2-ene-4,1-diyl]imino}]tris[3-(1H-indol-3-yl)propanoate] (**12**).*

Prepared by general procedure B from trisallene **3** in CH_3CN and heating for 18 h. Flash chromatography eluting with EtOAc gave Z,Z,Z-product **12** (82%) as a pale yellow froth; $[\alpha]_D^{27}$ + 23.0 (c, 10 mg/1 mL $CHCl_3$); mp 87-88 °C; δ_H (300 MHz, $CDCl_3$); 8.25 (3H, br s, 3 × indolyl-NH), 7.52 (3H, d, *J* 7.6, 3 × indolyl-H), 7.28-7.31 (6H, m, 3 × phenyl-H), 7.23-7.25 (3H, m, 3 × indolyl-H), 7.17-7.21 (9H, m, 3 × phenyl-H), 7.07 (3H, t, *J* 7.0, 3 × indolyl-H), 7.04 (3H, t, *J* 7.0, 3 × indolyl-H), 6.85 (3H, d, *J* 2.1 3 × indolyl-H), 5.70 (3H, t, *J* 6.6, 3 × NCH_2CH=), 4.60-4.45 (6H, m, 3 × NCH_2CH=), 3.84 (3H, d, *J* 12.6, 3 × =CCH_2N), 3.59-3.71 (3H, m, 3 × $CHCO_2Me$), 3.66 (9H, s, 3 × CO_2Me), 3.61 (3H, d, *J* 13.1, 3 × =CCH_2N), 3.18 (3H, dd, *J* 5.4 and 14.2, 3 × CH_ACHCO_2Me), 3.03 (3H, dd, *J* 8.2 and 14.2, 3 × CH_BCHCO_2Me), 1.86 (3H, br, 3 × NH); δ_C (75 MHz, $CDCl_3$); 175.1, 148.5, 141.6, 140.6, 136.1, 128.3, 127.5, 127.2, 126.2, 124.1, 123.2, 121.8, 119.2, 118.6, 111.1, 110.8, 61.4, 51.8, 46.8, 41.2, 29.2; υ_{max}/cm^{-1} (film); 3407, 3015, 2951, 1751, 1690, 1456, 1357, 1216, 1011; *m/z* (ESI^+) 1190.5 (100% MNa^+), (Found MNa^+, 1190.5132 $C_{69}H_{69}N_9NaO_9$ requires 1190.5110). NOE data ($CDCl_3$) for **12**:

	% Enhancement					
Irradiated proton	1-H	2-H	4-H	phenyl-H	Indolyl-CH_2	Indolyl-H
1-H		2.51	2.84	-	-	-
2-H	1.88		-	7.36 (δ 7.3)	-	-
4-H	-	-		1.12 (δ 7.2)	1.01 (δ 3.0-3.2)	0.42 (δ 6.8), 0.89 (δ 7.5)

*4.6. Trimethyl (2S,2'S,2''S)-2,2',2''-[(2,4,6-trioxo-1,3,5-triazinane-1,3,5-triyl)tris{[(2Z)-2-(4-methoxyphenyl)but-2-ene-4,1-diyl]imino}]tris[3-(1H-indol-3-yl)propanoate] (**13**).*

Prepared by general procedure B from trisallene **3** in CH_3CN and heating for 24 h. Flash chromatography eluting with EtOAc gave Z,Z,Z-isomer **13** (73%) as a pale yellow froth; $[\alpha]_D^{27}$ + 96.0 (c, 10 mg/1 mL $CHCl_3$); mp 95-96 °C; δ_H (500 MHz, $CDCl_3$); 8.29 (3H, br s, indolyl-NH), 7.50-7.52 (3H, m, 3 × indolyl-H), 7.20-7.22 (3H, m, 3 × indolyl-H), 7.21 (6H, d, *J* 8.7, 3 × phenyl-H), 7.10 (3H, t, *J* 7.3, 3 × indolyl-H), 7.04 (3H, t, *J* 7.3, 3 × indolyl-H), 6.87 (3H, br s, 3 × indolyl-H), 6.69 (6H, d, *J* 8.7, 3 × phenyl-H), 5.64 (3H, t, *J* 6.6, 3 × NCH_2CH=), 5.62-4.52 (6H, m, 3 × NCH_2CH=), 3.80 (3H, d, *J* 12.8, 3 × =CCH_2N), 3.76 (9H, s, 3 × OMe), 3.64-3.74 (3H, m, 3 × $CHCO_2Me$), 3.66 (9H, s, 3 × CO_2Me), 3.60 (3H, d, *J* 12.8, 3 × =CCH_2N), 3.17 (3H, dd, *J* 5.4 and 14.5, 3 × CH_ACHCO_2Me), 3.03 (3H, dd, *J* 7.7 and 14.5, 3 × CH_BCHCO_2Me), 1.91 (3H, br, 3 × NH); δ_C (75 MHz, $CDCl_3$); 175.1, 159.0, 148.5, 140.8, 136.1, 132.7, 127.3, 123.3, 121.7, 119.2, 118.6, 113.6, 111.1, 110.6, 109.8, 61.4, 55.2, 51.9, 46.6, 41.2, 29.1; υ_{max}/cm^{-1} (film); 3404, 2951, 1731, 1689, 1511, 1457, 1248, 1217; *m/z* (ESI^+) 1258.5 (32%, MH^+), (Found MH^+, 1258.5611. $C_{72}H_{76}N_9O_{12}$ requires 1258.5608).

*4.7. Trimethyl (2*S*,2'*S*,2''*S*)-2,2',2''-[(2,4,6-trioxo-1,3,5-triazinane-1,3,5-triyl)tris({(2*Z*)-2-[4-(trifluoromethyl)phenyl]but-2-ene-4,1-diyl}imino)]tris[3-(1*H*-indol-3-yl)propanoate] (**14**).*

Prepared by general procedure B from trisallene **3** in CH_3CN and heating for 19 h. Flash chromatography eluting with 95:5 v/v $CHCl_3$/MeOH gave Z,Z,Z-product **14** (79%) as a pale yellow froth; $[\alpha]_D^{27}$ + 7.5 (c, 10 mg/1 mL $CHCl_3$); mp 86-87 °C; δ_H (500 MHz, $CDCl_3$); 8.26 (3H, br, 3 × indolyl-NH), 7.51 (3H, d, *J* 7.8, 3 × indolyl-H), 7.33 (6H, d, *J* 8.2, 3 × phenyl-H), 7.29 (6H, d, *J* 8.2, 3 × phenyl-H), 7.22 (3H, d, *J* 6.8, 3 × indolyl-H), 7.12 (3H, t, *J* 7.3, 3 × indolyl-H), 7.04 (3H, t, *J* 7.3, 3 × indolyl-H), 6.81 (3H, br s, 3 × indolyl-H), 5.71 (3H, t, *J* 6.8, 3 × NCH_2CH=), 4.52-4.6 (6H, m, 3 × NCH_2CH=), 3.83 (3H, d, *J* 12.8, 3 × =CCH_2N), 3.70-3.63 (3H, m, 3 × $CHCO_2Me$), 3.68 (9H, s, 3 × CO_2Me), 3.58 (3H, d, *J* 13.2, 3 × =CCH_2N), 3.18 (3H, dd, *J* 5.0 and 14.6, 3 × CH_ACHCO_2Me), 2.99 (3H, dd, *J* 8.2 and 14.6, 3 × CH_BCHCO_2Me), 1.87 (3H, br, 3 × NH); δ_C (125 MHz, $CDCl_3$); 175.1, 148.4, 144.0 (br s), 140.0, 136.2, 129.5 (*J* 31.1), 127.7, 126.5 (br s), 125. 7, 125.1 (*J* 10.9), 124.1 (*J* 271.2), 123.1, 121.9, 119.3, 118.6, 111.3 (br s), 110.8, 61.3, 51.9, 46.6, 41.1, 29.2; υ_{max}/cm^{-1} (film); 3405, 2952, 1732, 1692, 1456, 1325, 1215, 1165, 1119, 1068; *m/z* (ESI^+) 1394.4 (100%, MNa^+), (Found MNa^+, 1394.4668. $C_{72}H_{66}F_9N_9NaO_9$ requires 1394.4737).

*4.8. Trimethyl (2*S*,2'*S*,2''*S*)-2,2',2''-[(2,4,6-trioxo-1,3,5-triazinane-1,3,5-triyl)tris({(2*Z*)-2-[3,5-bis(trifluoromethyl)phenyl]but-2-ene-4,1-diyl}imino)]tris[3-(1*H*-indol-3-yl)propanoate] (**15**).*

Prepared by general procedure B from trisallene **3** in CH_3CN and heating for 19 h. Flash chromatography eluting with 9:1 v/v $CHCl_3$/MeOH gave Z,Z,Z-product **15** (79%) as a pale yellow froth; $[\alpha]_D^{27}$ + 8.0 (c, 10 mg/1 mL $CHCl_3$); mp 90-91 °C; δ_H (300 MHz, $CDCl_3$); 8.21 (3H, br s, 3 × indolyl-NH), 7.86 (6H, br s, 3 × phenyl-H), 7.70 (3H, br s, 3 × phenyl-H), 7.49 (3H, d, *J* 7.6, 3 × indolyl-H), 7.23 (3H, br s, 3 × indolyl-H), 7.10 (3H, dt, *J* 1.0 and 8.2, 3 × indolyl-H), 7.02 (3H, t, *J* 7.6, 3 × indolyl-H), 6.93 (3H, d, *J* 2.1, 3 × indolyl-H), 5.79 (3H, t, *J* 6.6, 3 × NCH_2CH=), 4.60 (6H, d, *J* 6.6 3 × NCH_2CH=), 3.84 (3H, d, *J* 12.6, 3 × =CCH_2N), 3.62-3.73 (3H, m, 3 × $CHCO_2Me$), 3.7 (9H, s, 3 × CO_2CH_3), 3.57 (3H, d, *J* 12.6, 3 × =CCH_2N), 3.19 (3H, dd, *J* 4.9 and 14.2, 3 × CH_ACHCO_2Me), 3.04 (3H, dd, *J* 7.6 and 14.2, 3 × CH_BCHCO_2Me), 1.86 (3H, br s, 3 × NH); δ_C (125 MHz, $CDCl_3$); 175.1, 148.4, 142.8, 139.5, 136.0, 131.4 (*J* 33.1), 128.7, 127.2, 126.4 (*J* 2.2), 123.3 (*J* 273), 121.4 (*J* 3.3), 122.9, 121.9, 119.3, 118.4, 111.1, 110.9, 61.5, 51.9, 46.7, 41.1, 29.2; υ_{max}/cm^{-1} (film); 3408, 3016, 2953, 1731, 1693, 1457, 1381, 1279, 1179, 1133; *m/z* (ESI^+) 1598.4 (100% MNa^+), (Found MNa^+ 1598.4330 $C_{75}H_{63}F_{18}N_9NaO_9$ requires 1598.4354).

*4.9. Trimethyl (2*S*,2'*S*,2''*S*)-2,2',2''-[(2,4,6-trioxo-1,3,5-triazinane-1,3,5-triyl)tris({(2*Z*)-2-[4-(1*H*-pyrrol-1-yl)phenyl]but-2-ene-4,1-diyl}imino)]tris[3-(1*H*-indol-3-yl)propanoate] (**16**).*

Prepared by general procedure B from trisallene **3** in CH_3CN and heating for 21 h. Flash chromatography eluting with EtOAc gave Z,Z,Z-product **16** (60%) as a pale yellow froth; $[\alpha]_D^{27}$ – 10.0 (c, 10 mg/1 mL $CHCl_3$); mp 100-101 °C; δ_H (300 MHz, $CDCl_3$); 8.27 (3H, br, 3 × indolyl-NH), 7.53 (3H, d, *J* 7.6, 3 × indolyl-H), 7.26 (6H, d, *J* 8.5, 3 × phenyl-H), 7.12-7.23 (9H, m, 3 × indolyl-H), 7.10 (6H, d, *J* 8.5, 3 × phenyl-H), 7.03 (6H, t, *J* 2.1, 3 × pyrol-H), 6.84 (3H, d, *J* 2.1, 3 × indolyl-H), 6.34 (6H, t, *J* 2.1, 3 × pyrol-H), 5.71 (3H, t, *J* 6.8, 3 × NCH_2CH=), 4.63-4.56 (6H, m, 3 × NCH_2CH=), 3.84 (3H, d, *J* 13.1, 3 × =CCH_2N), 3.80 (3H, d, *J* 13.1, 3 × =CCH_2N), 3.67 (3H, m, 3 × $CHCO_2Me$), 3.69 (9H, br s, 3 × CO_2Me), 3.20 (3H, dd, *J* 4.3 and 14.2, 3 × CH_ACHCO_2Me), 3.01 (3H, dd, *J* 8.2 and 14.2, 3 × CH_BCHCO_2Me), 1.89 (3H, br s, 3 × NH); δ_C (75 MHz, $CDCl_3$); 175.1, 148.5, 140.7, 139.7, 137.4, 136.2, 127.3, 123.7, 123.3, 121.9, 119.7, 119.3, 119.0, 118.6, 111.2, 110.7, 110.5, 61.3, 51.9, 46.5, 41.2, 29.2; υ_{max}/cm^{-1} (film); 3403, 2950, 1731, 1689, 1521, 1456, 1330, 1215, 1070; *m/z* (ESI^+) 1385.5 (100%, MNa^+); (Found MNa^+, 1385.5909. $C_{81}H_{78}N_{12}NaO_9$ requires 1385.5907).

*4.10. Trimethyl (2*S*,2'*S*,2''*S*)-2,2',2''-[(2,4,6-trioxo-1,3,5-triazinane-1,3,5-triyl)tris({(2*Z*)-2-[4-(1*H*-pyrrol-1-yl)phenyl]but-2-ene-4,1-diyl}imino)]tris(3-hydroxypropanoate) (**17**).*

Prepared by general procedure B from trisallene **3** in CH_3CN and heating for 20 h. Flash chromatography eluting with EtOAc then 1:1 v/v EtOAc:MeOH gave Z,Z,Z-isomer **17** (60%) as a pale yellow froth; $[\alpha]_D^{27}$ + 75.0 (c, 10 mg/1 mL $CHCl_3$); mp 89-91 °C; δ_H (500 MHz, $CDCl_3$); 7.50 (6H, d, *J* 8.5, phenyl-H), 7.34 (6H, d, *J* 8.5, phenyl-H), 7.07 (6H, br s, pyrol-H), 6.33 (6H, br s, pyrol-H), 5.89 (3H, t, *J* 7.0, 3 × NCH_2CH=), 4.88-4.77 (6H, m, 3 × NCH_2CH=), 3.93 (3H, d, *J* 11.8, =CCH_2N), 3.81 (3H, dd, *J* 4.1 and 11.4, $CHCO_2Me$), 3.74 (3H, d, *J* 11.8, =CCH_2N), 3.71 (9H, s, CO_2Me), 3.60 (3H, dd, *J* 6.4 and 10.5, CH_AOH), 3.43-3.45 (3H, m, CH_BOH), 2.0 (3H, br, 3 x NH); δ_C (75 MHz, $CDCl_3$); 173.2, 148.8, 141.2, 140.1, 137.7, 127.6, 123.6, 120.1, 119.1, 110.6, 62.9, 62.7, 52.1, 46.5, 41.4; υ_{max}/cm^{-1} (film); 3324, 2952, 1735, 1687, 1522, 1458, 1330, 1200, 1069; *m/z* (ESI^+) 1088.4 (100%, MNa^+), (Found MNa^+, 1088.4501. $C_{57}H_{63}N_9NaO_{12}$ requires 1088.4488).NOE data ($CDCl_3$) for **17**:

	% Enhancement			
Irradiated proton	1-H	2-H	4-H	phenyl-H
1-H	-	2.55	0.77	-
2-H	1.08	-	-	5.82 (δ 7.5)

*4.11. 1,3,5-Tris[(2Z)-3-(4-methoxyphenyl)-4-(tricyclo[3.3.1.1^{3,7}]dec-1-ylamino)but-2-en-1-yl]-1,3,5-triazinane-2,4,6-trione (**18**).*

Prepared by general procedure A from trisallene **3** in CH_3CN and heating for 2 h. Flash chromatography eluting with EtOAc then 19:1 v/v EtOAc/MeOH gave Z,Z,Z-isomer **18** (72%) as a pale yellow froth; mp 103-105 °C; δ_H (500 MHz, $CDCl_3$); 7.42 (6H, d, *J* 8.7, 3 × phenyl-H), 6.83 (6H, d, *J* 8.7, 3 × phenyl-H), 5.74 (3H, t, *J* 7.1, 3 × NCH_2CH=), 4.72 (6H, d, *J* 7.1, 3 × NCH_2CH=), 3.79 (9H, s, 3 × OCH_3), 3.75 (6H, s, 3 × =CCH_2N), 2.07 (9H, br s, 9 × adamantyl-CH), 1.70 (18H, br s, 9 × adamantyl-CH_2), 1.65 (18H, br q, *J* 11.9, 9 × adamantyl-CH_2), 1.23 (3H, br s, 3 × NH), δ_C (75 MHz, $CDCl_3$); 159.1, 148.8, 142.7, 133.4, 127.5, 121.0, 113.7, 55.2, 50.8, 42.5, 41.5, 39.1, 36.8, 29.6; υ_{max}/cm^{-1} (film); 2904, 2847, 1688, 1607, 1510, 1455, 1309, 1246, 1179; *m/z* (ESI^+) 1057.6 (100%, MH^+); (Found MH^+, 1057.6495. $C_{66}H_{85}N_6O_6$ requires 1057.6525). NOE data ($CDCl_3$) for **18**:

	% Enhancement				
Irradiated proton	1-H	2-H	4-H	phenyl-H	adamantyl-CH_2
1-H		2.22	2.15	-	-
2-H	1.87		-	7.90 (δ 7.4)	-
4-H	2.25	-		4.38 (δ 7.4)	5.41 (δ 1.7)

*4.12. 1,3,5-Tris[(2Z)-3-phenyl-4-(tricyclo[3.3.1.1^{3,7}]dec-1-ylamino)but-2-en-1-yl]-1,3,5-triazinane-2,4,6-trione (**19**).*

Prepared by general procedure A from trisallene **3** in CH_3CN and heating for 2 h. Flash chromatography eluting with EtOAc

then 7:3 v/v EtOAc/MeOH gave Z,Z,Z-product **19** (63%) as a colourless froth, mp 108-110 °C; δ_H (500 MHz, $CDCl_3$); 7.48 (6H, d, *J* 7.8, 3 × phenyl-H), 7.22-7.30 (9H, m, 3 × phenyl-H), 5.80 (3H, t, *J* 7.1, 3 × NCH_2CH=), 4.74 (6H, d, *J* 7.1, 3 × NCH_2CH=), 3.77 (6H, s, 3 × =CCH_2N), 2.07 (9H, br s, 9 × adamantyl-CH), 1.71 (18H, br s, 9 × adamantyl-CH_2), 1.64 (18H, br q, *J* 11.4, 9 × adamantyl-CH_2), 1.26 (3H, br s, 3 × NH), δ_C (125 MHz, $CDCl_3$); 148.7, 143.4, 141.1, 128.3, 127.5, 126.4, 122.7, 50.8, 42.6, 41.5, 39.3, 36.8, 29.6; υ_{max}/cm^{-1} (film); 3428, 2904, 2847, 1688, 1567, 1455, 1309, 1215, 1097; *m/z* (ESI^+) 967.6 (18%, MH^+); (Found MH^+, 967.6190. $C_{63}H_{79}N_6O_3$ requires 967.6208); 484.3 (100%, $[M+2H]^{2+}$, (Found $[M+2H]^{2+}$, 484.3158 $C_{63}H_{80}N_6O_3$ requires 484.3140); 323.2 (26%, $[M+3H]^{3+}$, (Found $[M+3H]^{3+}$, 323.2118 $C_{63}H_{81}N_6O_3$ requires 323.2128). NOE data ($CDCl_3$) for **19**:

	% Enhancement				
Irradiated proton	1-H	2-H	4-H	phenyl-H	adamantyl-CH_2
1-H		4.08	3.06	-	-
2-H	2.59		-	9.75 (δ 7.4)	-
4-H	3.18	-		5.95 (δ 7.4)	7.02 (δ 1.6)

*4.13. 1,3,5-Tris[(2Z)-3-[3,5-bis(trifluoromethyl)phenyl]-4-(tricyclo[3.3.1.1^{3,7}]dec-1-ylamino)but-2-en-1-yl]-1,3,5-triazinane-2,4,6-trione (**20**).*

Prepared by general procedure A from trisallene **3** in CH_3CN and heating for 2.5 h. Flash chromatography eluting with $CHCl_3$ then 9:1 v/v $CHCl_3$/MeOH gave the product **20** as a 87:13 mixture of *Z,Z,Z*- and *Z,Z,E*-isomers (57%) as a colourless froth. Major Z,Z,Z isomer δ_H (500 MHz, $CDCl_3$); 8.0 (6H, br s, 3 × phenyl-H), 7.70 (3H, br s, 3 × phenyl-H), 5.85 (3H, t, *J* 6.8, 3 × NCH_2CH=), 4.75 (6H, d, *J* 6.8, 3 × NCH_2CH=), 3.7 (6H, s, 3 × =CCH_2N), 2.0 (9H, br s, 3 × adamantyl-CH), 1.5-1.8 (36H, m, 3 × adamantyl-CH_2), 1.26 (3H, br s, 3 × NH).; δ_C (125 MHz, $CDCl_3$); 148.6, 143.5, 141.3, 131.3 (*J* 34), 126.6 (br s), 123.4 (*J* 271), 121.2 (*J* 3.6), 50.9, 42.7, 41.4, 39.5, 36.7, 29.6; υ_{max}/cm^{-1} (film); 2909, 2850, 1693, 1456, 1383, 1310, 1278, 1179, 1235; *m/z* (ESI^+) 1375.5 (72%, MH^+); (Found MH^+, 1375.5472. $C_{69}H_{73}F_{18}N_6O_3$ requires 1375.5451).

*4.14. 1,3,5-Tris[(2Z)-3-(4-methylphenyl)-4-(tricyclo[3.3.1.1^{3,7}]dec-1-ylamino)but-2-en-1-yl]-1,3,5-triazinane-2,4,6-trione (**21**).*

Prepared by general procedure A from trisallene **3** in CH_3CN and heating for 2 h. Flash chromatography eluting with EtOAc gave **21** as a single *Z,Z,Z*-isomer (72%) as a colourless froth. mp 97-99 °C; δ_H (500 MHz, $CDCl_3$); 7.35 (6H, d, *J* 7.8, 3 × phenyl-H), 7.10 (6H, d, *J* 7.8, 3 × phenyl-H), 5.79 (3H, t, *J* 7.1, 3 × NCH_2CH=), 4.73 (6H, d, *J* 7.1, 3 × NCH_2CH=), 3.81 (6H, s, 3 × =CCH_2N), 2.32 (9H, s, 3 × Me) 2.08 (9H, br s, 9 × adamantyl-CH), 1.64 (18H, br q, *J* 12.3, 9 × adamantyl-CH_2), 1.25 (3H, br s, 3 × NH); δ_C (125 MHz, $CDCl_3$); 148.8, 143.2, 138.1, 137.2, 129.0, 126.3, 121.9, 110.8, 50.8, 42.6, 41.5, 39.2, 36.8, 29.7, 21.1; υ_{max}/cm^{-1} (film); 2904, 2847, 1687, 1454, 1309, 1096; *m/z* (ESI^+) 1009.6 (100%, MH^+); (Found MH^+, 1009.6728. $C_{66}H_{85}N_6O_3$ requires 1009.6678). NOE data ($CDCl_3$) for **21**:

	% Enhancement				
Irradiated proton	1-H	2-H	4-H	phenyl-H	adamantyl-CH_2
1-H		2.54	2.06	-	-
2-H	1.64		-	7.95 (δ 7.3)	-
4-H	2.44	-		5.14 (δ 7.3)	5.79 (δ 1.6)

*4.15. 1,3,5-Tris{(2Z)-4-(tricyclo[3.3.1.1^{3,7}]dec-1-ylamino)-3-[4-(trifluoromethyl)phenyl]but-2-en-1-yl}-1,3,5-triazinane-2,4,6-trione (**22**).*

Prepared by general procedure A from trisallene **3** in CH_3CN and heating for 1.5 h. Flash chromatography eluting with 98:2 v/v $CHCl_3$/MeOH gave the product **22** as a 71:29 mixture of *Z,Z,Z*- and *Z,Z,E*-isomers (91%) as a colourless froth. Major *Z,Z,Z*-isomer: δ_H (500 MHz, $CDCl_3$); 7.61 (6H, d, *J* 8.2, 3 × phenyl-H), 7.54 (6H, d, *J* 8.2, 3 × phenyl-H), 5.85 (3H, t, *J* 7.1, 3 × NCH_2CH=), 4.77 (6H, d, *J* 7.1, 3 × NCH_2CH=), 3.75 (6H, s, 3 × =CCH_2N), 2.08 (9H, br s, 9 × adamantyl-CH), 1.70 (18H, br s, 9 × adamantyl-CH_2), 1.57-1.68 (18H, m, 9 × adamantyl-CH_2), 1.3 (3H, br s, 3 × NH), δ_C (75 MHz, $CDCl_3$); 148.8, 144.8 (br s), 142.5, 129.5 (*J* 33), 129.0 (*J* 272), 126.6 (br s), 124.3, 111.1 (*J* 9.9), 50.9, 42.5, 41.4, 39.3, 36.7, 29.6; υ_{max}/cm^{-1} (film); 2905, 2848, 1690, 1457, 1325, 1164, 1124, 1068; *m/z* (ESI^+) 1170.5 (39%, MH^+); (Found MH^+, 1171.5813. $C_{66}H_{76}F_9N_6O_3$ requires 1171.5835).

*4.16. 1,3,5-Tris[(2Z)-4-(adamantan-1-ylamino)-3-(pyridin-3-yl)but-2-en-1-yl]-1,3,5-triazinane-2,4,6-trione (**23**).*

Prepared by general procedure A from trisallene **3** in CH_3CN and heating for 2 h. Flash chromatography eluting with EtOAc then 10:3 v/v EtOAc/MeOH gave the product **23** (66%) as a single Z,Z,Z-isomer which crystallized from $CHCl_3$ as a colourless fine needles, mp 111-113 °C; δ_H (300 MHz, $CDCl_3$); 8.75 (3H, d, *J* 1.9, 3 × pyridyl-H), 8.49 (3H, dd, *J* 1.9 and 4.8, 3 × pyridyl-H), 7.85 (3H, td, *J* 1.9, 8.1, 3 × pyridyl-H), 7.22 (3H, dd, *J* 4.8 and 8.1, 3 × pyridinyl-H), 5.85 (3H, t, *J* 7.2, 3 × NCH_2CH=), 4.78 (6H, d, *J* 7.2, 3 × NCH_2CH=), 3.76 (6H, s, 3 × =CCH_2N), 2.08 (9H, br s, 9 × adamantyl-CH), 1.71 (18H, br d, *J* 1.9, 9 × adamantyl-CH_2), 1.65 (18H, br q, *J* 10.5, 9 × adamantyl-CH_2); δ_C (75 MHz, $CDCl_3$); 148.7, 148.69, 147.7, 140.8, 136.8, 133.7, 123.9, 123.1, 50.9, 42.6, 41.4, 39.3, 36.8, 29.6; υ_{max}/cm^{-1} (film); 3318, 2905, 2848, 1693, 1567, 1455, 1357, 1310, 1215; *m/z* (ESI^+) 970.6 (33%, MH^+); (Found MH^+, 970.6069. $C_{60}H_{76}N_9O_3$ requires 970.6066).

*4.17. 1,3,5-Tris[(2Z)-3-[4-(1H-pyrrol-1-yl)phenyl]-4-(tricyclo[3.3.1.1^{3,7}]dec-1-ylamino)but-2-en-1-yl]-1,3,5-triazinane-2,4,6-trione (**24**).*

Prepared by general procedure A from trisallene **3** in CH_3CN and heating for 2 h. Flash chromatography eluting with $CHCl_3$ then 9:1 v/v $CHCl_3$/MeOH gave the product **24** as a single Z,Z,Z-isomer (85%) as a pale yellow froth. mp 134-137 °C.; δ_H (500 MHz, $CDCl_3$); 7.56 (6H, d, *J* 8.7, 3 × phenyl-H), 7.32 (6H, d, *J* 8.7, 3 × phenyl-H), 7.07 (6H, t, d, *J* 2.2, 3 × pyrol-H), 6.33 (6H, t, *J* 2.2, 3 × pyrol-H), 5.84 (3H, t, *J* 6.8, 3 × NCH_2CH=), 4.77 (6H, d, *J* 6.8, 3 × NCH_2CH=), 3.77 (6H, s, 3 × =CCH_2N), 2.09 (9H, br s, 9 × adamantyl-CH), 1.73 (18H, br s, 9 × adamantyl-CH_2), 1.66 (18H, br q, *J* 11.4, 9 × adamantyl-CH_2), 1.26 (3H, br s, 3 × NH); δ_C (125 MHz, $CDCl_3$); 148.8, 142.5, 140.0, 138.4, 127.5, 122.4, 120.1, 119.1, 110.5, 50.9, 42.6, 41.5, 39.3, 36.8, 29.7; υ_{max}/cm^{-1} (film); 2904, 2848, 1689, 1608, 1520, 1455, 1330, 1215, 1069; *m/z* (ESI^+) 1162.6 (100%, MH^+); (Found MH^+, 1162.6960. $C_{75}H_{88}N_9O_3$ requires 1162.7005).

*4.18. 1,3,5-Tris[(2Z)-4-(8-fluoro-1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indol-2-yl)-3-phenylbut-2-en-1-yl]-1,3,5-triazinane-2,4,6-trione (**25**).*

Prepared by general procedure A from trisallene **3** in CH_3CN and heating for 2 h. Flash chromatography eluting with $CHCl_3$

then 9:1 v/v $CHCl_3$/MeOH gave the product **25** as a 87:13 mixture of Z,Z,Z- and Z,Z,E-isomers (82%) as a colourless froth. Major Z,Z,Z-isomer: δ_H (500 MHz, $CDCl_3$); 7.72 (3H, br s, 3 × pyridoindolyl-NH), 7.43 (6H, td, *J* 1.6 and 7.6, 3 × phenyl-H), 7.25-7.17 (9H, m, 3 × phenyl-*H*), 7.05 (3H, dd *J*, 4.3 and 8.7, 3 × pyridoindolyl-H), 7.0 (3H, dd *J*, 2.1 and 9.3, 3 × pyridoindolyl-H), 6.78 (3H, dt, *J* 2.1 and 11.5, 3 × pyridoindolyl-H), 5.89 (3H, t, *J* 6.6, 3 × NCH_2CH=), 4.75 (6H, d, *J* 6.6, 3 × NCH_2CH=), 3.75 (6H, br s, 3 × =CCH_2N), 3.64 (6H, br s, 3 × pyridoindolyl-CH_2), 2.79 (6H, br s, 3 × pyridoindolyl-CH_2), 2.58 (6H, br s, 3 × pyridoindolyl-CH_2); δ_C (125 MHz, $CDCl_3$); 156.7 (*J* 237.7), 148.9, 141.9, 134.3, 132.3, 128.2, 127.4, 126.6 (*J* 9.1), 125.9, 111.6 (*J* 9.1), 109.1 (*J* 23.4), 108.8 (*J* 3.66), 102.7 (*J* 23.4), 56.2, 49.6, 49.3, 41.5, 23.6; υ_{max}/cm^{-1} (film); 3415, 2918, 1686, 1595, 1458, 1365, 1323, 1232, 1181, 1147, 1085; *m/z* (ESI^+) 1084.4 (100%, MH^+); (Found MH^+, 1084.4811. $C_{66}H_{61}F_3N_9O_3$ requires 1084.4844).

*4.19. 1,3,5-Tris[(2Z)-3-[3,5-bis(trifluoromethyl)phenyl]-4-(8-fluoro-1,3,4,5-tetrahydro-2*H*-pyrido[4,3-*b*]indol-2-yl)but-2-en-1-yl]-1,3,5-triazinane-2,4,6-trione (**26**).*

Prepared by general procedure A from trisallene **3** in CH_3CN and heating for 2.5 h. Flash chromatography eluting with 19:1 then 9:1 v/v $CHCl_3$/MeOH gave the product **26** as a 87:13 mixture of Z,Z,Z- and Z,Z,E-isomers (64%) as a colourless froth. Major Z,Z,Z-isomer: δ_H (300 MHz, $CDCl_3$); 7.92 (6H, br s, 3 × pyridoindolyl-NH and 3 × phenyl-H), 7.75 (6H, d, *J* 13.1, phenyl-H), 7.11 (3H, dd, *J* 4.3 and 8.7, 3 × pyridoindolyl-H), 7.02 (3H, dd, *J* 2.1 and 9.3, 3 × pyridoindolyl-H), 6.80 (6H, dt, *J* 2.1 and 11.5, 3 × pyridoindolyl-H), 6.0 (3H, t, *J* 6.4, 3 × NCH_2CH=), 4.84 (6H, d, *J* 6.4, 3 × NCH_2CH=), 3.80 (6H, br s, 3 × =CCH_2N), 3.70 (6H, br s, 3 × pyridoindolyl-CH_2), 2.92 (6H, br s, 3 × pyridoindolyl-CH_2), 2.74 (6H, br s, 3 × pyridoindolyl-CH_2); δ_C (75 MHz, $CDCl_3$); 157.7 (*J* 233.3), 148.7, 143.4, 138.9, 134.0, 132.3, 131.8 (*J* 33.1), 128.4, 126.8 (*J* 3.3), 126.3 (*J* 9.9), 123.3 (*J* 273.1), 121.2 (*J* 3.3), 111.0 (*J* 9.9), 109.1 (*J* 26.5), 108.7 (*J* 4.4), 102.7 (*J* 24.3), 55.7, 49.9, 48.8, 41.4, 23.5; υ_{max}/cm^{-1} (film); 3468, 3413, 3022, 2927, 2837, 1695, 1597, 1456, 1382, 1278, 1181, 1134; *m/z* (ESI^+) 1492.4 (100%, MH^+); (Found MH^+, 1492.4094. $C_{72}H_{55}F_{21}N_9O_3$ requires 1492.4087).

*4.20. 1,3,5-Tris{(2Z)-4-(8-fluoro-1,3,4,5-tetrahydro-2*H*-pyrido[4,3-*b*]indol-2-yl)-3-[4-(1*H*-pyrrol-1-yl)phenyl]but-2-en-1-yl}-1,3,5-triazinane-2,4,6-trione (**27**).*

Prepared by general procedure A from trisallene **3** in CH_3CN and heating for 2 h. Flash chromatography eluting with $CHCl_3$ then 9:1 v/v $CHCl_3$/MeOH gave the product **27** as a 87:13 mixture of Z,Z,Z-and Z,Z,E-isomers (73%) as a pale yellow froth. Major Z,Z,Z isomer: δ_H (500 MHz, $CDCl_3$); 7.73 (3H, br s, 3 × pyridoindolyl-NH), 7.50 (6H, d, *J* 8.2, 3 × phenyl-H), 7.24 (6H, d, *J* 8.2, 3 × phenyl-H), 7.09 (3H, dd, *J* 4.1 and 8.7, 3 × pyridoindolyl-H), 7.04 (6H, t, *J* 1.8, pyrol-H and 3 × pyridoindolyl-H), 6.82 (3H, dt, *J* 2.2 and 11.6, 3 × pyridoindolyl-H), 6.32 (6H, t, *J* 1.8, pyrol-H), 5.94 (3H, t, *J* 6.4, 3 × NCH_2CH=), 4.79 (6H, d, *J* 6.4, 3 × NCH_2CH=), 3.78 (6H, br s, 3 × =CCH_2N), 3.69 (6H, br s, pyridoindolyl-CH_2), 2.84 (6H, br s, pyridoindolyl-CH_2), 2.66 (6H, br s, pyridoindolyl-CH_2); δ_C (75 MHz, $CDCl_3$); 157.7 (*J* 233.3), 148.7, 140.2, 139.8, 138.8, 134.2, 132.3, 127.7, 126.3 (*J* 9.9), 125.5, 119.9, 119.1, 111.6, 111.3 (*J* 9.9), 110.4, 108.8 (*J* 4.4), 102.7 (*J* 24.3), 55.9, 49.6, 49.2, 41.5, 23.6. υ_{max}/cm^{-1} (film); 3395, 1691, 1520, 1455, 1328, 1183, 1070; *m/z* (ESI^+) 1279.5 (100%, MH^+); (Found MH^+, 1279.5662. $C_{78}H_{70}F_3N_{12}O_6$ requires 1279.5640).

*4.21. 1,3,5-Tris[(2Z)-4-(8-fluoro-1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indol-2-yl)-3-(pyridin-3-yl)but-2-en-1-yl]-1,3,5-triazinane-2,4,6-trione (**28**).*

Prepared by general procedure A from trisallene **3** in CH_3CN and heating for 2 h. Flash chromatography eluting with EtOAc then 5:1 v/v EtOAc/MeOH gave the product **28** as a 86:14 mixture of Z,Z,Z-and Z,Z,E-isomers (70%) as a colourless froth. Major Z,Z,Z isomer: δ_H (300 MHz, DMSO); 10.86 (3H, s, 3 × NH), 8.71 (3H, d, *J* 1.4, 3 × pyridyl-H), 8.41 (3H, dd, *J* 1.4 and 4.8, 3 × pyridyl-H), 7.89 (3H, td, *J* 1.4 and 8.1, 3 × pyridyl-H), 7.30 (3H, dd, *J* 4.8 and 8.1, 3 × pyridyl-H), 7.21 (3H, dd, *J* 4.5 and 9.1, 3 × pyridoindolyl-H), 7.07 (3H, dd, *J* 2.5 and 10.0, 3 × pyridoindolyl-H), 6.79 (3H, dt, *J* 2.5 and 9.1, 3 × pyridoindolyl-H), 6.07 (4H, t, *J* 5.7, 3 × NCH_2CH=), 4.77 (6H, d, *J* 5.7, 3 × NCH_2CH=), 3.76 (6H, br s, 3 × =CCH_2N), 3.63 (6H, br s, 3 × pyridoindolyl 1-CH_2), 2.84 (6H, br s, 3 × pyridoindolyl-CH_2), 2.68 (6H, br s, 3 × pyridoindolyl-CH_2); δ_C (75 MHz, DMSO); 156.6 (*J* 231.6), 149.0, 148.1, 147.5, 136.5, 136.0, 134.9, 133.7, 132.4, 128.1, 125.7 (*J* 9.9), 123.1, 111.4 (*J* 9.9), 107.8 (*J* 24.2), 107.5 (*J* 4.4), 101.9 (*J* 24.2), 54.9, 49.5, 48.9, 40.8, 23.5; υ_{max}/cm^{-1} (solid); 3183, 2923, 2385, 1688, 1634, 1588, 1455, 1369, 1324, 1286, 1234; *m/z* (ESI^+) 1087.5 (52%, MH^+); (Found MH^+, 1087.4675. $C_{63}H_{58}F_3N_{12}O_3$ requires 1087.4701). NOE data (DMSO) for **28**:

	% Enhancement				
Irradiated proton	1-H	2-H	4-H	Pyridyl-H	pyridoindolyl-CH_2
1-H		-10.6	-5.8	-	-
2-H	-11.2		-	-3.0 (δ 8.71) -1.9 (δ 7.89)	-
4-H	-4.7	-		-	-4.2 (δ 3.63), 4.8 (δ 2.84), 3.1 (δ 2.68)

*4.22. 1,3,5-Tris[(2Z)-4-(8-fluoro-1,3,4,5-tetrahydro-2*H*-pyrido[4,3-*b*]indol-2-yl)-3-(4-methoxyphenyl)but-2-en-1-yl]-1,3,5-triazinane-2,4,6-trione (**29**).*

Prepared by general procedure A from trisallene **3** in CH_3CN and heating for 2 h. Flash chromatography eluting with EtOAc gave the product **29** as a 79:21 mixture of Z,Z,Z- and Z,Z,E-isomers (78%) as a colourless froth. Major Z,Z,Z-isomer: δ_H (500 MHz, $CDCl_3$); 7.75 (3H, br s, 3 × pyridoindolyl-NH), 7.39 (6H, d, *J* 8.7, 3 × phenyl-H), 7.09 (3H, dd, *J* 4.1 and 8.4, 3 × pyridoindolyl-H), 7.01 (3H, d, *J* 9.1, 3 × pyridoindolyl-H), 6.78 (6H, d, *J* 8.7, 3 × phenyl-H), 6.78 (3H, m, 3 × pyridoindolyl-H), 5.85 (3H, t, *J* 6.6, 3 × NCH_2CH=), 4.74 (6H, d, *J* 6.6, 3 × NCH_2CH=), 3.74 (15H, br s, 3 × =CCH_2N and OCH_3), 3.66 (6H, br s, 3 × pyridoindolyl-CH_2), 2.82 (6H, br s, 3 × pyridoindolyl-CH_2), 2.64 (6H, br s, 3 × pyridoindolyl-CH_2); δ_C (125 MHz, $CDCl_3$); 159.0, 157.6 (J 232.3), 148.8, 140.4, 134.3, 132.3, 127.7, 126.4 (*J* 9.1), 113.6 (*J* 9.1), 110.9 (*J* 23.8), 108.9 (*J* 3.6), 102.6 (*J* 23.8), 56.1, 55.2, 49.5, 49.3, 41.5, 23.7; υ_{max}/cm^{-1} (film); 3405, 2932, 2836, 1690, 1606, 1511, 1458, 1323, 1247, 1181, 1147, 1084, 1035; *m/z* (ESI^+) 1174.5 (100%, MH^+); (Found MH^+, 1174.5184. $C_{69}H_{67}F_3N_9O_6$. requires 1174.5161). NOE data ($CDCl_3$) for **29**:

	% Enhancement			
Irradiated proton	1-H	2-H	4-H	phenyl-H
1-H	-	-4.67	-	-
2-H	-3.33	-	-	-1.80 (δ 6.78), -1.57 (δ 7.39)
4-H	-1.89	-0.75	-	-2.58 (δ 6.78)

*4.23. 1,3,5-Tris[(2Z)-4-[3-(3-isopropyl-5-methyl-4H-1,2,4-triazol-4-yl)-8-azabicyclo[3.2.1]oct-8-yl]-3-(pyridin-3-yl)but-2-en-1-yl]-1,3,5-triazinane-2,4,6-trione (**30**).*

Prepared by general procedure A from **3** in CH_3CN and heating for 3 h. Flash chromatography eluting with 10:7 v/v EtOAc/MeOH and then 1:1 v/v EtOAc/MeOH gave **30** as a 62:38 mixture of Z,Z,Z and Z,Z,E-isomers (69%) as a colourless froth; Major Z,Z,Z isomer: δ_H (300 MHz, $CDCl_3$); 8.86 (3H, d, *J* 2.4, 3 × pyridyl-H), 8.51 (3H, dd, *J* 1.4 and 4.8, 3 × pyridyl-H), 7.78 (3H, td, *J* 1.4 and 9.5, 3 × pyridyl-H), 7.26 (3H, dd, *J* 4.8 and 9.5, 3 × pyridyl-H), 5.91 (3H, t, *J* 6.7, 3 × NCH_2CH=), 4.82 (6H, d, *J* 6.7, 3 × NCH_2CH=), 4.28-4.15 (3H, m, 3 × azabicyclooctyl-H), 3.64 (6H, s, 3 × =CCH_2N), 3.36 (6H, br s, 6 × azabicyclooctyl-H), 2.94-2.84 (3H, m, 3 × triazolyl 3-$CH(CH_3)_2$), 2.34 (9H, s, 3 × triazolyl 5-CH_3), 2.23-2.13 (6H, m, 6 × azabicyclooctyl-H), 2.03-1.92 (6H, m, 6 × azbicyclooctyl-H), 1.69-1.59 (12H, m, 12 × azabicyclooctyl-H), 1.32 (18H, d, *J* 7.2, 3 × triazolyl 3-$CH(CH_3)_2$); υ_{max}/cm^{-1} (film) (isomeric mixture); 3383, 2965, 2878, 1693, 1567, 1514, 1462, 1417, 1345, 1315, 1286, 1251, 1215; *m/z* (ESI^+) (isomeric mixture) 1219.8 (50%, MH^+); (Found MH^+, 1219.7538. $C_{69}H_{91}N_{18}O_3$ requires 1219.7516).
NOE data (DMSO) for **30**:

	% Enhancement				
Irradiated proton	1-H	2-H	4-H	Pyridyl-H	pyridoindolyl-CH_2
1-H		-10.6	-5.8	-	-
2-H	-11.2		-	-3.0 (δ 8.71), -1.9 (δ 7.89)	-
4-H	-4.7	-		2.5 (δ 8.41)	-4.2 (δ 3.63), 4.8 (δ 2.84), 3.1 (δ 2.68)

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