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Sulfolenoporphyrins: synthons for refunctionalization of porphyrins

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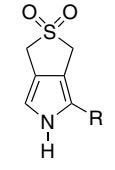
Abstract—Using sulfolenopyrroles (**4**) and (**11**) methods are developed for the synthesis of *opp*- (**15**,**18**,**19**) and *adj*- (**25**) bis-sulfolenoporphyrins; such compounds are useful building blocks for the refunctionalization of the porphyrin system, and readily undergo Diels–Alder cycloaddition reactions.

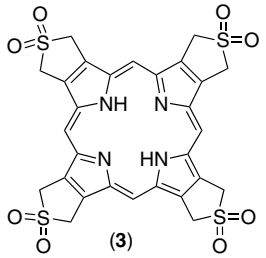
The β,β′-fused sulfolenopyrrole (**1**) was introduced into pyrrole and porphyrin chemistry by Vicente et al. in 1997.[1] It was shown to react thermally as a potent masked diene with dienophiles (such as phenylvinylsulfone), and a new route to tetrabenzoporphyrins was developed. These workers also cyclotetramerized the reduction product (**2**) to give the symmetrical tetrasulfolenoporphyrin (**3**),[1] but this was found to suffer solubility problems in organic solvents. The benzyl ester (**4**) of the sulfolenopyrrole was subsequently used by Gunter et al.[2,3] to prepare a mono-sulfolenoporphyrin (**5**) using the [3+1] variant[4–6] of the MacDonald synthesis,[7] and this was used in Diels–Alder cycloadditions with common dienophiles such as dimethyl acetylenedicarboxylate (DMAD) and norbornadiene. Montforts and co-workers also used pyrrole (**4**) to prepare an open-chain sulfolenobilin, which was cyclized to give a sulfolenochlorin and, after Diels–Alder cycloaddition, a fullerenochlorin.[8,9] At about the same time, Kräutler and co-workers synthesized the soluble zinc(II) 5,10,15,20-tetra-aryl-tetra-sulfolenoporphyrin (**6**),[10] and eventually managed to accomplish stepwise Diels–Alder cycloadditions of up to four fullerenes.[11]

Gunter et al.[2,3] successfully prepared porphyrins (e.g., **5**) bearing one sulfolenopyrrole subunit, but ambitions to construct a library of polysulfoleno building blocks for use in fabrication of superstructured porphyrin assemblies were not realized.[3] The electron-withdrawing effect of the β,β′-fused sulfolene moiety significantly reduced the nucleophilicity of the intermediate pyrrole, and this is a critically important issue in pyrrole-coupling reactions.[12] In no case (except for the tetramerization reaction of Vicente, Kräutler and co-workers)[1,10,11] was it found possible to prepare building blocks with more than one sulfolenopyrrole subunit, and therefore accessibility to 'linear' and 'stepped' porphyrin oligomers and adducts was thwarted.

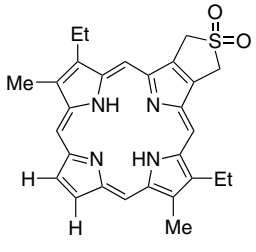
Gunter et al.[2,3] successfully prepared symmetrical tripyrranes, using the Sessler method,[13] bearing either



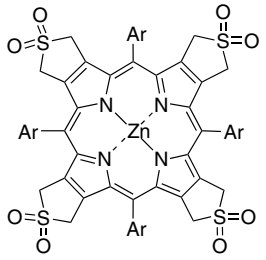
(**1**) R = CO_2Et
(**2**) R = CH_2OH
(**4**) R = CO_2CH_2Ph



(**3**)



(**5**)



(**6**) Ar = 3,5-di(*tert*-butyl)phenyl

Keywords: Benzoporphyrin; Diels–Alder cycloaddition; Porphyrin synthon; Sulfolenoporphyrin; Sulfolenopyrrole.
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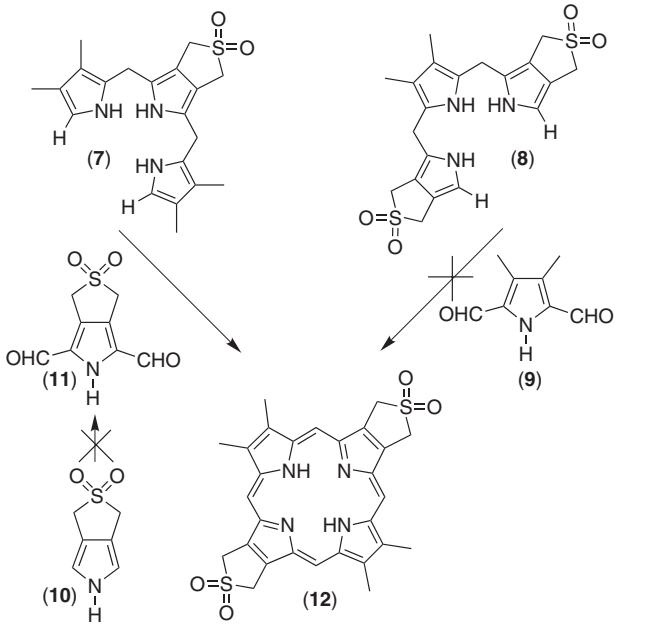
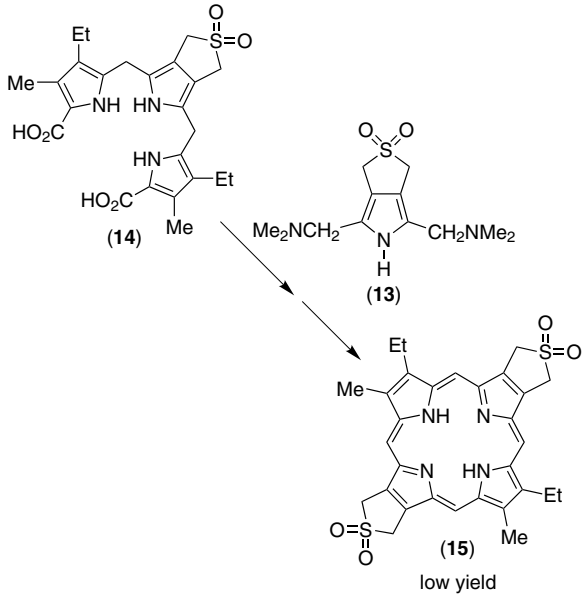


Scheme 1. Unsuccessful routes to *opp*-bis(sulfolenopyrrole)porphyrin (**12**).



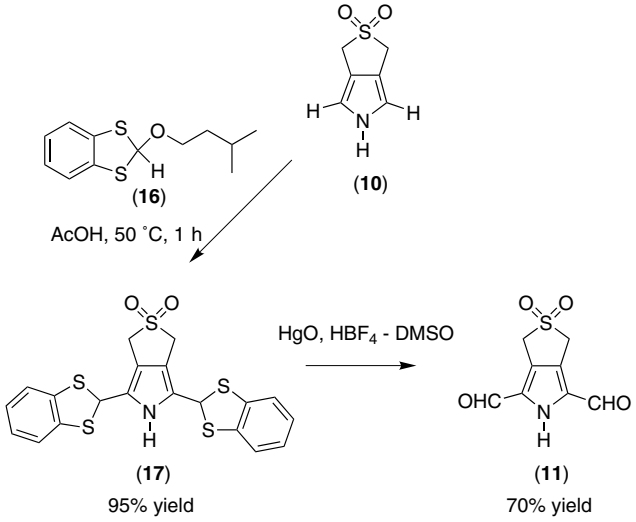
Scheme 2. Synthesis of *opp*-bis-sulfolenoporphyrin (**15**).

one sulfolenepyrrole in the middle (Scheme 1, **7**), or two sulfolenepyrroles, one at each end of the tripyrrane (Scheme 1, **8**). The latter was not sufficiently nucleophilic to react with a 2,5-diformylpyrrole (**9**) in the [3+1] protocol. We have ourselves shown that sulfolenopyrrole (**10**) does not undergo double formylation, so a monopyrrole (**11**) was not available for reaction with the mono-sulfolenopyrrole-tripyrrane (**7**) to give the *opp*-bis(sulfolenopyrrole)porphyrin (**12**).

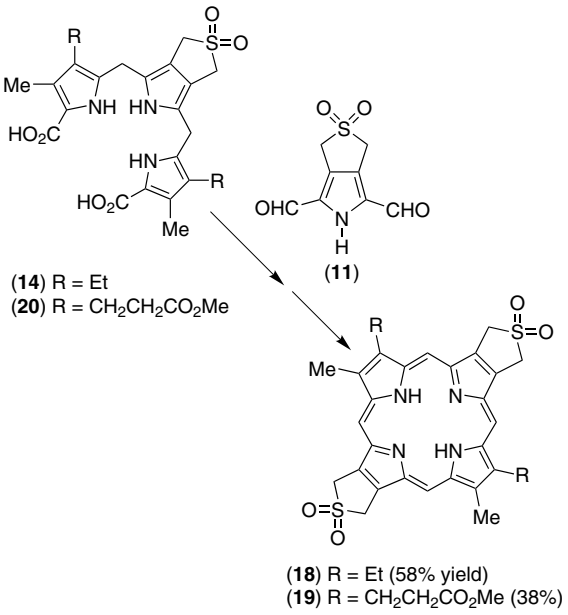
Herein we report methodology that overcomes the previously identified electronic problems, and permits the synthesis of porphyrins bearing more than one and less than four sulfolenopyrrole subunits. We demonstrate the effectiveness of the methodology in the synthesis of both *adj* - and *opp*-bis(sulfoleno)porphyrins.

The standard [3+1] approach to porphyrins requires[4,5] a 2,5-diformylpyrrole and a tripyrrane (as in Scheme 1). The sulfolenopyrrole (**10**), is not sufficiently nucleophilic to be formylated more than once under Vilsmeier conditions, and when one electronegative formyl (or imine salt moiety) is inserted, it certainly could not be formylated a second time. Neither, in our hands, could pyrrole (**10**) be 2,5-diformylated using TFA and trimethyl orthoformate.[14] In our published version of the [3+1] route to porphyrins,[6] the tripyrrane is treated with a monopyrrole subunit bearing 2- and 5-*N*,*N*-dimethylaminomethylene substituents. Thus, treatment[6,15] of (**10**)[3] with an excess of Eschenmoser's salt (Aldrich) gave a 50% yield of the required sulfolenopyrrole (**13**). This pyrrole reacted with the tripyrrane dicarboxylic acid (**14**) (Scheme 2), but only a small amount of porphyrin (**15**) was obtained and this approach was abandoned. Clearly (see Scheme 1), another avenue for success in the synthesis of *opp*-bis(sulfoleno)porphyrins would be a viable route to the 2,5-diformylsulfolenopyrrole (**11**). This was accomplished as follows: pyrrole (**10**) was treated with 2-isopentlyoxy-1,3-benzodithole (**16**)[16–18] to give a 95% yield of the bis-adduct (**17**).[19] With HgO/HBF_4/DMSO, (**17**) was converted into the required 2,5-diformyl-sulfolenopyrrole (**11**)[19] in 70% yield (Scheme 3).

Thus, pyrrole (**11**) was condensed under [3+1] conditions with the tripyrrane-1,14-dicarboxylic acid (**14**) to give a 58% yield of the *opp*-bis-sulfolenoporphyrin (**18**)[19] (Scheme 4); this porphyrin was not particularly soluble in common organic solvents, so the analogous porphyrin (**19**)[19] was also prepared from (**11**) and the tripyrrane (**20**), in an unoptimized 38% yield.



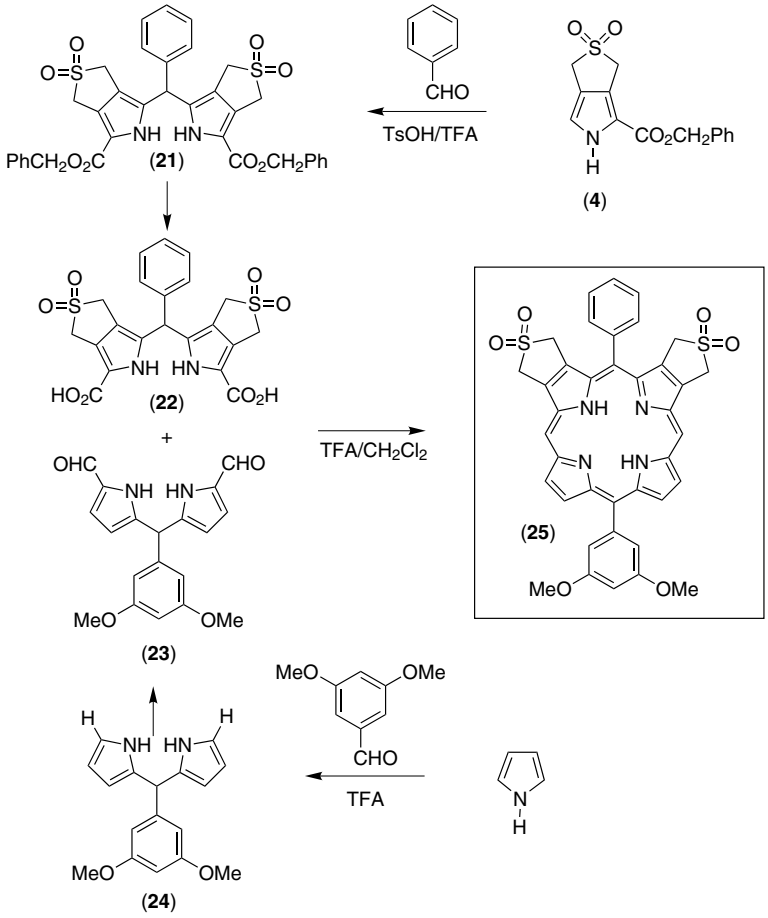
Scheme 3. Synthesis of 2,5-diformylsulfolenopyrrole (**11**).



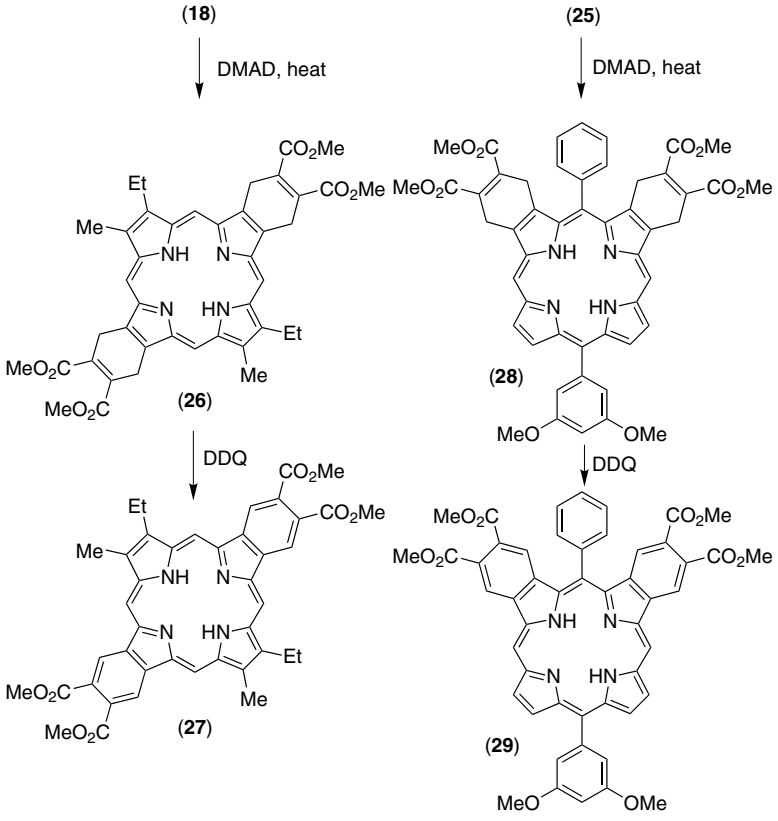
Scheme 4. Synthesis of *opp*-bis-sulfolenoporphyrins (**18**) and (**19**).

Our attention next turned to methodology for synthesis of an *adj*-bis-sulfolenoporphyrin. The sulfolenopyrrole (**4**) was treated with benzaldehyde in the presence of TsOH and TFA in dichloromethane to give a 60% yield of the dipyrromethane (**21**). This was catalytically denbenzylated (95% yield) to give the dipyrromethane 1,9-dicarboxylic acid (**22**). Compound (**22**) was treated with the generic 1,9-diformyldipyrromethane (**23**) [obtained by the reaction of 3,5-dimethoxybenzaldehyde with pyrrole {40% yield of 1,9-diunsubstituted dipyrromethane (**24**)} followed by double Vilsmeier formylation (70% yield)] to give porphyrin (**25**)[19] in 15% yield (Scheme 5).

Finally, susceptibility of the *opp*- (**18**,**19**) and *adj*-bis-sulfolenoporphyrins (**25**) toward Diels–Alder cycloaddition reactions was readily established. For example (Scheme 6), the *opp*-porphyrin (**18**) reacted (at 110 °C in trichlorobenzene) with DMAD to give the bis-adduct (**26**). With DDQ this gave an overall 85% yield [from (**18**)] of the *opp*-dibenzoporphyrin (**27**).[19] As was predictable based on steric arguments, Diels–Alder cycloaddition reactions of the *adj*-bis-sulfolenoporphyrin (**25**) were more difficult to accomplish. With DMAD at 214 °C in trichlorobenzene, the bis-adduct (**28**) was obtained, and after DDQ treatment, a 40% overall yield [from (**25**)] of the *adj*-dibenzoporphyrin (**29**)[19] was obtained.



Scheme 5. Synthesis of *adj*-bis-sulfolenoporphyrin (**25**).



Scheme 6. Diels–Alder cycloaddition reactions of (**18**) and (**25**).

Acknowledgements

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19. Selected data for **11**: ^{1}H NMR (DMSO-d_6), δ ppm: 4.48 (s, 4H), 9.76 (s, 2H); ^{13}C NMR (DMSO-d_6), δ ppm 52.2, 123.0, 130.0, 181.7; HRMS (TOF ES+): Calcd for $C_8H_7NO_4$ M+Na = 235.9993, found: *m*/*z* 235.9986; Anal. Calcd for $C_8H_7NO_4S{\cdot}0.25H_2O$: C, 44.13; H, 3.47; N, 6.43. Found: C, 44.20; H, 3.44; N, 6.21.
Selected data for **17**: ^{1}H NMR ($CDCl_3$), δ ppm 3.85 (s, 4H), 6.39 (d, J = 6.6 Hz, 2H), 7.12 (m, 4H), 7.35 (m, 4H), 11.43 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 47.5, 52.6, 112.5, 122.3, 125.6, 126.0, 136.5; HRMS (TOF ES+): Calcd for $C_{20}H_{15}NO_2S_5$ M+Na = 483.9604, found: *m*/*z* 483.9603; Anal. Calcd for $C_{20}H_{15}NO_2S_5$: C, 52.04; H, 3.28; N, 3.03. Found: C, 51.97; H, 3.35; N, 2.96.
Selected data for **18**: UV–vis λ_{max} (CH_2Cl_2) 399 nm (ε 360,000), 503 (36,000), 541 (39,000), 562 (32,000); ^{1}H NMR ($CDCl_3$+TFA), δ ppm −3.00 (br, 2H), 1.64 (t, J = 9.2 Hz, 3H), 3.58 (s, 3H), 4.04 (q, J = 9.2 Hz, 2H), 5.68

(s, 4H), 5.69 (s, 4H), 10.63 (2, 2H), 10.65 (s, 2H); ^{13}C NMR ($CDCl_3$+TFA), δ ppm 11.9, 16.4, 20.2, 55.7, 101.0, 101.4, 107.3, 111.8, 116.4, 134.6, 137.7, 139.5, 143.1, 143.9, 146.0, 153.1, 158.9, 159.6; HRMS (TOF ES+): Calcd for $C_{30}H_{30}N_4O_4S_2$ M+H = 575.1786, found: *m/z* 575.1786.

Selected data for **19**: UV–vis λ_{max} (CH_2Cl_2) 401 nm (ε 149,000), 504 (25,800), 543 (25,800); ^{1}H NMR ($CDCl_3$+TFA), δ ppm −3.50 (br, 2H), 3.16 (t, J = 7.3 Hz, 4H), 3.67 (s, 6H), 3.68 (s, 6H), 4.46 (t, J = 7.3 Hz, 4H), 5.75 (s, 4H), 5.81 (s, 4H), 10.66 (s, 2H), 10.90 (s, 2H); ^{13}C NMR ($CDCl_3$+TFA), ppm 11.7, 21.7, 29.9, 30.6, 35.4, 53.4, 56.0, 102.0, 102.2, 135.1, 135.6, 137.7, 138.1, 142.0, 143.3, 176.2.

Selected data for **25**: UV–vis λ_{max} (CH_2Cl_2) 408 nm (ε 106,000), 502 (11,300), 576 (7000); ^{1}H NMR ($CDCl_3$), δ ppm −3.22 (s, 2H), 4.01 (s, 6H), 4.51 (s, 4H), 5.63 (s, 4H), 6.95 (s, 1H), 7.42 (d, J = 2.2 Hz, 2H), 7.85–8.00 (m, 5H), 9.20 (d, J = 4.7 Hz, 2H), 9.38 (d, J = 4.7 Hz, 2H), 10.12 (s, 2H); ^{13}C NMR (CH_2Cl_2), δ ppm 55.9, 56.2, 58.7, 100.6, 104.1, 114.7, 118.2, 121.1, 129.2, 130.5, 132.4, 132.6, 133.0, 135.0, 136.7, 139.4, 140.0, 141.3, 142.8, 146.3, 148.9, 160.0; HRMS (TOF ES+): Calcd for $C_{38}H_{31}N_4O_8S_2$M−$2SO_2$+H = 575.2447, found: *m/z* 575.2231; Anal. Calcd for $C_{38}H_{30}N_4O_6S_2{\cdot}1.5H_2O$: C, 62.55; H, 4.55; N, 7.67. Found: C, 62.65; H, 4.35; N, 7.51.

Selected data for **27**: UV–vis λ_{max} (CH_2Cl_2) 419 nm (ε 500,000), 497 (31,500), 567 (84,800), 581 (63,600), 636 (34,800); ^{1}H NMR ($CDCl_3$), δ ppm −6.73 (s, 2H), 1.58 (s, 6H), 1.66 (t, J = 7.6 Hz, 6H), 3.22 (s, 6H), 3.71 (q, J = 7.6 Hz, 4H), 4.33 (s, 6H), 4.34 (s, 6H), 9.13 (s, 4H), 9.28 (s, 2H), 9.34 (s, 2H); ^{13}C NMR ($CDCl_3$) δ ppm 11.1, 17.5, 19.4, 53.4, 53.6, 94.5, 94.6, 121.5, 121.7, 130.1, 130.2, 132.5, 134.5, 135.3, 139.4, 141.5, 141.7, 146.1, 146.2, 169.4, 169.5; HRMS (TOF ES+): Calcd for $C_{42}H_{38}N_4O_8$+H = 749.2587, found: *m/z* 749.2579; Anal. Calcd for $C_{42}H_{38}N_4O_8{\cdot}1.5H_2O$: C, 68.57; H, 5.34; N, 7.61. found: C, 68.31; H, 5.38; N, 7.41.

Selected data for **29**: UV–vis λ_{max} (CH_2Cl_2) 431 nm (ε 440,000), 534 (37,600), 569 (50,900), 594 (33,000), 650 (28,000). ^{1}H NMR ($CDCl_3$) δ ppm −2.45 (s, 1H), −2.22 (br s, 1H), 4.02 (s, 6H), 4.04 (s, 6H), 4.20 (s, 6H), 6.97 (t, J = 2.0 Hz, 1H), 7.46 (d, J = 2.0 Hz, 2H), 7.49 (s, 2H), 7.64–7.72 (m, 4H), 7.98 (t, J = 6.1 Hz, 1H), 9.11 (d, J = 4.6 Hz, 2H), 9.24 (d, J = 4.6 Hz, 2H), 9.67 (s, 2H), 10.37 (s, 2H). ^{13}C NMR ($CDCl_3$) δ ppm 52.9, 53.3, 55.9, 100.3, 114.1, 114.6, 122.0, 127.0, 128.8, 129.1, 129.8, 130.9, 131.1, 131.2, 132.3, 137.3, 138.4, 139.3, 140.1, 141.9, 145.1,146.5, 159.6, 168.2, 169.0. HRMS (TOF ES+): Calcd for $C_{50}H_{39}N_4O_{10}$ M+H = 855.2666, found: *m/z* 855.2595.