Synthesis and Structures of Novel Multi-armed Molecules Involving Benzene as a Core and 4-Phenylthiazole, 4-Pyrazolylthiazole, or Thiadiazole Units as Arms

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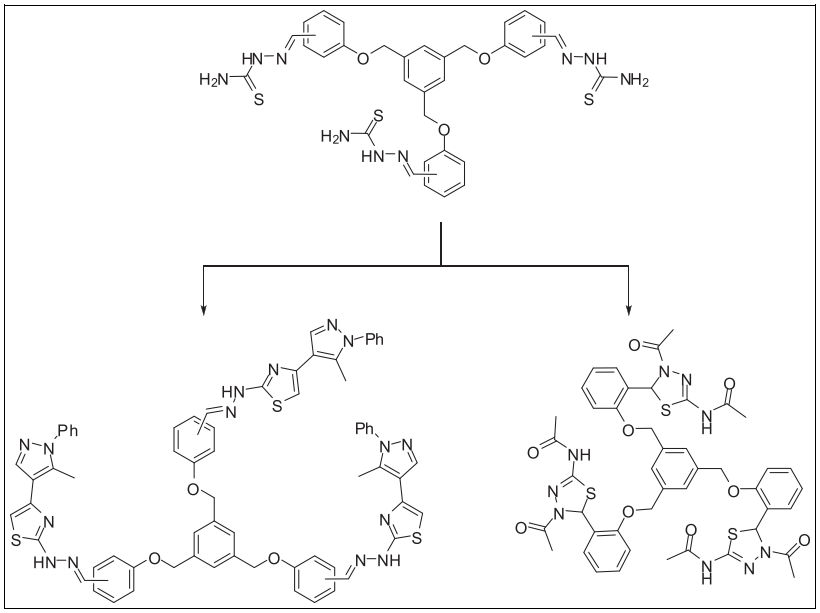

A synthesis of novel three-, four-, and sixfold branched 4-phenylthiazolylhydrazones, 4-pyrazolylthiazolyl hydrazones, and thiadiazoles which are linked to a benzene core *via* phenoxymethyl spacers was reported. The synthetic methodology includes initially formation of poly(aldehyde thiosemicarbazones) **9**, **14**, and **15** by acid catalyzed condensation of thiosemicarbazide (**8**) with the appropriate poly(aldehydes) **3, 5,** and **7,** respectively. Subsequent reaction of **9, 14,** and **15** with each of 2-bromo-1-phenylethanone (**10a**) and 2-bromo-1-(**4**-chlorophenyl)ethanone (**10b**) in refluxing ethanol in the presence of few drops of TEA afforded **11, 16,** and **18,** respectively, in good yields. On the other hand, the synthesis of the novel poly(4,5-dihydro-1,3,4-thiadiazolyl) derivatives **20, 21a,b,** and **22** was performed by cyclization of **9b, 14a,b,** and **15a,** respectively, in refluxing acetic anhydride.

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INTRODUCTION

Since the pioneering work of Vögtle and Weber [1] as well as that of MacNicol *et al*. [2] on multi-armed molecules, much attention have been paid to the synthesis of such compounds for their wide range of applications [3–8]. This class of compounds is considered important hosts for constructing microporous networks possessing selective inclusion properties and their applications in supramolecular host–guest chemistry have been recently reported [9]. Some related compounds have also been used for the formation of discotic mesogens [10], organic electronic and optoelectronic materials [11–13]. They have also been used as building units for dendrimers [14]. Furthermore, thiazole derivatives were reported to exhibit numerous pharmacological and biological applications, such as anti-HIV, anti-inflammatory, antimicrobial, antihypertensive, analgesic, and herbicidal activity [15].

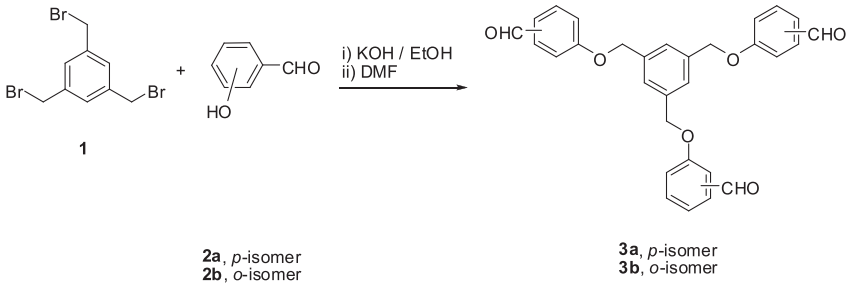
Moreover, pyrazole system is also considered as an important class of heterocyclic compounds not only for being the core unit in a variety of drugs such as celecobix (Celebrex) [16], sildenafil (Viagra) [17], and rimonabant (Acomplia) [18], but also for possessing a wide range of activities such as antifungal [19], anti-inflammatory [20], antimicrobial [21], antidepressant [22], antiparasitic [23], antiviral [24], and antitumor activities [25].

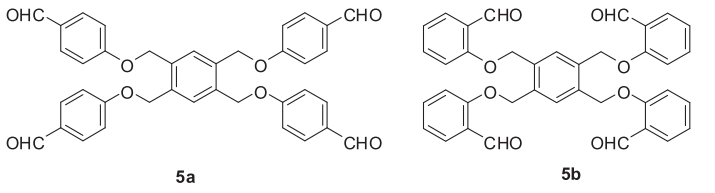
In addition, 1,3,4-thiadiazole derivatives have also attracted much attention in the last decades for their wide spectrum of biological activities including anti-inflammatory

[26], antimicrobial [27], antituberculosis [28], anticancer [29], antidepressant and anxiolytic [30], antihypertensive [31], antioxidant [32], anticonvulsants [33], and antifungal activities [34].

In connection with these findings, we report herein on the synthesis of novel three-, four-, and sixfold branched 4-phenylthiazolylhydrazones, 4-pyrazolylthiazolylhydrazones,

Scheme 1. Synthesis of tris-(formylphenoxymethyl)benzenes **3a,b**.





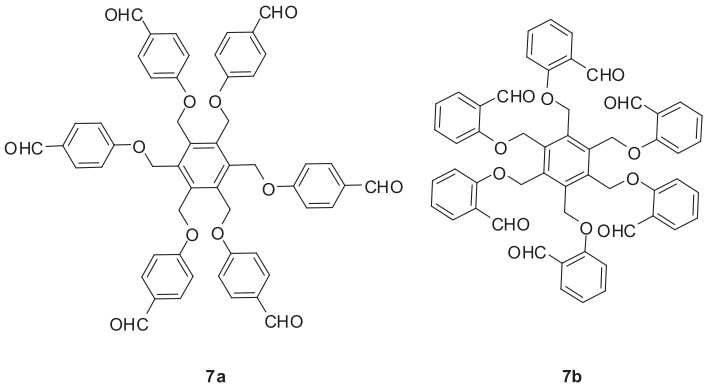
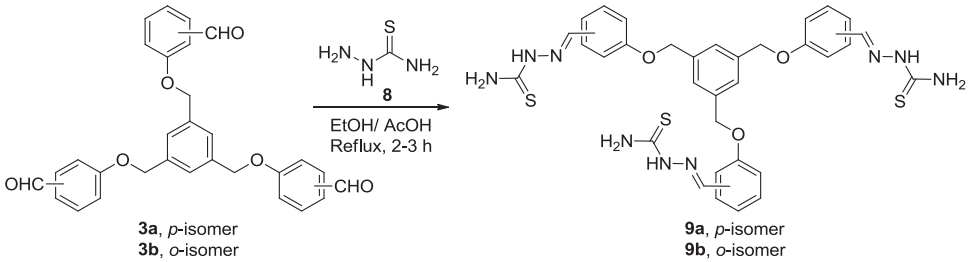


Figure 1. Tetrakis- and hexakis(formylphenoxymethyl)benzenes **5a,b** and **7a,b**.

Scheme 2. Synthesis of tris(aldehyde thiosemicarbazones) **9a** and **9b**.



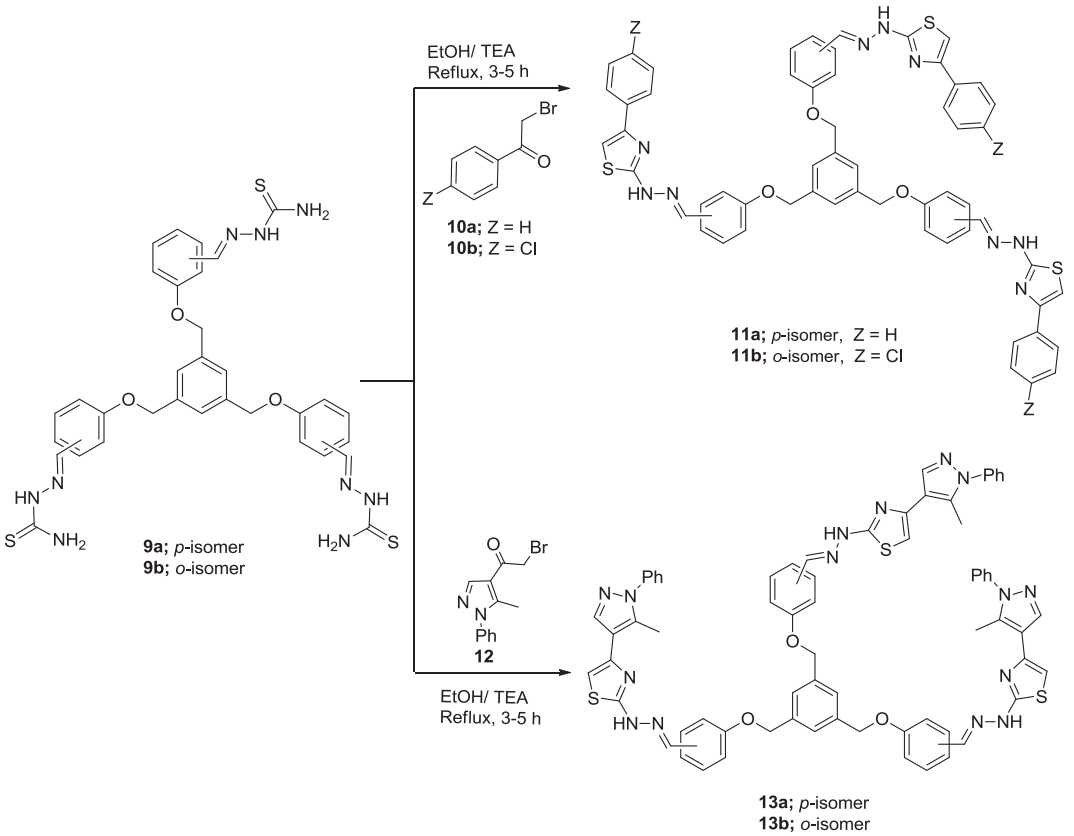
and thiadiazoles which are linked to a benzene core *via* phenoxymethyl spacers.

RESULTS AND DISCUSSION

We first synthesized the required aldehydes **3a**,**b**, **5a**,**b**, and **7a**,**b** following reported methods, described by our group or after modification of literature procedure described by other groups. Thus, tris(formylphenoxymethyl)benzenes **3a**,**b** were prepared by reacting the potassium salt of 4-hydroxybenzaldehyde (**2a**) or salicylaldehyde (**2b**) with tris (bromomethyl)benzene (**1**) in refluxing DMF (Scheme 1) [35].

Similarly, the tetrakis(formylphenoxymethyl)benzenes **5a** and **5b** were prepared, by fourfold substitution of tetrakis

Scheme 3. Reaction of compounds **9a,b** with the appropriate 2-bromo-Ethanone derivatives.



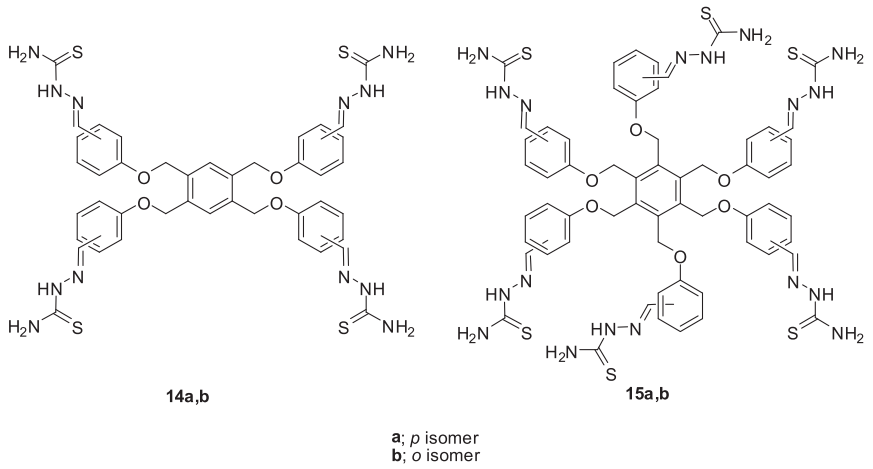


Figure 2. Tetrakis- and hexakis (aldehyde thiosemicarbazones) **14a,b** and **15a,b**.

(bromomethyl)benzenes (**4**) with four equivalents of the potassium salt of 4-hydroxybenzaldehyde (**2a**) or salicylaldehyde (**2b**), respectively. With the same reaction sequence, the hexakis(formylphenoxymethyl)benzenes **7a** and **7b** were prepared, by sixfold substitution of hexakis(bromomethyl) benzenes (**6**) with six equivalents of the potassium salt of 4-hydroxybenzaldehyde or salicylaldehyde, respectively (Fig. 1) [35].

The synthetic utility of aldehydes **3**, **5**, and **7** as building blocks for novel tris-, tetrakis-, and hexakis(thiazoles), in which the 4-phenylthiazolylhydrazone or 4-pyrazolylthiazolylhydrazone is linked to benzene core *via* phenoxymethyl group, was investigated. Thus, the tris(aldehyde thiosemicarbazones) **9a** and **9b** were first synthesized in 77 and 72% yields, respectively, by acid catalyzed condensation of thiosemicarbazide (**8**) with the appropriate tris (aldehydes) **3a** and **3b**, respectively (Scheme 2).

Reaction of the latter compounds with each of 2-bromo-1-phenylethanone (**10a**) and 2-bromo-1-(4-chlorophenyl) ethanone (**10b**) in refluxing ethanol in the presence of few drops of TEA afforded **11a** and **11b** in 67 and 69% yields, respectively (Scheme 3). In analogy, reaction of compounds **9a,b** with 2-bromo-1-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)ethanone (**12**) in refluxing ethanol in the presence of few drops of TEA afforded **13a** and **13b** in 70 and 64% yields, respectively (Scheme 3). Compound **12** was

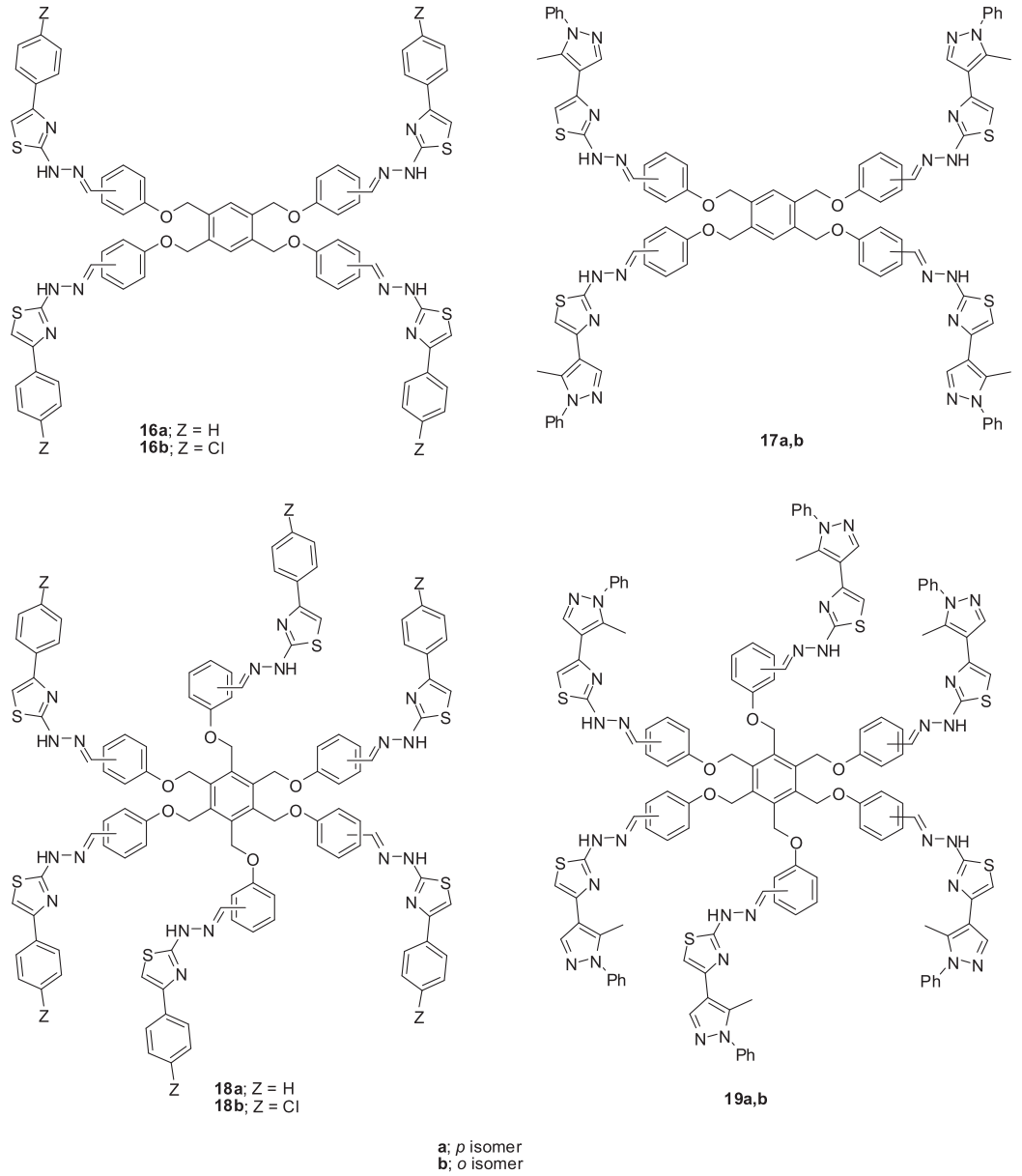


Figure 3. Tetrakis- and hexakis(thiazoles) **16a,b**, **17a,b**, **18a,b** and **19a,b**.

synthesized by the reaction of phenylhydrazine with ((dimethylamino)methylene)pentane-2,4-dione, obtained upon treatment of acetylacetone with dimethylformamide dimethylacetal (DMFDMA), followed by bromination upon treatment with Br_2 in AcOH [36].

The same methodology was extended to the preparation of tetrakis- and hexakis(thiazoles) **16–19**. Thus, compounds **16–19** were successfully prepared, from **5a,b** and **7a,b** firstly by reaction with thiosemicarbazide (**8**) in refluxing EtOH containing few drops of AcOH to give **14a,b** and **15a,b** in 70, 73 and 68, 64% yields, respectively (Fig. 2).

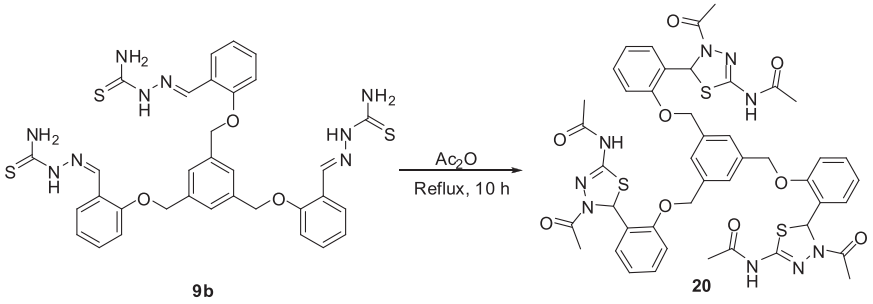
Subsequent reaction of the latter compounds with the appropriate bromoacetyl compounds **10a**,**b** and **12** in refluxing ethanol in the presence of few drops of TEA afforded the corresponding tetrakis(thiazoles) **16a**,**b** and **17a**,**b** in 65, 69 and 66, 68% yields, respectively, as well as hexakis(thiazoles) **18a**,**b** and **19a**,**b** in 63, 65 and 66, 67% yields, respectively (Fig. 3).

Our study was extended to include the synthesis of the novel tris(4,5-dihydro-1,3,4-thiadiazolyl) derivative **20** in which the thiadiazolyl moiety is linked to the benzene core *via* phenoxymethyl group, in good yield, by cyclization of tris(aldehyde thiosemicarbazone) **9b** in refluxing acetic anhydride (Scheme 4).

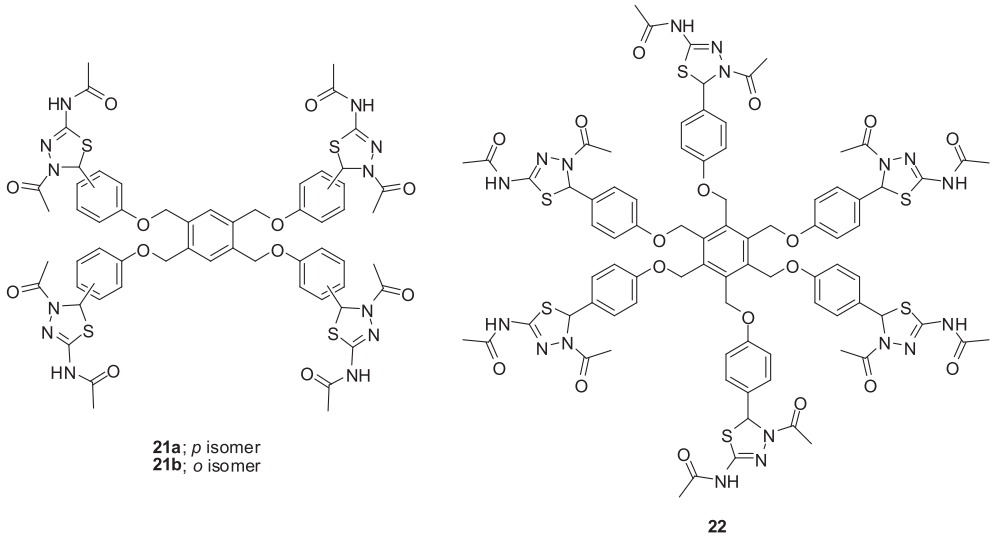
Encouraged by the above results, we expanded the scope of this reaction to prepare novel fourfold branched (4,5-dihydro-1,3,4-thiadiazolyl) derivatives **21a** and **21b** and sixfold branched (4,5-dihydro-1,3,4-thiadiazolyl) derivative **22** (Fig. 4) by cyclization of the appropriate tetrakis(aldehyde thiosemicarbazones) **14a** and **14b** and hexakis(aldehyde thiosemicarbazone) **15a,** respectively, with acetic anhydride.

The structures of the new synthesized compounds were confirmed by IR, NMR, and mass spectra as well as elementary analyses. The IR spectrum of tris (thiazolylhydrazone) **11a** as a representative example of these class of compounds revealed an absorption band at 3431 cm^{-1} because of (NH). Its ^1H NMR spectra showed the presence of a characteristic singlet signal at 7.99 ppm because of one methine proton (—N=CH—). Mass spectrum of compound **11a** showed the molecular ion peaks at *m/z* 999 (M^+) in agreement with its respective molecular formula. The spectra of other bis(thiazoles) **11b**, **16a**,**b**,

Scheme 4. Synthesis of tris(4,5-dihydro-1,3,4-thiadiazolyl) derivative **20** from **9b**.



9b **20**



21a; *p* isomer
21b; *o* isomer

22

Figure 4. Tetrakis- and hexakis (4,5-dihydro-1,3,4-thiadiazolyl) derivatives **21a,b** and **22**.

and **18a**,**b** showed similar spectral data which are listed in the experimental part.

The symmetry of compounds **19a**,**b** is manifested by a single set of signals characteristic of the six equivalent OCH_2 and six methyl groups in the ^{1}H-NMR spectra. Similarly, compounds **21a**,**b** are characterized by a single set of signals characteristic of the four equivalent OCH_2, four acetyl (CH_3CO), four acetamido ($NHCOCH_3$), and four methine (CH) groups.

CONCLUSIONS

We developed a simple method for the preparation of novel three-, four-, and sixfold branched 4-phenylthiazolylhydrazones, 4-pyrazolylthiazolylhydrazones, and thiadiazoles which are linked to a benzene core *via* phenoxymethyl spacers. Full characterization of these compounds is reported. The new synthesized compounds are interesting both in their own right as unusual molecules and for their promising pharmacological and biological activities as well as for their expected inclusion properties. The extension of the scope of this method to cover additional multi-armed heterocyclic compounds is now under study.

EXPERIMENTAL

General. Melting points were determined in open glass capillaries with a Gallenkamp apparatus. The infrared spectra were recorded in potassium bromide disks on a Pye Unicam SP 3-300 and Shimadzu FTIR 8101 PC infrared spectro photometer. NMR spectra were recorded in deuterated dimethyl sulfoxide (DMSO-d6) with a Varian Mercury VXR-300 NMR spectrometer at 300 MHz (^{1}H NMR) and at 75 MHz (^{13}C NMR). Mass spectra (EI) were obtained at 70 eV with a type Shimadzu GCMQP 1000 EX spec trometer. Analytical thin-layer chromatography was per formed using pre-coated silica gel 60778 plates (Fluka), and the spots were visualized with UV light at 254 nm. The elemental analyses were performed at the Micro analytical center, Cairo University.

Synthesis of poly(thiosemicarbazones) 9a,**b**, **14a**,**b**, and **15a**,**b**.

General procedure. To a solution of poly(aldehydes) **3a**,**b** or **5a**,**b** or **7a**,**b** (1 mmol) in absolute ethanol (25 mL) containing few drops of acetic acid, thiosemicarbazide (**8**) (3 or 4 or 6 mmol) was added. The reaction mixture was heated under reflux for 3 h. The solid formed upon cooling was collected and recrystallized from ethanol/DMF to give the corresponding.poly(thiosemicarbazones) **9a**,**b**, **14a**,**b**, and **15a**,**b**.

2,2′,2′′-(4,4′,4′′-(Benzene-1,3,5-triyltris(methylene))tris(oxy) tris(benzene-4,1-diyl))-tris(methan-1-yl-1-ylidene)tris (hydrazinecarbothioamide) 9a. Pale yellow powder, (77% yield), mp. 204–205°C; IR: (potassium bromide) 3421, 3367 (NH_2), 3254 (NH), 1601 (C=N) cm^{-1}; ^{1}H-NMR: δ 5.19 (s, 6H, 3 CH_2O), 7.03–7.99 (m, 21H, ArH + 3 NH_2), 8.07 (s, 3H, 3 CH=N), 11.26 (s, 3H, 2 NH); ms: *m/z* (%) 699 (9.5, M^+) 389 (54.2), 151 (100), 135 (29.3), 57 (93.5), 43 (82.6). *Anal*. Calcd. for $C_{33}H_{33}N_9O_3S_3$: C, 56.63; H, 4.75; N, 18.01; S, 13.74. Found: C, 56.55; H, 4.66; N, 17.91; S, 13.68.

2,2′,2′′-(2,2′,2′′-(Benzene-1,3,5-triyltris(methylene))tris(oxy) tris(benzene-2,1-diyl))tris(methan-1-yl-1-ylidene)tris (hydrazinecarbothioamide) 9b. Pale yellow powder, (72% yield), mp. 200–202°C; IR: (potassium bromide) 3421, 3366 (NH_2), 3251 (NH), 1595 (C=N) cm^{-1}; ^{1}H-NMR: δ 5.26 (s, 6H, 3 CH_2O), 6.96–8.13 (m, 21H, ArH + 3 NH_2), 8.51 (s, 3 CH=N), 11.39 (s, 3H, 3 NH); ms: *m/z* (%) 699 (10.2, M^+), 630 (60.2), 321 (100), 310 (47.2), 55 (40.3). *Anal*. Calcd. for $C_{33}H_{33}N_9O_3S_3$: C, 56.63; H, 4.75; N, 18.01; S, 13.74. Found: C, 56.52; H, 4.69; N, 17.95; S, 13.66.

2,2′,2′′,2′′′-(4,4′,4′′,4′′′-(Benzene-1,2,4,5-tetrayltetrakis(methylene)) tetrakis (oxy)-tetrakis(benzene-4,1-diyl))tetrakis(methan-1-yl-1-ylidene) tetrakis (hydrazinecarbo-thioamide) 14a. Pale yellow powder, (73% yield), mp. 246–248°C; IR: (potassium bromide) 3425, 3364 (NH_2), 3254 (NH), 1594 (C=N) cm^{-1}; ^{1}H-NMR: δ 5.29 (s, 8H, 4 CH_2O), 7.03–7.98 (m, 26H, ArH + 4 NH_2), 8.07 (s, 4H, 4 CH=N), 11.29 (s, 4H, 4 NH); ms: *m/z* (%) 906 (24.9, M^+), 815 (100), 801 (31.3), 481 (21.9), 249 (12.2), 57 (11.8). *Anal*. Calcd. for $C_{42}H_{42}N_{12}O_4S_4$: C, 55.61; H, 4.67; N, 18.53; S, 14.14. Found: C, 55.51; H, 4.53; N, 18.39; S, 14.01.

2,2′,2′′,2′′′-(2,2′,2′′,2′′′-(Benzene-1,2,4,5-tetrayltetrakis (methylene))tetrakis (oxy)tetrakis(benzene-2,1-diyl))tetrakis(methan-1-yl-1-ylidene)tetrakis (hydrazine-carbothioamide) 14b. Pale yellow powder, (70% yield), mp. 203–205°C; IR: (potassium bromide) 3430, 3275 (NH_2), 3150 (NH), 1595 (C=N) cm^{-1}; ^{1}H-NMR: δ 5.41 (s, 8H, 4 CH_2O), 6.93–8.11 (m, 26H, ArH + 4 NH_2), 8.51 (s, 4H, CH=N), 11.42 (s, 4H, 4 NH); ms: *m/z* (%) 906 (14.9, M^+), 816 (47.6), 814 (100), 801 (31.3), 481 (21.9), 250 (12.2), 59 (12.8). *Anal*. Calcd. for $C_{42}H_{42}N_{12}O_4S_4$: C, 55.61; H, 4.67; N, 18.53; S, 14.14. Found: C, 55.44; H, 4.45; N, 18.41; S, 13.88.

2,2′,2′′,2′′′,2′′′′,2′′′′′-(4,4′,4′′,4′′′,4′′′′,4′′′′′-(Benzene-1,2,3,4,5,6-hexaylhexakis (methylene))hexakis(oxy)hexakis(benzene-4,1-diyl)) hexakis(methan-1-yl-1-ylidene)hexakis(hydrazinecarbothioamide) 15a. Pale yellow powder, (68% yield), mp. > 300°C; IR: (potassium bromide) 3423, 3271 (NH_2), 3159 (NH), 1601 (C=N) cm^{-1}; ^{1}H-NMR: δ 5.32 (s, 12H, 6 CH_2O), 6.93–7.94 (m, 36H, ArH + 6 NH_2), 8.05 (s, 6H, CH=N), 11.26 (s, 6H, 6 NH). *Anal*. Calcd. for $C_{60}H_{60}N_{18}O_6S_6$: C, 54.53; H, 4.58; N, 19.08; S, 14.56. Found: C, 54.40; H, 4.43; N, 18.91; S, 14.44.

2,2′,2′′,2′′′,2′′′′,2′′′′′-(2,2′,2′′,2′′′,2′′′′,2′′′′′-(Benzene-1,2,3,4,5,6-hexaylhexakis (methylene))hexakis(oxy)hexakis(benzene-2,1-diyl)) hexakis(methan-1-yl-1-ylidene)hexakis(hydrazinecarbothioamide) 15b. Pale yellow powder, (64% yield), mp. 240–242°C; IR: (potassium bromide) 3418, 3260 (NH_2), 3145 (NH), 1600

(C=N) cm^{-1}; ^{1}H-NMR: δ 5.52 (s, 12H, 6 CH_2O), 6.95–8.11 (m, 36H, ArH + 6 NH_2), 8.39 (s, 6H, 6 CH=N), 11.31 (s, 6H, 6 NH). *Anal*. Calcd. for $C_{60}H_{60}N_{18}O_6S_6$: C, 54.53; H, 4.58; N, 19.08; S, 14.56. Found: C, 54.40; H, 4.42; N, 19.19; S, 14.72.

Synthesis of poly(thiazoles) 11a,b, 16a,b, and 18a,b. ***General procedure.*** To a solution of poly(thiosemicarbazones) **9a,b** or **14a,b** or **15a,b** (1 mmol) in absolute ethanol (25 mL) containing few drops of TEA, 2-bromo-1-phenylethanone (**10a**) or 2-bromo-1-(4-chlorophenyl) ethanone (**10b**) (3 or 4 or 6 mmol) was added. The reaction mixture was heated under reflux for 5 h. The solid product formed upon cooling was collected and recrystallized from ethanol/DMF to give the corresponding poly (thiazoles) **11a,b**, **16a,b**, and **18a,b.**

1,3,5-Tris((4-(2-(4-phenylthiazol-2-yl)hydrazono)methyl) phenoxy)methyl)benzene 11a. Orange powder, (67% yield), mp. 210–212°C; IR: (potassium bromide) 3431 (NH), 1603 (C=N) cm^{-1}; ^{1}H-NMR: δ 5.20 (s, 6H, 3 CH_2O), 7.01–7.85 (m, 33H, ArH + 3 thiazole-H), 7.99 (s, 3H, 3 CH=N), 11.98 (s, 3H, 3 NH); ms: *m/z* (%) 999 (4.5, M^+), 992 (100), 815 (67.1), 481 (21.9), 249 (12.2), 57 (11.8). *Anal*. Calcd. for $C_{57}H_{45}N_9O_3S_3$: C, 68.45; H, 4.53; N, 12.60; S, 9.62. Found: C, 68.29; H, 4.38; N, 12.45; S, 9.44.

1,3,5-Tris((2-((2-(4-(4-chlorophenyl)thiazol-2-yl)hydrazono) methyl)phenoxy)-methyl)benzene 11b. Yellow powder, (69% yield), mp. 180–182°C; IR: (potassium bromide) 3436 (NH), 1599 (C=N) cm^{-1}; ^{1}H-NMR: δ 5.30 (s, 6H, 3 CH_2O), 7.01–7.95 (m, 30H, ArH + 3 thiazole-H), 8.47 (s, 3H, 3 CH=N), 12.11 (s, 3H, 3 NH); ms: *m/z* (%) 1101 (5.6, M^+), 1067 (9.1), 603 (100), 339 (59.4), 264 (62.6), 55 (64.5). *Anal*. Calcd. for $C_{57}H_{42}Cl_3N_9O_3S_3$: C, 62.04; H, 3.84; N, 11.42; S, 8.72. Found: C, 61.95; H, 3.79; N, 11.31; S, 8.62.

1,2,4,5-Tetrakis((4-((2-(4-phenylthiazol-2-yl)hydrazono) methyl)phenoxy)methyl)-benzene 16a. Orange powder, (65% yield), mp. > 300°C; IR: (potassium bromide) 3433 (NH), 1602 (C=N) cm^{-1}; ^{1}H-NMR: δ 5.32 (s, 8H, 4 CH_2O), 7.08–7.84 (m, 42H, ArH + 4 thiazole-H), 7.98 (s, 4H, 4 CH=N), 11.99 (s, 4H, 4 NH). ^{13}C-NMR: δ 66.9, 104.5, 115.1, 127.9, 128.4, 129.2, 129.3, 130.6, 131.3, 131.6, 134.6, 135.0, 135.3, 155.7, 159.4. *Anal*. Calcd. for $C_{74}H_{58}N_{12}O_4S_4$: C, 67.97; H, 4.47; N, 12.85; S, 9.81. Found: C, 67.83; H, 4.31; N, 12.67; S, 9.69.

1,2,4,5-Tetrakis((2-((2-(4-(4-chlorophenyl)thiazol-2-yl) hydrazono)methyl) phenoxy)methyl)benzene 16b. Yellow powder, (69% yield), mp. 190–192°C; IR: (potassium bromide) 3438 (NH), 1598 (C=N) cm^{-1}; ^{1}H-NMR: δ 5.45 (s, 8H, 4 CH_2O), 7.00–7.86 (m, 38H, ArH + 4 thiazole-H), 8.46 (s, 4H, 4 CH=N), 12.10 (s, 4H, 4 NH). ^{13}C-NMR: δ 67.5, 104.2, 112.8, 121.1, 122.7, 125.1, 127.1, 128.0, 130.5, 131.8, 133.4, 135.1, 136.8, 149.2, 155.9, 162.2, 168.2. *Anal*. Calcd. for $C_{74}H_{54}Cl_4N_{12}O_4S_4$: C, 61.49; H, 3.77; N, 11.63; S, 8.87. Found: C, 61.36; H, 3.65; N, 11.44; S, 8.73.

1,2,3,4,5,6-Hexakis((4-((2-(4-phenylthiazol-2-yl)hydrazono) methyl)phenoxy) methyl)benzene 18a. Orange powder, (63% yield), mp. > 300°C; IR: (potassium bromide) 3428 (NH), 1602 (C=N) cm^{-1}; ^{1}H-NMR: δ 5.32 (s, 12H, 6 CH_2O), 7.01–7.80 (m, 60H, ArH + 6 thiazole-H), 7.95 (s, 6H, 6 CH=N), 11.96 (s, 6H, 6 NH). *Anal*. Calcd. for $C_{108}H_{84}N_{18}O_6S_6$: C, 67.48; H, 4.40; N, 13.12; S, 10.01. Found: C, 67.28; H, 4.18; N, 12.90; S, 9.87.

1,2,3,4,5,6-Hexakis((2-((2-(4-(4-chlorophenyl)thiazol-2-yl) hydrazono) methyl)phenoxy)methyl)benzene 18b. Yellow powder, (65% yield), mp. 208–210°C; IR: (potassium bromide) 3433 (NH), 1599 (C=N) cm^{-1}; ^{1}H-NMR: δ 5.55 (s, 12H, 6 CH_2O), 6.94–7.77 (m, 54H, ArH + 6 thiazole-H), 8.35 (s, 6H, 6 CH=N), 11.88 (s, 6H, NH); ^{13}C-NMR: δ 64.3, 104.2, 112.8, 120.5, 120.7, 123.0, 127.0, 128.3, 129.3, 130.3, 131.7, 133.4, 149.2, 155.8, 162.2, 168.0. *Anal*. Calcd. For $C_{108}H_{78}Cl_6N_{18}O_6S_6$: C, 60.93; H, 3.69; N, 11.84; S, 9.04. Found: C, 60.67; H, 3.52; N, 11.71; S, 8.89.

Synthesis of Poly(pyrazolylthiazoles) 13a,b, 17a,b and 19a,b. ***General procedure.*** To a solution of poly (thiosemicarbazones) **9a,b** or **14a,b** or **15a,b** (1 mmol) in absolute ethanol (25 mL) containing few drops of TEA, 2-bromo-1-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)ethanone (**12**) (3 or 4 or 6 mmol) was added. The reaction mixture was heated under reflux for 5 h. The solid product formed upon cooling was collected and recrystallized from ethanol/DMF to give the corresponding poly(pyrazolylthiazoles) **13a,b**, **17a,b**, and **19a,b**.

1,3,5-Tris((4-((2-(4-(5-methyl-1-phenyl-1H-pyrazol-4-yl)thiazol-2-yl)hydrazono) methyl)phenoxy)methyl)benzene 13a. Orange powder, (70% yield), mp. 220–222°C; IR: (potassium bromide) 3424 (NH), 1601 (C=N) cm^{-1}; ^{1}H-NMR: δ 2.49 (s, 9H, 3 CH_3), 5.20 (s, 6H, 3 CH_2O), 6.84 (s, 3H, 3 thiazole-H), 7.08–7.61 (m, 30H, ArH), 7.91 (s, 3H, CH=N), 7.98 (s, 3H, 3 pyrazole-H), 11.95 (s, 3H, 3 NH); ^{13}C-NMR: δ 11.9, 69.1, 101.4, 115.2, 116.7, 120.2, 124.8, 125.2, 126.4, 127.4, 129.3, 135.4, 137.4, 138.7, 139.2, 141.0, 144.3, 159.1, 168.1; ms: *m/z* (%) 1239 (9.5, M^+), 992 (100), 815 (67.1), 481 (21.9), 249 (12.2), 57 (11.8). *Anal*. Calcd. for $C_{69}H_{57}N_{15}O_3S_3$: C, 66.81; H, 4.63; N, 16.94; S, 7.75. Found: C, 66.69; H, 4.52; N, 16.85; S, 7.58.

1,3,5-Tris((2-(2-(4-(5-methyl-1-phenyl-1H-pyrazol-4-yl) thiazol-2-yl)hydrazono)-methyl)phenoxy)methyl)benzene 13b. Orange powder, (64% yield), mp. > 300°C; IR: (potassium bromide) 3433 (NH), 1597 (C=N) cm^{-1}; ^{1}H-NMR: δ 2.50 (s, 9H, 3 CH_3), 5.30 (s, 6H, 3 CH_2O), 6.86 (s, 3H, 3 thiazole-H), 7.01–7.83 (m, 30H, ArH), 7.90 (s, 3H, 3 CH=N), 8.46 (s, 3H, 3 pyrazole-H), 12.08 (s, 3 NH); ms: *m/z* (%) 1239 (11.4, M^+), 992 (100), 874 (10.7), 249 (12.2), 57 (11.8). *Anal*. Calcd. for $C_{69}H_{57}N_{15}O_3S_3$: C, 66.81; H, 4.63; N, 16.94; S, 7.75. Found: C, 66.71; H, 4.51; N, 16.79; S, 7.93.

1,2,4,5-Tetrakis((4-((2-(4-(5-methyl-1-phenyl-1H-pyrazol-4-yl) thiazol-2-yl)hydrazono)methyl)phenoxy)methyl)benzene 17a. Orange powder, (66% yield), mp. > 300°C; IR: (potassium bromide) 3447 (NH), 1588 (C=N) cm^{-1}; ^{1}H-NMR: δ 2.49 (s, 12H, 4 CH_3), 5.32 (s, 8H, 4 CH_2O), 6.83 (s, 4H, 4 thiazole-H), 7.08–7.61 (m, 38H, ArH), 7.90 (s, 4H, 4 CH=N), 7.98 (s, 4H, 4 pyrazole-H), 11.95 (s, 4H, 4 NH). ^{13}C-NMR: δ 11.9, 66.8, 101.4, 115.2, 116.7, 124.8, 127.5, 127.7, 129.1, 134.8, 135.4, 138.7, 139.2, 140.9, 144.3, 159.0, 168.1. *Anal*. Calcd. for $C_{90}H_{74}N_{20}O_4S_4$: C, 66.40; H, 4.58; N, 17.21; S, 7.88. Found: C, 66.55; H, 4.66; N, 17.07; S, 8.01.

1,2,4,5-Tetrakis((2-((2-(4-(5-methyl-1-phenyl-1H-pyrazol-4-yl)thiazol-2-yl)hydrazono)methyl)phenoxy) methyl)benzene 17b. Orange powder, (68% yield), mp. > 300°C; IR: (potassium bromide) 3434 (NH), 1599 (C=N) cm^{-1}; ^{1}H-NMR: δ 2.49 (s, 12H, 4 CH_3), 5.45 (s, 8H, 4 CH_2O), 6.84 (s, 4H, 4 thiazole-H), 7.00–7.80 (m, 38H, ArH), 7.88 (s, 4H, 4 CH=N), 8.46 (s, 4H, 4 pyrazole-H), 12.06 (s, 4H, 4 NH). *Anal*. Calcd. for $C_{90}H_{74}N_{20}O_4S_4$: C, 66.40; H, 4.58; N, 17.21; S, 7.88. Found: C, 66.17; H, 4.34; N, 17.39; S, 7.65.

1,2,3,4,5,6-Hexakis((4-((2-(4-(5-methyl-1-phenyl-1H-pyrazol-4-yl)thiazol-2-yl)hydrazono)methyl)phenoxy)methyl)benzene 19a. Orange powder, (66% yield), mp. > 300°C; IR: (potassium bromide) 3432 (NH), 1600 (C=N) cm^{-1}; ^{1}H-NMR: δ 2.49 (s, 18H, 6 CH_3), 5.35 (s, 12H, 6 CH_2O), 6.78 (s, 6H, 6 thiazole-H), 7.01–7.53 (m, 54H, ArH), 7.89 (s, 6H, 6 CH=N), 7.94 (s, 6H, 6 pyrazole-H), 11.93 (s, 6H, 6 NH). *Anal*. Calcd. for $C_{132}H_{108}N_{30}O_6S_6$: C, 65.98; H, 4.53; N, 17.49; S, 8.01. Found: C, 65.80; H, 4.69; N, 17.25; S, 7.78.

1,2,3,4,5,6-Hexakis((2-((2-(4-(5-methyl-1-phenyl-1H-pyrazol-4-yl)thiazol-2-yl)hydrazono)methyl)phenoxy)methyl)benzene 19b. Orange powder, (67% yield), mp. 286–288°C; IR: (potassium bromide) 3431 (NH), 1597 (C=N) cm^{-1}; ^{1}H-NMR: δ 2.39 (s, 18H, 6 CH_3), 5.57 (s, 12H, 6 CH_2O), 6.76 (s, 6H, 6 thiazole-H), 6.79–7.80 (m, 54H, ArH), 7.95 (s, 6H, 6 CH=N), 8.35 (s, 6H, 6 pyrazole-H), 11.89 (s, 6H, NH). *Anal*. Calcd. for $C_{132}H_{108}N_{30}O_6S_6$: C, 65.98; H, 4.53; N, 17.49; S, 8.01. Found: C, 66.21; H, 4.76; N, 17.64; S, 8.26.

Synthesis of poly(4,5-dihydro-1,3,4-thiadiazolyl) derivatives 20b, 21a,b, and 22a. ***General procedure.*** A solution of each of poly(thiosemicarbazones) **9b**, **14a**,**b**, or **15a** in acetic anhydride (20 mL) was heated under reflux for 7–10 h. The reaction mixture was then cooled and poured into crushed ice. The solid residue was collected and recrystallized from ethanol/ethylacetate to give poly(4,5-dihydro-1,3,4-thiadi azolyl) derivatives **20**, **21a**,**b**, and **22.**

N,N′,N″-(5,5′,5″-(2,2′,2″-(Benzene-1,3,5-triyltris(methylene) tris(oxy)tris-(benzene-2,1-diyl))tris(4-acetyl-4,5-dihydro-1,3,4-thiadiazole-5,2-diyl))-triacetamide 20. Colorless crystal, (64% yield), mp. 198–200°C; IR: (potassium bromide) 3427 (NH), 1710 (C=O), 1662 (C=O), 1606 (C=N) cm^{-1}; ^{1}H-NMR: δ 2.03, 2.38 (2 s, 18H, 6 CH_3CO), 5.14 (s, 6H, 3 CH_2O), 6.77 (s, 3H, 3 thiadiazole-H), 6.96–7.47 (m, 15H, ArH), 11.69 (s, 3H, 3 NH); ms: *m/z* (%) 951 (11, M^+), 920 (66.4), 800 (100), 400 (24.6), 232 (19), 139 (7.6). *Anal*. Calcd. for $C_{45}H_{45}N_9O_9S_3$: C, 56.77; H, 4.76; N, 13.24; S, 10.10. Found: C, 56.65; H, 4.52; N, 13.09; S, 9.87.

N,N′,N″,N‴-(5,5′,5″,5‴-(4,4′,4″,4‴-(Benzene-1,2,4,5-tetrayltetrakis-(methylene))tetrakis(oxy)tetrakis(benzene-4,1-diyl))tetrakis(4-acetyl-4,5-dihydro-1,3,4-thiadiazole-5,2-diyl)) tetraacetamide 21a. Colorless powder, (68% yield), mp. 242–245°C; IR: (potassium bromide) 3448 (NH), 1705 (C=O), 1644 (C=O), 1605 (C=N) cm^{-1}; ^{1}H-NMR: δ 1.98, 2.24 (2 s, 24H, 8 CH_3CO), 5.43 (s, 8H, 4 CH_2O), 6.92 (s, 4H, 4 thiadiazole-H), 7.26–7.94 (m, 18H, ArH), 11.62 (s, 4H, 4 NH); ^{13}C-NMR: δ 21.7, 22.4, 61.6, 67.2, 112.6, 120.8, 124.1, 128.5, 129.3, 146.6, 153.7, 167.3, 169.1; ms: *m/z* (%) 1242 (10.4, M^+), 1148 (7.5), 991 (100), 815 (67.1), 249 (12.2), 58 (12.8). *Anal*. Calcd. for $C_{58}H_{58}N_{12}O_{12}S_4$: C, 56.02; H, 4.70; N, 13.52; S, 10.32. Found: C, 55.88; H, 4.57; N, 13.28; S, 10.19.

N,N′,N″,N‴-(5,5′,5″,5‴-(2,2′,2″,2‴-(Benzene-1,2,4,5-tetrayltetrakis-(methylene))tetrakis(oxy)tetrakis(benzene-2,1-diyl))tetrakis(4-acetyl-4,5-dihydro-1,3,4-thiadiazole-5,2-diyl)) tetraacetamide 21b. Colorless powder, (66% yield), mp. 203–205°C; IR: (potassium bromide) 3444 (NH), 1728 (C=O), 1669 (C=O), 1607 (C=N) cm^{-1}; ^{1}H-NMR: δ 2.17, 2.38 (2 s, 24H, 8 CH_3CO), 5.20 (s, 8H, 4 CH_2O), 6.77 (s, 4H, 4 thiadiazole), 6.95–7.66 (m, 18H, ArH), 11.69 (s, 4H, NH); ms: *m/z* (%) 1242 (23.4, M^+), 1127 (9.8), 991 (100), 815 (60.9), 297 (11.2), 60 (4.3). *Anal*. Calcd. for $C_{58}H_{58}N_{12}O_{12}S_4$: C, 56.02; H, 4.70; N, 13.52; S, 10.32. Found: C, 55.97; H, 4.66; N, 13.44; S, 10.27.

N,N′,N″,N‴,N⁗,N⁗′-(5,5′,5″,5‴,5⁗,5⁗′-(4,4′,4″,4‴,4⁗,4⁗′-(Benzene-1,2,3,4,5,6-hexaylhexakis(methylene))hexakis(oxy) hexakis(benzene-4,1-diyl))hexakis(4-acetyl-4,5-dihydro-1,3,4-thiadiazole-5,2-diyl))hexa-acetamide 22. Colorless powder, (67% yield), mp. 230–232°C; IR: (potassium bromide) 3433 (NH), 1702 (C=O), 1662 (C=O), 1607 (C=N) cm^{-1}; ^{1}H-NMR: δ 2.02, 2.16 (2 s, 36H, 12 CH_3CO), 5.17 (s, 12H, 6 CH_2O), 6.72 (s, 6H, 6 thiadiazole-H), 6.85–7.11 (m, 24H, ArH), 11.67 (s, 6H, 6 NH); ^{13}C-NMR: δ 21.8, 22.5, 63.6, 65.4, 114.6, 126.6, 134.0, 137.3, 145.9, 157.9, 167.2, 169.2. *Anal*. Calcd. For $C_{84}H_{84}N_{18}O_{18}S_6$: C, 55.25; H, 4.64; N, 13.81; S, 10.54. Found: C, 55.18; H, 4.75; N, 13.72; S, 10.43.

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