Bis([1,3,4]thiadiazolo)[1,3,5]triazinium halides 4:[1] syntheses of azole-substituted guanidines and bis(azolyl)alkanes

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Abstract

The reaction of bis([1,3,4]thiadiazolo)[1,3,5]triazinium bromides **3** with 1*H*[1,2,4]triazole **6**, imidazole **7**, 1-methylimidazole **8**, and benzimidazole **9** in pyridine solution yielded product mixtures containing the highly substituted guanidines *N*-[[(1*H*-azolyl)[1,3,4]thiadiazol-3(2*H*)-yl]methylene][1,3,4]thiadiazol-2-amines **10**, **11**, **12** as main products, and varying amounts 2-[[1,3,4]thiadiazol-2-yl)imino][1,3,4]thiadiazol-3(2*H*-yl][1,3,4]thiadiazol-2(3*H*)-ones **13**, **14**, **15**, and bis[2,3-dihydro[(5-methyl[1,3,4]thiadiazol-2-yl)imino][1,3,4]thiadiazol-3-yl]methanes **16**, **17**, **18** [bis(azolyl)alkanes, "aminals"], which were easily separated by column chromatography. The formation of the products appears to be the result of a novel S_N(ANRORC) reaction cascade which competes with an azole catalyzed reaction. The latter causes partially ring destruction of **3**.

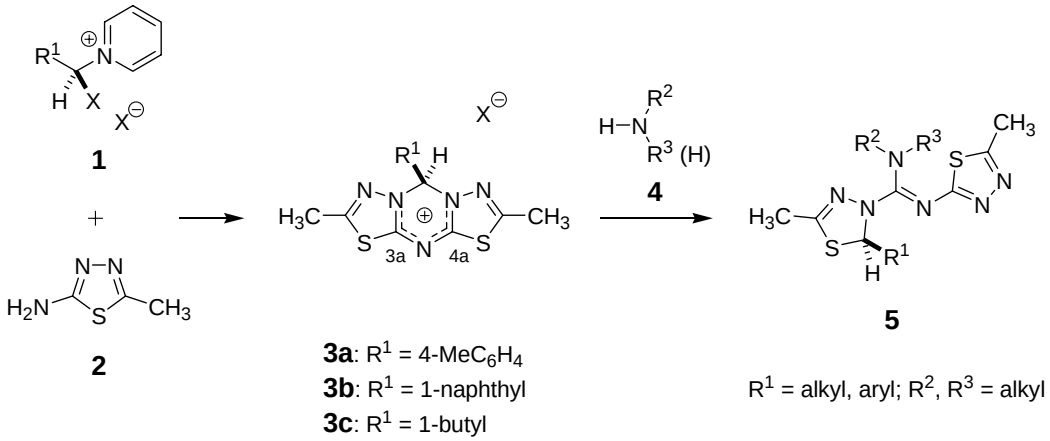
Keywords: Nitrogen-sulfur heterocycles, rearrangement reactions, S_N(ANRORC), guanidines, bis(azolyl)alkanes

Introduction

The reaction of some pyridinium halides **1**[2] with 2-amimo-5-methyl[1,3,4]thiadiazole **2**[3] has been used for the synthesis of 9*H*-bis([1,3,4]thiadiazolo)[2,3-*d*:3',2'-*a*][1,3,5]triazin-8-ium halides **3**.[4] These novel tricyclic 5/6/5-heterocycles possess a remarkable electrophilicity[5,6] at both the 3a-C and 4a-C positions of the central triazinium ring and react with nitrogen nucleophiles such as primary or secondary aliphatic amines **4** to give novel guanidine derivatives **5** in excellent yields (Scheme 1).[7,8]

To our knowledge, there are only few reports on the preparation of guanidine derivatives bearing three different nitrogen heterocycles directly integrated within the guanidine unit (cf. ref. 7, and the literature cited therein). Because the guanidine functionality resembles a key scaffold of numerous natural compounds exhibiting significant biological activity, the number of reagents for their preparation is increasing.[9]

In this paper we describe our studies on the reactivity of 1*H*[1,2,4]triazole **6**, imidazole **7**, 1-methylimidazole **8**, and benzimidazole **9** towards the cationic 5/6/5-heterocycles **3a−c**. The results are compared with those of our recently published investigations.[7]



Scheme 1

Results and Discussion

The reactions of azoles **6–9** with the tricyclic cations **3a–**c were performed in pyridine solution by varying both reaction time and temperature (Table 1). While reactions of primary or secondary aliphatic/alicyclic amines **4** yielded up to 85% of the highly substituted guanidines **5**[7,8] as the result of novel examples for S_N(ANRORC) reaction,[10] the analogous reactions of azoles **6–9** with **3** led to product mixtures. These mixtures contained variable amounts of the novel azole-substituted guanidines **10–12**. Furthermore, the novel aminals **13–15**, and **16–18** (Table 1) were formed. Notably, compounds **16–18** (ca. 12%) had been isolated previously[4] from the product mixture resulting from the initial cyclization reaction, which transforms **1a–c** and **2** into **3**.

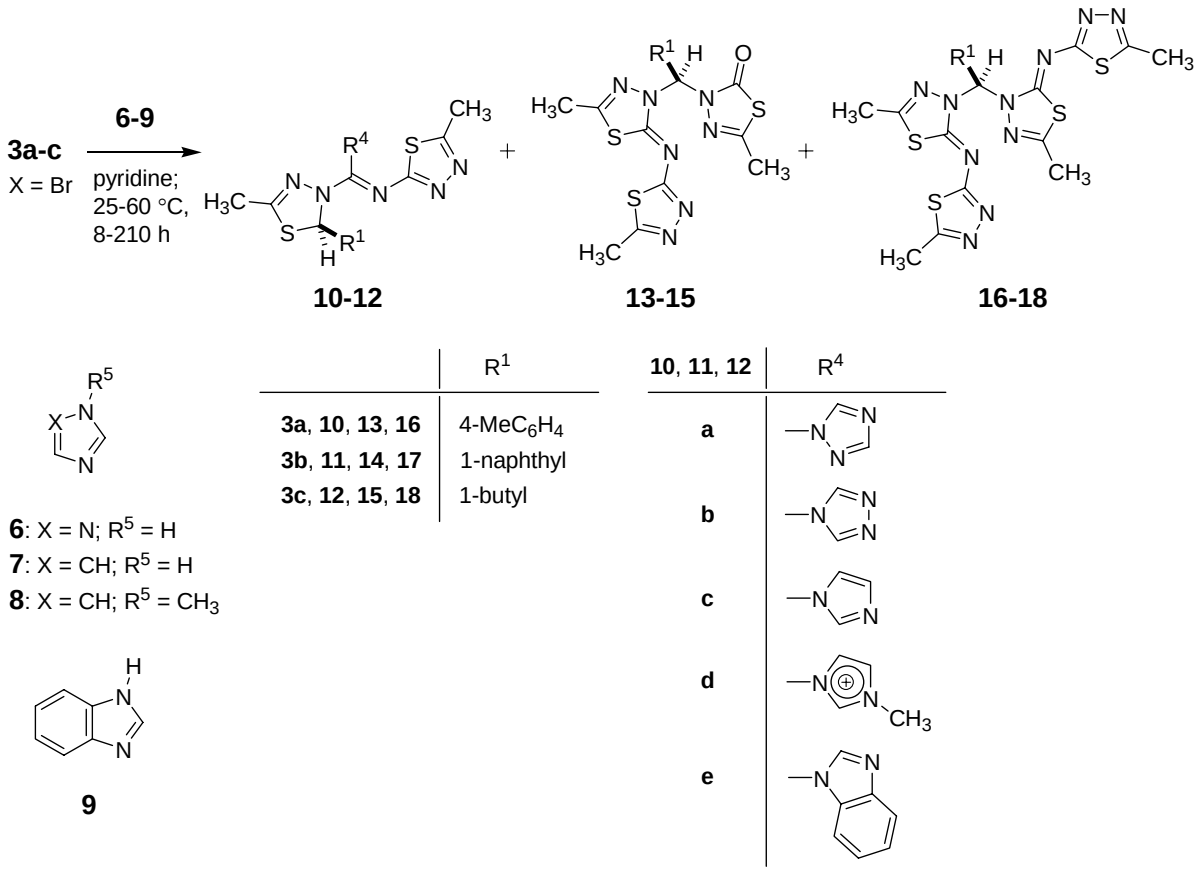
Table 1. Products **10**−**18** from the reaction of **3a–c** with azoles **6–9**

Reaction	Overall yield [%][a]	Products **10**−**18** (yield [%])				Reaction time [h] / Temperature [°C]
3a + **6**	80	**10a** (49)[b]	**10b** (18)[b]	**13** (20)[b]	**16** (5.4)[b]	14 / 60
3b + **6**	92	**11a** (41)[c]	**11b** (26)[c]	**14** (29)[c]	**17** (4.1)[c]	18 / 60
3c + **6**	58	**12a** (8)[b]	**12b** (22)[b]	**15** (25)[b]	**18** (8.0)[b]	8 / 60
3a + **7**	96	**10c** (82)[c]		**13** (17)[c]	**16** (trace)[c]	72 / 25
3b + **7**	93	**11c** (42)[b]		**14** (29)[b]	**17** (7.8)[b]	210 / 25
3c + **7**	85	**12c** (25)[b]		**15** (21)[b]	**18** (27)[b]	40 / 25

Table 1. Continue

3a + 8	85	**10d** (38)[c]	**13** (48)[c]	**16** (trace)[c]	30 / 50
3b + 8	94	**11d** (37)[b]	**14** (39)[b]	**17** (7.8)[b]	30 / 50
3c + 8	91	**12d** (49)[b]	**15** (7)[b]	**18** (17)[b]	15 / 60
3a + 9	97	**10e** (62)[c]	**14** (34)[b]	**16** (trace)[c]	12 / 60
3b + 9	96	**11e** (52)[b]	**13** (38)[c]	**17** (trace)[b]	12 / 55
3c + 9	98	**12e** (83)[c]	**15** (9)[c]	**18** (8)[c]	12 / 60

[a] Based on **3**. [b] Determined by column chromatography. [c] Determined by ^{1}H NMR spectroscopy.

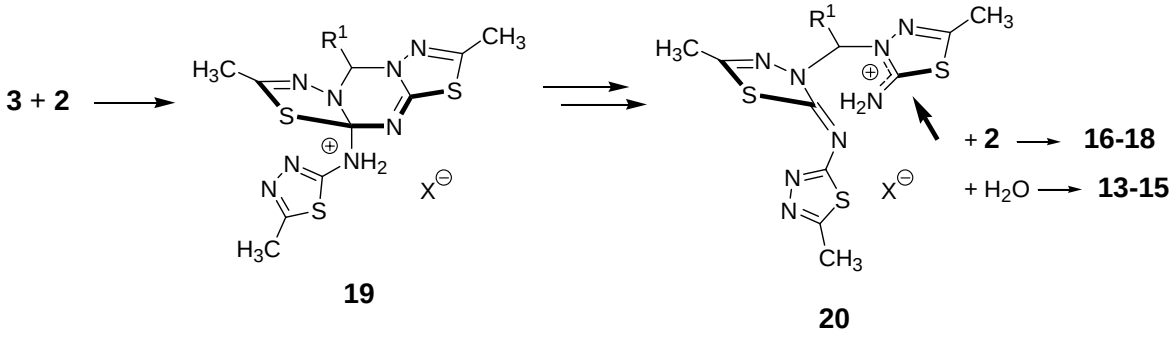


Scheme 2

The formation of products **13–18** (Scheme 2) could be caused by the well-known acid-base properties (bifunctional catalysis) of azoles.[11] In our case, these azole properties give rise to a catalytic hydrolysis reaction of cations **3** (caused by atmospheric moisture) which is followed by ring destruction and by the formation of both the components used for the synthesis of **3** and **1**, i.e. the 2-aminothiadiazole **2** and the corresponding aldehydes (4-methylbenzaldehyde, 1-naphthaldehyde, pentanal). The aldehydes as well as thiadiazole **2** have been qualitatively identified in the reaction mixtures (GC, DC, IR, formation of 2,4-dinitrophenylhydrazones). This

hydrolysis competes with the formation of the main products (guanidines **10–12**) and interferes with the above mentioned S_N(ANRORC) reaction.

As expected, an excess of **2** reacts with cations **3** giving the adduct **19** (Scheme 3): The amine group of **2** reacting as the nucleophile attacks the electrophilic carbon atom 3a-C of **3**. After another multi-step reaction sequence, which presumably includes several intra- and inter-molecular proton migrations followed by a ring-opening reaction, the intermediate **20** is formed; **20** is then attacked either by water − resulting in the formation of **13–15** − or by an additional 2-aminothiadiazole molecule **2** giving rise to the formation of **16–18** with concomitant elimination of NH_4Br.



Scheme 3

The novel compounds **13–15** are representatives of a specific class of bis(azolyl)alkanes[12] ("aminals"). Interestingly, only few derivatives have been reported with 3*H*[1,3,4]thiadiazol-2-one moieties being part of an aminal structure.[13,14] The structure assignments of the guanidines **10–12**, of the novel aminals **13–15**, and of **17** are based on NMR data, mass spectra (CI), IR spectra, and elemental analyses. The formation of the [1,2,4]triazolyl isomers, the guanidines **10a** and **10b**, **11a** and **11b**, **12a** and **12b** is not unexpected owing to the fact that [1,2,4]triazole **6** is an ambident nucleophilic species.[15]

Both the simple separation procedure for the isomeric products by column chromatography and the reliable structure determination by $^1H/^{13}C$ NMR correlation spectroscopy (HMQC, HMBC, DEPT) qualifies these compounds for future investigations. We believe that due to the biological significance of some azoles an increasing interest in the synthesis of such highly azole-substituted compounds can be expected.[16] Especially, we are interested to use such compounds for modifying the biologically active sites of zinc complexes to study the chemistry of zinc by the modulation of its coordination environment.[17] These investigations are underway.

Experimental Section

General Procedures. Column chromatography was carried out on Merck silica gel 60 (0.063–0.200 mm). Melting points were determined on a Büchi Melting Point B-540 or Micro-Melting point apparatus Boetius. NMR spectra were recorded on Bruker DRX 400 and Bruker Avance 250 at 250/400 MHz and 62.5/100 MHz for proton and carbon, respectively; $CDCl_3$ (δ_H 7.24; δ_C 77.0) was used as solvent with TMS as internal standard. The IR-spectra (KBr) were recorded on a Thermo-Nicolet spectrometer AVATAR 320 E.S.P. FT-IR. DCI/H_2O-MS**:** Finnigan MAT SSQ 710. Elemental analyses (C, H, N, S): Leco CHNS-932 and Vario EL III; halogens were determined by the Schöninger method through potentiometric titration.

Compounds **3** (R^1 = 4-MeC_6H_4; 1-naphthyl; 1-butyl), **16** and **18** have been described in the literature.[4] Azoles **6–9** are commercial products (Sigma-Aldrich Fine Chemicals) and were used as acquired**.**

General procedure for the reaction of azoles 6–9 with the 5/6/5-heterocycles 3

To a suspension of **3a−c** (5 mmol) in pyridine (60 mL) was added the azole **6**, **7**, **9** (10.15 mmol) or **8** (5.10 mmol) (reaction temperature and time cf. Table 1). The suspension gradually changed to a clear solution. The solvent was evaporated in vacuo, and the residue was washed with ice water. The resulting crude product mixture was subjected to column chromatography (eluent: ethyl acetate). The separation of the products **10–18** was monitored by pre-coated plastic sheets for TLC (Polygram® SIL G/UV_{254}, 0.2 mm silica gel).

5-Methyl-*N*-[[5-methyl-2-(4-methylphenyl)[1,3,4]thiadiazol-3(2H)-yl](1*H*[1,2,4]triazol-1-yl)-methylene][1,3,4]thiadiazol-2-amine (10a). White powder, mp 238 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.38 (3H, s), 2.50 (3H, s), 2.68 (3H, s), 7.20–7.29 (AA', BB', 2,6-, 3,5-H C_6H_4), 8.04 (1H, s, triazol-1-yl), 8.30 (1H, s, triazol-1-yl), 8.34 (1H, s, thiadiazol-3(2H)-yl). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 16.7, 17.2, 21.6, 71.9, 127.8, 130.2, 130.9, 140.9, 144.7, 152.6, 153.0, 160.4, 161.2, 171.6. IR (KBr): $\tilde{\nu}$ 1572 cm^{-1} (C=N exocyclic). CIMS: *m/z* (%) 385 (40) [MH^+]. Anal. Calcd for $C_{16}H_{16}N_8S_2$ (384.47): C, 49.98; H, 4.19; N, 29.14; S, 16.68. Found: C, 49.90; H, 4.16; N, 28.76; S, 16.60.

5-Methyl-*N*-[[5-methyl-2-(4-methylphenyl)[1,3,4]thiadiazol-3(2*H*)-yl](4*H*[1,2,4]triazol-4-yl)-methylene][1,3,4]thiadiazol-2-amine (10b). White powder, mp 198 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.40 (3H, s), 2.50 (3H, s), 2.69 (3H, s), 7.24, 7.27 (AA', 2,6-H C_6H_4), 7.06, 7.09 (X,X', 3,5-H C_6H_4), 8.30 (1H, s, thiadiazol-3(2H)-yl); 8.45 (2H, s, triazol-4-yl). ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.8, 17.2, 21.6, 67.4, 127.2, 130.2, 130.9, 140.5, 2x143.0, 153.9, 160.6, 161.5, 171.2; IR (KBr): $\tilde{\nu}$ 1574 cm^{-1} (C=N exocyclic). CIMS: *m/z* (%) 385 (30) [MH^+]. Anal. Calcd for $C_{16}H_{16}N_8S_2$ (384.47): C, 49.98; H, 4.19; N, 29.14; S, 16.68. Found: C, 49.71; H, 4.33; N, 29.14; S, 16.68.

***N*-[1*H*-Imidazol-1-yl[5-methyl-2-(4-methylphenyl)[1,3,4]thiadiazol-3(2*H*)-yl]methylene]-5-methyl[1,3,4]thiadiazol-2-amine (10c).** Yellow powder, mp 148 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.34 (3H, s), 2.44 (3H, s), 2.64 (3H, s), 7.19, 7.16, (AA', 2,6-H C_6H_4), 7.01, 6.99, (X,X', 3,5-H C_6H_4), 7,76, 7.16, 7.08 (AMX, $^3J = {}^4J$ = 1.2 Hz, 3H, imidazol-1-yl,), 8.09 (1H, s, thiadiazol-3(2H)-yl). ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.3, 16.8, 21.1, 68.4, 118.9, 126.8, 2x129.5, 131.8, 137.5, 139.3, 152.4, 160.4, 160.6, 171.2. IR (KBr): $\tilde{\nu}$ 1569 cm^{-1} (C=N exocyclic). CIMS: *m/z* (%384(18) [MH$^+$].Anal. Calcd for $C_{17}H_{17}N_7S_2$ (383.48): C, 53.24; H, 4.47; N, 25.57; S, 16.72. Found: C, 52.88; H, 4.80; N, 25.61; S, 16.88.

1-Methyl-3-[[5-methyl-2-(4-methylphenyl)[1,3,4]thiadiazol-3(2*H*)-yl][(5-methyl[1,3,4]thiadiazol-2-yl)imino]methyl]-1*H*-imidazol-3-ium bromide (10d). Yellow powder, mp 138 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.34 (3H, s), 2.49 (3H, s), 2.62 (3H, s), 4.20 (3H, s), 7.22–7.14 (AA'BB', 2,6-, 3,5-H C_6H_4), 10.32, 7.58, 7.35 (3H, imidazol-1-yl, coupling not resolved), 8.39 (1H, s) ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 16.3, 17.1, 21.2, 37.5, 70.4, 120.9, 124.1, 127.5, 128.7, 130.1, 138.0, 140.6, 154.2, 159.7, 161.7, 170.5. IR (KBr): $\tilde{\nu}$ 1578 cm^{-1} (C=N exocyclic). CIMS: *m/z*(%): 478 (9) [M$^+$]. Anal. Calcd for $C_{18}H_{20}BrN_7S_2 \cdot H_2O$ (496.44): C, 43.55; H, 4.47; Br, 16.10; N, 19.75; S, 12.92. Found: C, 43.26; H, 4.64; Br, 15.88; N, 19.82; S, 13.41.

***N*-[1*H*-Benzimidazol-1-yl[5-methyl-2-(4-methylphenyl)[1,3,4]thiadiazol-3-(2*H*)yl]-methylene]-5-methyl[1,3,4]thiadiazol-2-amine (10e).** Beige powder, mp 197 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.37 (3H, s), 2.41 (3H, s), 2.66 (3H, s), 7.23, 7.21 (AA' 2,6-H C_6H_4), 7.14, 7.12 (X,X', 3,5-H C_6H_4), 7.26–7.83 (4H, m), 8.41 (1H, s, thiadiazol-3(2H)-yl), 8.05 (1H, s, benzimidazol-1-yl). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 16.3, 16.8, 21.1, 67.0, 110.5, 120.5, 122.9, 123.5, 127.1, 129.7, 130.9, 133.4, 139.5, 143.0, 143.5, 152.6, 160.4, 160.6, 171.3. IR (KBr): $\tilde{\nu}$ 1572 cm^{-1} (C=N exocyclic). CIMS: *m/z* (%) 434 (7) [MH$^+$]. Anal. Calcd for $C_{21}H_{19}N_7S_2$ (433.54): C, 58.18; H, 4.42; N, 22.61; S, 14.79. Found: C, 58.31; H, 4.45; N, 22.48; S, 14.52.

5-Methyl-*N*-[[5-methyl-2-(1-naphthyl)[1,3,4]thiadiazol-3(2*H*)-yl](1*H*[1,2,4]triazol-1-yl)methylene][1,3,4]thiadiazol-2-amine (11a). Pale yellow powder, mp 202 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.48 (3H, s), 2.69 (3H, s), 7.38–8.01 (7H, m), 8.14 (1H, s, triazol-1-yl), 8.10 (1H, s, triazol-1-yl), 8.95 (1H, s, thiadiazol-3(2H)-yl). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 16.9, 17.3, 69.7, 122.5,125.5, 126.2, 126.9, 128.2, 128.4, 129.6, 130.7, 131,3, 134.2, 145.1, 152.1, 152.9, 160.0, 161.4, 171.5. IR (KBr): $\tilde{\nu}$ 1575 cm^{-1} (C=N exocyclic). CIMS: *m/z* 421 (26) [MH$^+$]. Anal. Calcd for $C_{19}H_{16}N_8S_2$ (420.50): C, 54.27; H, 3.84; N, 26.65; S, 15.25. Found: C, 54.53; H, 3.96; N, 26.44; S, 15.07.

5-Methyl-*N*-[[5-methyl-2-(1-naphthyl)[1,3,4]thiadiazol-3(2*H*)-yl](4*H*[1,2,4]triazol-4-yl)methylene][1,3,4]thiadiazol-2-amine (11b). Pale yellow powder, mp 239 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.43 (3H, s), 2.68 (3H, s), 7.25–7.99 (7H, m), 8.40 (1H, s, triazol-4-yl), 8.78 (2H, s, thiadiazol-3(2H)-yl). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 16.7, 17.2, 66.0, 122.1, 125.4, 125.9, 127.0, 128.4, 129.3, 129.8, 130.2, 131.5, 134.2, 2x142.7, 153.7, 159.9, 161.7, 171.2. IR (KBr): $\tilde{\nu}$ 1578 cm^{-1} (C=N exocyclic). CIMS: *m/z* (%) 421 (6) [MH$^+$]. Anal. Calcd for $C_{19}H_{16}N_8S_2$ (420.50): C, 54.27; H, 3.84; N, 26.65; S, 15.25. Found: C, 53.78; H, 4.04; N, 26.83; S, 15.26.

***N*-[1H-Imidazol-1-yl[5-methyl-2-(1-naphthyl)[1,3,4]thiadiazol-3(2*H*)-yl]methylene]-5-methyl-[1,3,4]thiadiazol-2-amine (11c).** Beige powder, mp 219–221 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.39 (3H, s), 2.66 (3H, s), 7.22–7.92 (7H, m), 7.91, 7.16, 7.12 (3H, imidazol-1-yl, coupling not resolved), 8.65 (1H, s, thiadiazol-3(2H)-yl). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 16.3, 16.8, 67.2, 118.8, 122.1, 125.1, 125.6, 126.3, 127.6, 129.2, 130.0, 130.2, 130.4, 130.6, 133.8, 137.3, 152.4, 159.8, 160.9, 171.3. IR (KBr): $\tilde{\nu}$ 1572 cm^{-1} (C=N exocyclic). CIMS: *m/z* (%) 420 (68) [MH^+]. Anal. Calcd for $C_{20}H_{17}N_7S_2$ (419.52): C, 57.26; H, 4.08; N, 23.37; S, 15.28. Found: C, 57.06; H, 4.29; N, 23.14; S, 15.17.

1-Methyl-3-[[5-methyl-2-(1-naphthyl)[1,3,4]thiadiazol-3(2*H*)-yl]](5-methyl[1,3,4]thiadiazol-2-yl)imino]methyl]-1*H*-imidazol-3-ium bromide (11d). Beige powder, mp 187 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.46 (3H, s), 2.65 (3H, s), 4.28 (3H, s), 7.32–7.99 (7H, m), 10.58, 7.57, 7.34 (3H, imidazol-1-yl, coupling not resolved), 8.97 (1H, s, thiadiazol-3(2H)-yl). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ16.9, 17.7, 37.9, 69.2, 121.6, 122.2, 125.1, 125.5, 126.4, 127.2, 128.0, 128.7, 129.7, 130.2, 132.0, 134.1, 138.2, 154.9, 159.8, 162.0, 170.9. IR (KBr): $\tilde{\nu}$ 1579 cm^{-1} (C=N exocyclic). CIMS: *m/z* (%) 432 (3) [M^+]. Anal. Calcd for $C_{21}H_{20}BrN_7S_2 \cdot H_2O$ (532.47): C, 47.37; H, 4.16; Br, 15.01; N, 18.41; S, 12.04. Found: C, 47.07; H, 4.03; Br, 15.33, N, 18.82; S, 12.16.

***N*-[1*H*-Benzimidazol-1-yl[5-methyl-2-(1-naphthyl)[1,3,4]thiadiazol-3(2*H*)-yl]methylene]-5-methyl[1,3,4]thiadiazol-2-amine (11e).** Pale yellow powder, mp 282 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.44 (3H, s), 2.67 (3H, s), 7.26–7.96 (12H, m), 8.95 (1H, s, thiadiazol-3(2H)-yl). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 16.7, 17.2, 66.0, 110.3, 121.1, 122.6, 123.5, 124.2, 125.5, 126.2, 126.9, 128.1, 129.5, 129.6, 130.8, 131.2, 133.5, 134.3, 143.2, 144.1, 153.1, 160.4, 161.2, 171.7. IR (KBr): $\tilde{\nu}$ 1572 cm^{-1} (C=N exocyclic). CIMS: *m/z* (%) 470 (5) [MH^+]. Anal. Calcd for $C_{24}H_{19}N_7S_2$ (469.58); C, 61.39; H, 4.08; N, 20.88; S, 13.65. Found: C, 61.21; H, 4.25; N, 20.63; S, 13.38.

5-Methyl-*N*-[[5-methyl-2-(1-butyl)[1,3,4]thiadiazol-3(2*H*)-yl](1*H*[1,2,4]triazol-1-yl)methylene][1,3,4]thiadiazol-2-amine (12a). White powder, mp 139 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.92 (3H, t, *J* = 7.3 Hz), 1.30–1.45 (4H, m), 2.52–2.66 (2H, m), 2.50 (3H, s), 2.67 (3H, s), 6.96 (1H, t, *J* = 7.7 Hz, thiadiazol-3(2H)-yl), 7.96 (1H, s, triazol-1-yl), 8.43 (1H, s, triazol-1-yl). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 13.7, 16.7, 16.8, 21.8, 27.2, 32.0, 68.8, 143.4, 2x152.1, 160.0, 160.2, 171.0. IR (KBr): $\tilde{\nu}$ 1577 cm^{-1} (C=N exocyclic). CIMS: *m/z* (%) 351 (100) [MH^+]. Anal. Calcd for $C_{13}H_{18}N_8S_2$ (350.45): C, 44.55; H, 5.18; N, 31.97; S, 18.30. Found: C, 44.94; H, 5.24; N, 31.85; S, 18.30.

5-Methyl-*N*-{[5-methyl-2-(1-butyl)[1,3,4]thiadiazol-3(2*H*)-yl](4*H*[1,2,4]triazol-4-yl)methylene]-[1,3,4]thiadiazol-2-amine (12b). White powder, mp 189 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.94 (3H, t, *J* = 7.2 Hz), 1.33–1.49 (4H, m), 2.42–2.60 (2H, m), 2.50 (3H, s), 2.69 (3H, s), 6.85 (1H, t, *J* = 8.2 Hz, thiadiazol-3(2H)-yl), 8.46 (2H, s, triazol-4-yl). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 14.1, 16.7, 16.8, 22.3, 27.6, 33.3, 65.4, 2x141.3,153.0, 160.1, 160.2, 170.9. IR (KBr): $\tilde{\nu}$ 1577 cm^{-1} (C=N exocyclic). CIMS: *m/z* (%) 351 (63) [MH^+]. Anal. Calcd for $C_{13}H_{18}N_8S_2$ (350.45): C, 44.55; H, 5.18; N, 31.97; S, 18.30. Found: C, 44.56; H, 5.44; N, 31.55; S, 18.35.

***N*-[1*H*-Imidazol-1-yl[5-methyl-2-(1-butyl)[1,3,4]thiadiazol-3(2*H*)-yl]methylene]-5-methyl-[1,3,4]thiadiazol-2-amine (12c).** White powder, mp 150 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.87 (3H, t, *J* = 7.2 Hz), 1.19–1.42 (4H, m), 2.33–2.39 (2H, m), 2.45 (3H, s), 2.63 (3H, s), 6.76 (1H, t, *J* = 7.7 Hz, thiadiazol-3(2H)-yl), 7.77, 7.16, 7.00 (3H, imidazol-1-yl, coupling not resolved). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 13.7, 16.2, 16.6, 21.9, 27.4, 32.9, 66.7, 117.2, 129.6, 136.4, 152.0, 160.2, 160.4, 171.4. IR (KBr): $\tilde{\nu}$ 1573 cm^{-1} (C=N exocyclic). CIMS: *m/z* (%) 350 (100) [MH^+]. Anal. Calcd for $C_{14}H_{19}N_7S_2$ (349.47): C, 48.12; H, 5.48; N, 28.06; S, 18.35. Found: C, 48.02; H, 5.54; N, 27.96; S, 18.42.

1-Methyl-3-[[5-methyl-2-(1-butyl)[1,3,4]thiadiazol-3(2*H*)-yl][(5-methyl[1,3,4]thiadiazol-2-yl)-imino]methyl]-1*H*-imidazol-3-ium bromide (12d). White powder, mp 193 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.93 (3H, t, *J* = 7.2 Hz), 1.39–1.42 (4H, m), 2.63–2.69 (2H, m), 2.60 (3H, s), 2.73 (3H, s), 4.30 (3H, s), 7.07 (1H, t, *J* = 6.1 Hz, thiadiazol-3(2H)-yl), 7.46 (1H, d, *J* = 1.8 Hz, imidazol-1-ylium), 7.54 (1H, d, *J* = 1.6 Hz, imidazol-1-ylium), 10.70 (1H, s, imidazol-1-ylium). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 13.7, 16.3, 16.9, 21.8, 26.9, 32.4, 37.2, 69.0, 119.5, 124.2, 137.5, 153.6, 159.8, 161.5, 170.5. IR (KBr): $\tilde{\nu}$ 1579 cm^{-1} (C=N exocyclic). CIMS: *m/z* (%) 364 (9) [M^+]. Anal. Calcd for $C_{15}H_{22}BrN_7S_2$ (444.41): C, 40.54; H, 4.99; Br 17.98; N, 22.06; S, 14.43. Found: C, 39.82; H, 4.99; Br, 17.54; N, 21.92; S, 14.18.

***N*-[1*H*-Benzimidazol-1-yl[5-methyl-2-(1-butyl)[1,3,4]thiadiazol-3-(2*H*)-yl]methylene]-5-methyl-[1,3,4]thiadiazol-2-amine (12e).** White powder, mp 214 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.88 (3H, t, *J* = 7.1 Hz), 1.33–1.46 (4H, m), 2.55–2.78 (2H, m), 2.45 (3H, s), 2.67 (3H, s), 7.08–7.14 (1H, t, *J* = 7.9 Hz, thiadiazol-3(2H)-yl), 7.24–7.32 (2H, m), 7.73–7.80 (2H, m), 8.27 (1H, s). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 14.1, 22.3, 27.8, 32.9, 16.7, 17.1, 66.1, 111.2, 120.7, 123.2, 123.8, 141.7, 133.7, 143.5, 152.7, 160.6, 160.7, 171.8. IR (KBr): $\tilde{\nu}$ 1576 cm^{-1} (C=N exocyclic). CIMS: *m/z* (%) 400 (40) [MH^+]. Anal. Calcd for $C_{18}H_{21}N_7S_2$ (399.53): C, 54.11; H, 5.30; N, 24.54; S, 16.05. Found: C, 54.34; H, 5.51; N, 24.37; S, 15.92.

5-Methyl-3-[5-methyl-2-[(5-methyl[1,3,4]thiadiazol-2-yl)imino][1,3,4]thiadiazol-3(2*H*)-yl](4-methylphenyl)methyl[1,3,4]thiadiazol-2(3*H*)-one (13). Yellow powder, mp 150 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.33 (3H, s), 2.38 (3H, s), 2.45 (3H, s), 2.62 (3H, s), 7.18, 7.15 (AA'BB' 2,6-, 3,5-H C_6H_4), 8.13 (1H, s). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 16.2, 16.8, 18.4, 21.1, 67.5, 127.4, 127.8, 131.1, 138.9, 149.1, 151.3, 159.8, 160.6, 169.8, 171.5. IR (KBr): $\tilde{\nu}$ 1683 cm^{-1}, C=O, 1573 cm^{-1} (C=N exocyclic). CIMS: *m/z* (%) 432 (48) [MH^+]. Anal. Calcd for $C_{17}H_{17}N_7OS_3$ (431.54): C, 47.31; H, 3.97; N, 22.72; S, 22.29. Found: C, 47.66; H, 4.35; N, 22.70; S, 22.02.

5-Methyl-3-[5-methyl-2-[(5-methyl[1,3,4]thiadiazol-2-yl)imino][1,3,4]thiadiazol-3(2*H*)-yl](1-naphthyl)methyl[1,3,4]thiadiazol-2(3*H*)-one (14). Yellow powder, mp 252 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.35 (3H, s), 2.38 (3H, s), 2.63 (3H, s), 7.41–7.89 (7H, m, naphthyl), 8.64 (1H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.2, 16.8, 18.4, 66.2, 122.2, 125.1, 125.2, 126.0,127.3, 129.0, 130.0, 130.1, 130.2, 133.6, 149.6, 151.4, 159.2, 160.8, 169.9, 171.5. IR (KBr): $\tilde{\nu}$ 1686, (C=O), 1573 cm^{-1} (C=N exocyclic). CIMS: *m/z* (%) 468 (35) [MH^+]. Anal. Calcd for $C_{20}H_{17}N_7OS_3$ (467.58): C, 51.38; H, 3.66; N, 20.97; S, 20.57. Found: C, 51.01; H, 3.93; N, 20.95; S, 20.17.

5-Methyl-3-[1-[5-methyl-2-[(5-methyl[1,3,4]thiadiazol-2-yl)imino][1,3,4]thiadiazol-3(2*H*)-yl]-pentyl][1,3,4]thiadiazol-2(3*H*)-one (15). Yellow powder, mp 98 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.88 (3H, t, *J* = 7.2), 1.22–1.42 (4H, m), 2.34 (2H, m), 2.36 (3H,s), 2.47 (3H, s), 2.61 (3H, s), 6.85 (1H, t, *J* = 7.6). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 13.8, 16.3, 16.8, 18.4,22.1, 27.1, 32.2, 66.4, 149.0, 150.9, 159.5, 160.4, 169.9, 171.6. IR (KBr): $\tilde{\nu}$ 1676 (C=O), 1575 cm^{-1} (C=N exocyclic). CIMS: *m/z* (%) 398 (100) [MH^+]. Anal. Calcd for $C_{14}H_{19}N_7OS_3$ (349.47): C, 42.30; H, 4.82; N, 24.66; S, 24.19. Found: C, 42.49; H, 4.62; N, 24.64; S, 24.13.

Bis[2,3-dihydro-5-methyl-[(5-methyl[1,3,4]thiadiazol-2-yl)imino][1,3,4]thiadiazol-3-yl](1-naphthyl)methane (17). White powder, mp 239 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.34 (6H, s), 2.57 (6H, s), 7.35−7.86 (7H, m, naphthyl), 9.01 (1H, s).^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 16.6, 17.3, 68.6, 122.9, 125.6, 125.8, 126.5, 127.7, 129.4, 130.4, 130.6, 130.9, 134.1, 152.0, 159.9, 161.0, 172.0. IR (KBr): $\tilde{\nu}$ 1578 cm^{-1} (C=N exocyclic). CIMS: *m/z* (%) 565 (9) [MH^+]; 352 (28) [$C_{17}H_{14}N_5S_2$]. Anal. Calcd for $C_{23}H_{20}N_{10}S_4$ (564.71): C, 48.92; H, 3.57; N, 24.80; S, 22.71. Found: C, 48.73; H, 3.61; N, 24.52; S, 22.43.

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