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4*H*-[1,2,3]-THIADIAZOLO[3,4-*a*]BENZIMIDAZOLIUMIDES

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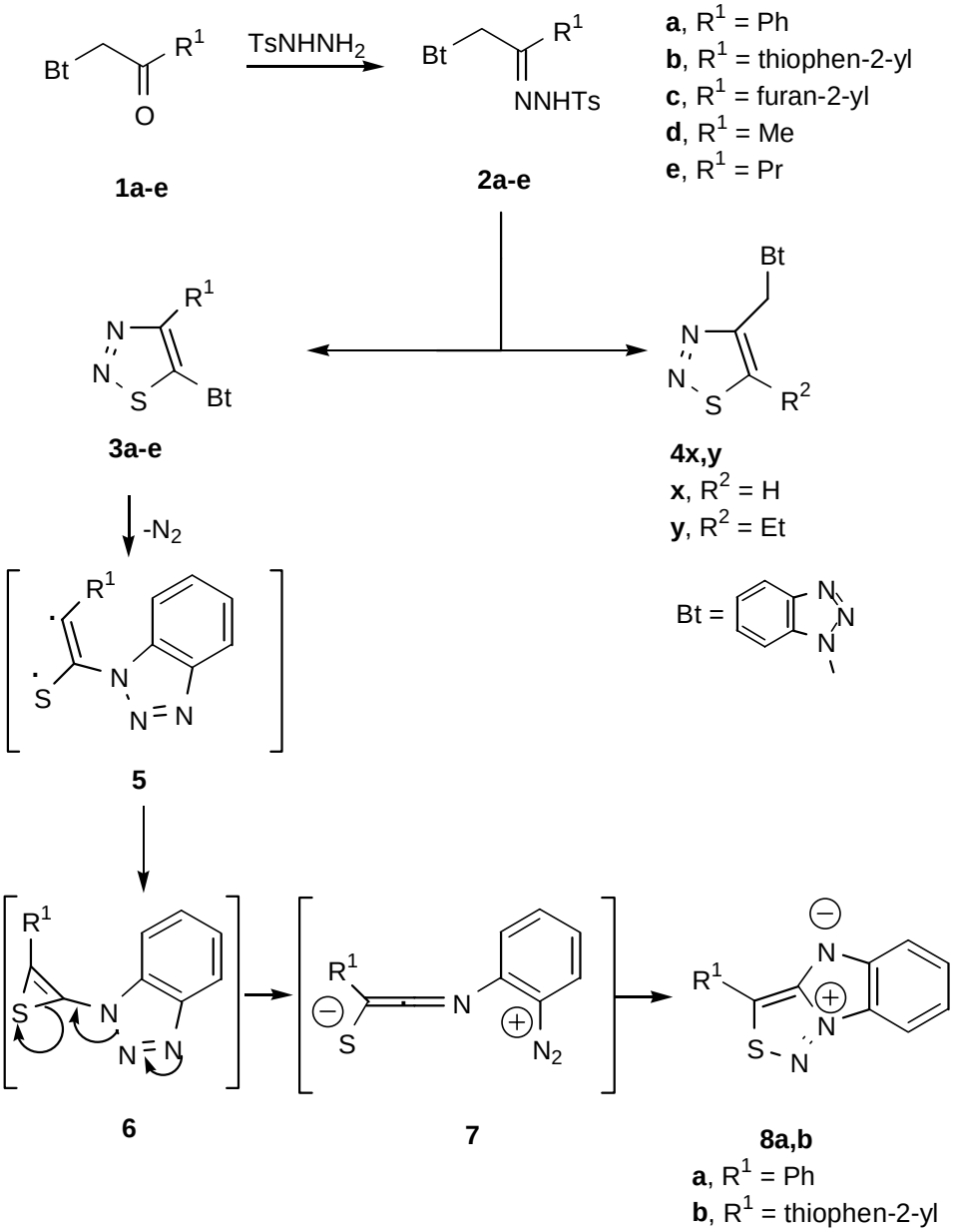
Abstract – Thermal rearrangements of 1-(1,2,3-thiadiazol-5-yl)-1*H*-1,2,3-benzotriazoles afford zwitterionic 3-phenyl-4*H*-[1,2,3]thiadiazolo[3,4-*a*]benzimidazol-2-ium-4-ides by intramolecular trapping of thiirene intermediates.

Bicyclic (5,5)-fused ring systems with one ring-junction nitrogen atom and one sulfur and two nitrogens as additional heteroatoms include (i) thiazolo-[4,3-*c*][1,2,4]-, -[2,3-*c*][1,2,4]-, -[3,2-*c*][1,2,3]-, -[3,4-*b*][1,2,4]-, -[2,3-*b*][1,3,4]-, -[3,2-*b*][1,2,4]triazoles; (ii) imidazo-[1,2-*d*][1,2,4]-, -[5,1-*b*][1,3,4]-thiadiazoles, -[2,1-*b*][1,3,4]- and -[1,2-*b*][1,2,4]-thiadiazoles. Such compounds have been found active as herbicides, were screened for antifungal activity, show insecticidal and pharmacological activity, and have found applications as liquid crystals and in photography. Comprehensive reviews about the synthesis, properties and structures through 1995 are available.[1a,b] However, no imidazo[3,4][1,2,3]thiadiazoles or their benzo-fused analogues have previously been reported. We now show that thermal intramolecular rearrangement of 1-(1,2,3-thiadiazol-5-yl)-1*H*-1,2,3-benzotriazoles leads to novel 4*H*-[1,2,3]thiadiazolo[3,4-*a*]benzimidazol-2-ium-4-ides.

Results and Discussion

Tosylhydrazones (**2a-e)** were prepared from readily accessible α-benzotriazolyl alkyl ketones (**1a-e)**[2a-d] according to the procedure reported earlier.[3] Subsequent cyclization with thionyl chloride converted **2a-c**

into the 1,2,3-thiadiazoles (**3a-c)** in good yields (Scheme 1), but aliphatic derivatives (**2d,e)** gave mixtures of the 1-(1,2,3-thiadiazol-5-yl)-1*H*-1,2,3-benzotriazoles (**3d,e)** with 1-(1,2,3-thiadiazol-4-ylmethyl)-1*H*-1,2,3-benzotriazoles (**4x,y)**. Compound (**4x)** was isolated as the hydrochloride salt.



Scheme 1

On heating (DMF, 150-170 °C), compounds (**3a,b)** evolved nitrogen and afforded 3-R-4*H*-[1,2,3]thiadiazolo[3,4-*a*]benzimidazol-2-ium-4-ides (**8a,b)** with structures supported by ^{1}H and ^{13}C NMR spectra, and elemental analyses. Structure (**8a)** was confirmed by single crystal X-Ray crystallography: it crystallizes as a hemi-hydrate in the monoclinic space group C2/c. Figure 1 shows a perspective view of **8a** with selected bond lengths and angles. Analysis of the bonding geometry (Figure 1) suggests that, as is commonly the case in non-classical heteropentalene structures,[4] the structure of compound (**8a)** cannot be adequately represented by a single resonance contributor. Coplanarity of the phenyl ring with the pentalene

ring system (angle between mean planes = 1.0(1)°) suggests conjugation between these two ring systems and significant localization of electron density at C1. The water solvate molecule lies on a crystallographic two-fold rotation axis and serves to connect adjacent molecules of **8a** in the crystal lattice by means of linear hydrogen bonds [H1···N3 = 2.06(2) Å, O1···N3 = 2.909(1) Å, O1-H1···N3 = 170(1) °C].

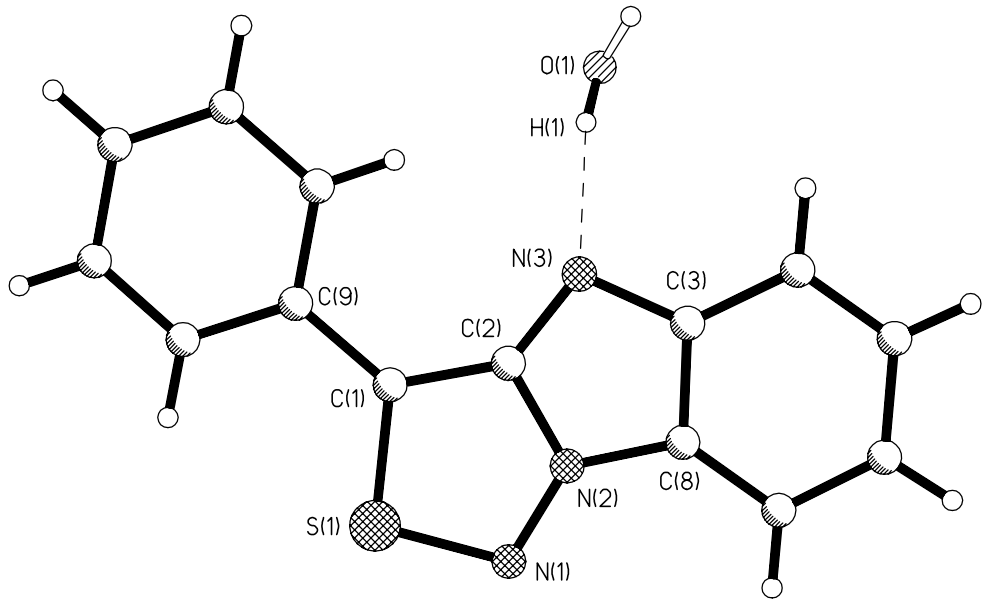


Figure 1. Perspective view and crystallographic atom labeling of the X-Ray crystal structure of **8a**. Selected bond lengths (Å) and angles (°): S1-N1 1.642(1), S1-C1 1.702(1), N1-N2 1.342(2), N2-C2 1.405(2), N2-C8 1.388(2), N3-C2 1.339(2), N3-C3 1.386(2), C1-C2 1.412(2), C1-C9 1.462(2), C3-C8 1.467(2), N1-S1-C1 98.57(6), N2-N1-S1 105.72(8), N1-N2-C8 132.8(1), N1-N2-C2 119.7(1), C8-N2-C2 107.5(1), C2-N3-C3 103.7(1), C2-C1-C9 128.4(1), C2-C1-S1 107.0(1), C9-C1-S1 124.6(1), N3-C2-N2 112.4(1), N3-C2-C1 138.6(1), N2-C2-C1 109.0(1), N3-C3-C8 112.8(1), N2-C8-C3 103.6(1).

Formation of the initial diradical (**5)** and its isomerization to 1-(3-substituted 2-thiirenyl)-1*H*-1,2,3-benzotriazole (**6)**, could be followed by opening the thiirene and benzotriazole rings to **7**. Final intramolecular [3+2] cycloaddition affords the zwitter-ionic products (**8a,b)** (Scheme 1). This is the first chemical evidence for the *intramolecular* heterocyclization of thiirene intermediates.

In conclusion, a novel transformation of 1-(1,2,3-thiadiazol-5-yl)-1*H*-1,2,3-benzotriazoles leading to 3-R-4*H*-[1,2,3]thiadiazolo[3,4-*a*]benzimidazol-2-ium-4-ides is described.

EXPERIMENTAL

Compounds (**2a,b, 3a,b)** were prepared as described in.[3]

General methods. Melting points were determined on a hot stage apparatus without correction. NMR spectra were recorded on a Varian Gemini-300 spectrometer at 300 MHz for ^{1}H and 75 MHz for ^{13}C NMR spectra with $CHCl_3$-*d* as a solvent if not stated otherwise. Chemical shift values are reported as δ downfield from TMS as the internal standard for ^{1}H and a solvent as the internal standard for ^{13}C.

General Procedure for the Preparation of Compounds (2c-e). A mixture of the corresponding 2-(1*H*-1,2,3-benzotriazol-1-yl)-1-R-1-ethanone (**1c-e)** (4.12 mmol) and *p*-tosylhydrazine (4.12 mmol) in benzene (50 mL) was heated under reflux overnight. The reaction mixture was cooled to rt, the crystalline product was filtered off and recrystallized from benzene.

***N'*-[2-(1*H*-1,2,3-Benzotriazol-1-yl)-1-(furan-2-yl)ethylidene]-4-methylbenzenesulfonhydrazide (2c).** White microcrystals, yield 72%, mp 205-207 °C; ^{1}H NMR δ 2.48 (s, 3H), 5.65 (s, 2H), 6.46 (t, *J* = 1.8 Hz, 1H), 7.07 (d, *J* = 3.9 Hz, 1H), 7.19–7.35 (m, 5H), 7.55 (d, *J* = 1.5 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 2H), 7.97 (d, *J* = 8.2 Hz, 1H), 9.87 (s, 1H); ^{13}C NMR δ 21.7, 52.2, 110.4, 112.0, 115.9, 119.8, 124.0, 127.5, 128.1, 129.7, 132.9, 133.4, 135.3, 144.4, 144.8, 146.2, 146.6. Anal. Calcd for $C_{19}H_{17}N_5O_3S$: C, 57.71; H, 4.34; N, 17.71. Found: C, 58.05; H, 4.71; N, 17.87.

***N'*-[2-(1*H*-1,2,3-Benzotriazol-1-yl)-1-methylethylidene]-4-methylbenzenesulfonhydrazide (2d).** White microcrystals, yield 84%, mp 208–209 °C; ^{1}H NMR (DMSO-d_6) δ 1.77 (s, 3H), 2.37 (s, 3H), 5.43 (s, 2H), 7.21 (d, *J* = 8.2 Hz, 1H), 7.33–7.42 (m, 5H), 8.04 (d, *J* = 8.4 Hz: 1H), 10.39 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 14.7, 21.1, 53.3, 110.6, 119.2, 123.9, 127.3, 127.4, 129.3, 133.1, 135.6, 143.2, 145.2, 151.9. Anal. Calcd for $C_{16}H_{17}N_5O_2S$: C, 55.96; H, 5.00; N, 20.40. Found: C, 55.74; H, 4.91; N, 20.32.

***N'*-[1-(1*H*-1,2,3-Benzotriazol-1-ylmethyl)butylidene]-4-methylbenzenesulfonhydrazide (2e).** White microcrystals, yield 92%, mp 172–173 °C; ^{1}H NMR δ 0.80 (t, *J* = 7.2 Hz, 3H), 1.35 (m, 2H), 2.04 (t, *J* = 8.6 Hz, 2H), 2.47 (s, 3H), 5.31 (s, 2H), 7.09 (d, *J* = 8.0 Hz, 1H), 7.23–7.39 (m, 4H), 7.72 (d, *J* = 8.4 Hz, 2H), 8.01 (d, *J* = 8.5 Hz, 1H), 8.30 (s, 1H); ^{13}C NMR δ 13.9, 18.1, 21.6, 29.1, 53.4, 109.9, 119.9, 124.1, 127.5, 128.0, 129.7, 133.0, 134.9, 144.4, 146.1, 152.9. Anal. Calcd for $C_{18}H_{21}N_5O_2S$: C, 58.20; H, 5.71; N, 18.86. Found: C, 58.31; H, 6.02; N, 18.92.

General Procedure for the Preparation of Compounds (3c-e) and (4x,y). The corresponding tosylhydrazone (**2)** (1 mmol) and thionyl chloride (10 mL) were stirred at rt for 12 h. The excess of thionyl chloride was removed *in vacuo*. The reaction mixture was diluted with ether or acetone (20 mL), and the obtained precipitate was filtered off and washed with ether (3 × 20 mL) to give compounds (**3)** or (**4)** which were further purified by column chromatography.

1-[4-(Furan-2-yl)-1,2,3-thiadiazol-5-yl]-1*H*-1,2,3-benzotriazole (3c). White microcrystals, (EtOAc:hexanes, 1:1), yield 83%, mp 160-161 °C; ^{1}H NMR δ 6.50 (d, *J* = 1.2 Hz, 1H), 7.02 (d, *J* = 3.3 Hz, 1H), 7.21 (d, *J* = 7.8 Hz, 1H), 7.30 (s, 1H), 7.49–7.54 (m, 2H), 8.18 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR δ 110.1, 111.8, 112.9, 120.6, 125.2, 129.4, 133.5, 142.1, 143.8, 144.4, 145.9, 146.1. Anal. Calcd for $C_{12}H_7N_5OS$: C, 53.52; H, 2.63; N, 26.01. Found: C, 53.38; H, 2.60; N, 25.92.

1-(4-Methyl-1,2,3-thiadiazol-5-yl)-1*H*-1,2,3-benzotriazole (3d). White microcrystals, (EtOAc:hexanes, 1:1), yield 35%, mp 107–109 °C; ^{1}H NMR δ 2.88 (s, 3H), 7.52–7.58 (m, 2H), 7.56 (t, *J* = 8.4 Hz, 1H), 8.20 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR δ 13.3, 109.5, 120.9, 125.4, 129.8, 133.4, 144.8, 145.9, 153.0. Anal. Calcd for $C_9H_7N_5S$: C, 49.75; H, 3.25; N, 32.24. Found: C, 49.76; H, 3.11; N, 32.05.

1-(4-Propyl-1,2,3-thiadiazol-5-yl)-1*H*-1,2,3-benzotriazole (3e). White microcrystals,(Et_2O:hexanes, 1:1), yield 28%, mp 40–42 °C; ^{1}H NMR δ 0.95 (t, *J* = 7.2 Hz, 3H), 1.89 (m, 2H), 3.11 (t, *J* = 7.8 Hz, 2H), 7.52–7.72 (m, 3H), 8.17 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR δ 13.5, 22.3, 28.9, 109.2, 120.6, 125.2, 129.5, 133.5, 144.2, 145.6, 157.5. Anal. Calcd for $C_{11}H_{11}N_5S$: C, 53.85; H, 4.53; N, 28.56. Found: C, 54.03; H, 4.47; N, 28.57.

1-(1,2,3-Thiadiazol-4-ylmethyl)-1*H*-1,2,3-benzotriazole hydrochloride (4x). White microcrystals, from EtOAc, yield 27%, mp 134-136 °C; ^{1}H NMR (DMSO-d_6) δ 6.54 (s, 2H), 7.42 (t, *J* = 7.5 Hz, 1H), 7.57 (t, *J* = 7.8 Hz, 1H), 7.97 (d, *J* = 8.4 Hz, 1H), 8.06 (d, *J* = 8.4 Hz, 1H), 9.37 (s, 1H), 10.50 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 45.3, 111.8, 120.2, 125.2, 128.6, 133.8, 138.9, 146.3, 158.2. Anal. Calcd for $C_9H_8N_5ClS$: N, 27.61. Found: N, 27.55.

1-[(5-Ethyl-1,2,3-thiadiazol-4-yl)methyl]-1*H*-1,2,3-benzotriazole (4y). White microcrystals, (EtOAc:hexanes, 1:1), yield 23%, mp 106–107 °C; ^{1}H NMR δ 1.28 (t, *J* = 7.5 Hz, 3H), 3.07 (q, *J* = 7.5 Hz, 2H), 6.27 (s, 2H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 8.03 (d, *J* = 8.3 Hz, 1H); ^{13}C NMR δ 16.3, 19.1, 44.1, 110.5, 120.1, 124.6, 128.2, 133.0, 146.5, 153.0, 160.1. Anal. Calcd for $C_{11}H_{11}N_5S$: C, 53.85; H, 4.53; N, 28.56. Found: C, 53.88; H, 4.48; N, 28.54.

3-Phenyl-4*H*-[1,2,3]thiadiazolo[3,4-*a*]benzimidazol-2-ium-4-ide (8a). 1-(4-Phenyl-1,2,3-thiadiazol-5-yl)-1*H*-1,2,3-benzotriazole (0.3 g, 1.08 mmol) in DMF (7 mL) was heated at 150-170 °C (oil bath) for 0.5 h, then cooled to rt. Chloroform (25 mL) was added and the reaction mixture was washed with water (3 × 50 mL). The organic layer was dried over $MgSO_4$, the solvent was evaporated, and the residue was purified by column chromatography (ether/hexanes, 1:1). Yield 0.09 g (39%), red crystals, mp 137-138.5 °C; ^{1}H NMR δ 7.26–7.32 (m, 1H), 7.42–7.59 (m, 4H), 7.96 (d, *J* = 8.5 Hz, 1H), 8.12 (d, *J* = 8.4 Hz, 1H), 8.23 (d, *J* = 7.1 Hz, 2H); ^{13}C NMR δ 113.3, 120.8, 121.4, 127.4, 128.2, 128.4, 128.5, 130.0, 130.7, 135.9, 152.1, 154.6. Anal. Calcd for $C_{14}H_9N_3S{\cdot}0.5H_2O$: C, 64.62; H 3.85; N, 16.15. Found: C, 65.61; H, 3.66 N, 16.40.

3-(Thiophen-2-yl)-4*H*-[1,2,3]thiadiazolo[3,4-*a*]benzimidazol-2-ium-4-ide (8b). 1-[4-(Thiophen-2-yl)-1,2,3-thiadiazol-5-yl]-1*H*-1,2,3-benzotriazole (3 g, 10.5 mmol) in DMF (20 mL) was heated at 150–200 °C (oil bath) for 2 h, and then cooled to rt. Chloroform (25 mL) was added and the reaction mixture was washed with water (3 × 50 mL). The organic layer was dried over $MgSO_4$, the solvent was evaporated, and the residue was purified by column chromatography (ether/hexanes 1:1). Yield 1.5 g (56%), brown crystals, mp 113–114 °C; ^{1}H NMR δ 7.20–7.32 (m, 2H), 7.52–7.57 (m, 2H), 7.94–7.98 (m, 2H), 8.10 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR δ 112.7, 120.4, 121.0, 127.7, 128.0, 128.2, 128.6, 128.7, 128.9, 129.8, 151.2, 153.9. Anal. Calcd for $C_{12}H_7N_3S_2$: C, 56.00, H 2.75, N, 16.33. Found: C, 56.16, H, 2.87, N, 16.16.

Crystal data for 8a: $C_{14}H_9N_3S\cdot 0.5H_2O$, FW 260.31, monoclinic, space group C2/c, *a* = 21.558(6), *b* = 6.867(2), *c* = 15.984(5) Å, *β* = 92.489(4) °, V = 2364(1) Å ^{3}, F(000) = 1080, Z = 8, T = -105 °C, μ (MoKα) = 0.26 mm^{-1}, D_{calcd} = 1.463 g.cm^{-3}, $2\theta_{max}$ 53° (CCD area detector, MoKα radiation), GOF = 1.05, wR(F^2) = 0.085 (all 2417 data), R = 0.029 (2197 data with I > 2σI).

Full crystallographic data have been submitted to the Cambridge Crystallographic Database.

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