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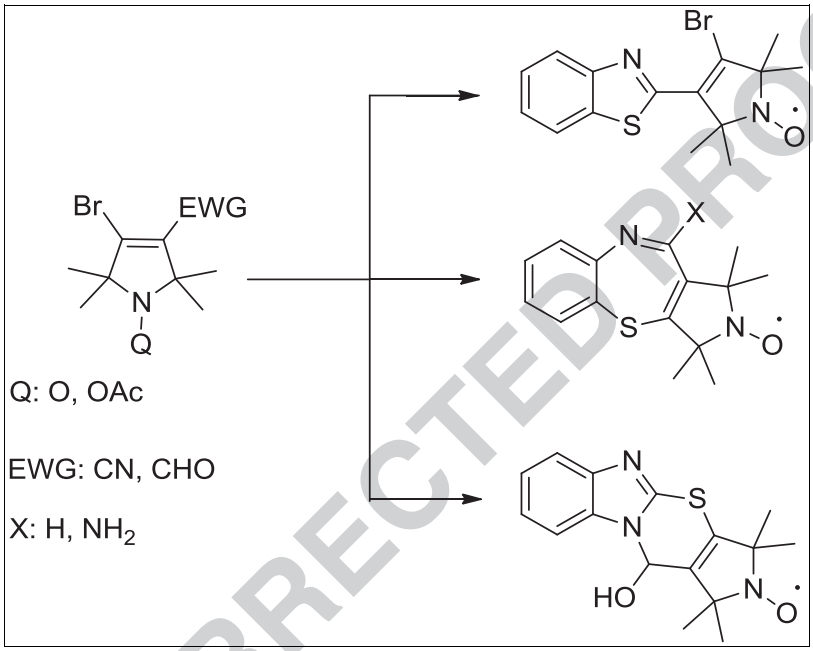

Reactions of β-bromo-β,γ-unsaturated pyrroline nitroxide aldehyde (**1**) or nitrile (**4**) or their diamagnetic forms (**5, 6**) with 2-aminothiophenol or 2-mercaptobenzimidazole were evaluated. The reaction could be reproduced more easily with the application of *O*-acetyl derivatives of nitroxides to generate 2-substituted-benzothiazole, pyrrolo[3,4-*b*]benzo[1,5]tiazepine scaffolds with 2-aminothiophenol and benzimidazo[2,1-*b*]pyrrolo[3,4-*e*]-[1,3]thiazine scaffold with 2-mercaptobenzimidazole.

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INTRODUCTION

Extensive studies of stable nitroxide free radicals have established the value of these unique compounds in applications such as spin labels [1], co-oxidants [2], building blocks for magnetic materials [3], synthesis of paramagnetic biomolecules [4], and mediators of polymerization [5]. These diverse applications were possible after M.B. Neiman and E.G. Rozantsev, and their group expanded the synthesis of nitroxide free radicals into a broad range of compounds [6], recognizing the limits of functionalization of TEMPO or F1 4-OXOTEMPO (Fig. 1).

To access further transformable stable nitroxide free radical building blocks, our laboratory started the synthesis of carbocycle and heterocycle condensed nitroxide free radicals, which offer many possible synthetic amendments. In these previous works, we synthesized thiophene [7], selenophene [8], pyridine [9], pyrrole [9,10], coumarin [11], phenanthrene [11], and polyheterocycles [12] condensed stable nitroxide free radicals. We reported the synthesis of 1,4-thiazepine derivative **2** [7] and 2-thienylbenzimidazole derivative **3** [13] by treatment of 4-bromo-3-formyl-2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrol-1-yloxyl radical **1** with cysteamine and 2-mercaptomethylbenzimidazole, respectively (Fig. 2). However, reactions of **1** with 2- F2 aminothiophenol resulted in the formation of a mixture of compounds.

In this article, we report the results of some reactions of β-bromo-β,γ-unsaturated pyrroline nitroxide aldehyde or nitrile with aromatic *N*-binucleophiles and *S*-binucleophiles

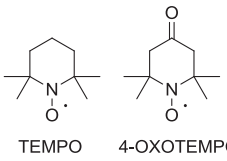


Figure 1. Structure of stable nitroxide free radicals TEMPO and 4-OXOTEMPO.

to elucidate their unusual performance in reactions and to find a pathway to synthesize the series of paramagnetically modified 1,5-benzothiazepine scaffolds, whose biological importance is well reported in the literature [14–18].

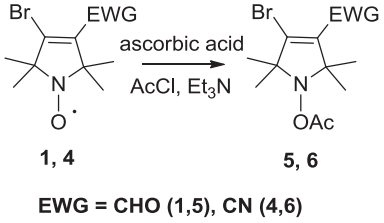
RESULTS AND DISCUSSION

Based on previous reports [19], our hypothesis was that nitroxides oxidize the aromatic thiols to the corresponding disulfides causing a nonreproducible reaction as in the case of compound **1** and 2-aminothiophenol.

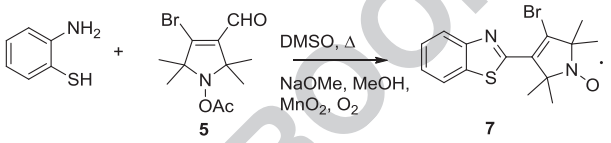
We proposed that a diamagnetic derivative of aldehyde **1** and nitrile **4** should be used in these reactions in such forms, which prevent the oxidation of aromatic thiols, because the formed aromatic disulfides cannot react further as *S*-nucleophiles. Therefore, compounds **1** and **4** were first converted to the *O*-acetyl derivatives **5** and **6** by a previously reported methodology [20], through the reduction to the corresponding hydroxylamine with ascorbic acid, followed by treatment with acetyl chloride **S1** in the presence of Et_3N in chloroform (Scheme 1).

Heating the 1:1 mixture of 2-aminothiophenol and compound **5** in the absence of a base in dimethyl sulfoxide in a (4 + 1) cyclocondensation generated 2-substituted benzothiazole. For more convenient isolation of compound **7**, the crude product was deacetylated with NaOMe in MeOH and oxidized with 0.1 equiv activated MnO_2 with bubbling through O_2 gas **S2** (Scheme 2). The (4 + 1) cyclocondensation was proven by elemental analysis and mass spectral measurements of the product, indicating the presence of bromine in

Scheme 1. Synthesis of diamagnetic *O*-acetyl derivatives of **1** and **6**.



Scheme 2. Reaction of compound **5** with 2-aminothiophenol in dimethyl sulfoxide (DMSO) in the absence of base.



molecular ion at 351/353/355 (M^+). The formation of benzothiazole is an acid-catalyzed process [21,22] initiated by the protonation of the imine with the participation of the SH acidic center, hence generating a nucleophilic thiolate and imine carbon more electrophilic than β-carbon.

Reaction of compound **5** and 2-aminothiophenol in acetonitrile in the presence of 1.1 equiv DBU gave 1,1,3,3-tetramethyl-2,3-dihydro-1*H*-pyrrolo[3,4-*b*] benzo[1,5]thiazepin-2-acetate **8** in an (4 + 3) cyclocondensation reaction. In this case, we propose that the bromine substitution with thiolate—generated in basic conditions—in the first stage be followed by the Schiff base formation. We assume the nucleophilic substitution of bromine atom to be the "push–pull" process with addition of thiolate to β-carbon, followed by halogen cleavage with C3–C4 double bond restoration. Deacetylation of compound **8**, as described earlier, offered compound **9**. Reduction of compound **9** with 1.2 equiv $NaBH_4$ in EtOH gave secondary amine **10.** This reduction is proven by appearance of CH_2 signal at 3.79 ppm in ^1H NMR spectrum, and this type of

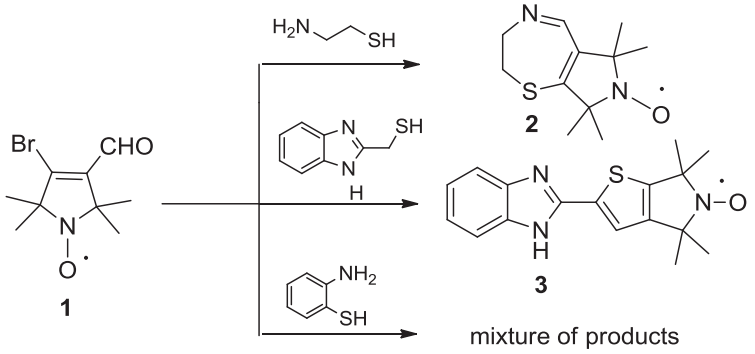
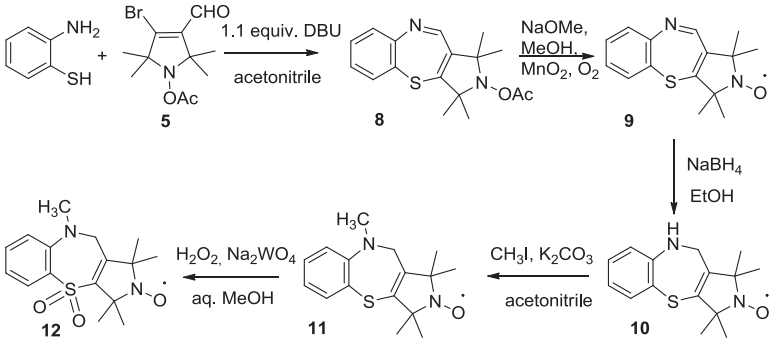
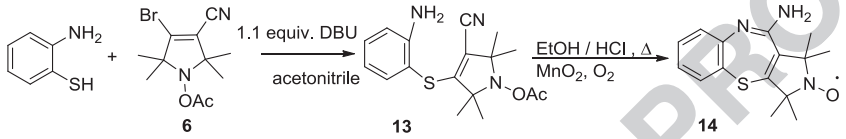


Figure 2. Reaction of aldehyde **1** with various *N*-binucleophiles and *S*-binucleophiles.

Scheme 3. Synthesis of paramagnetic benzo[1,5]thiazepine derivatives from aldehyde **5**.



Scheme 4. Synthesis of paramagnetic benzo[1,5]thiazepine derivative **14** from nitrile **6**.



transformation is well documented in the literature [23] as well. Methylation of compound **10** with CH_3I in acetonitrile in the presence of K_2CO_3 generated compound 1,1,3,3,9-pentamethyl-9,10-dihydro-1*H*-pyrrolo[3,4-*b*]benzo[1,5]thiazepin-2-yloxyl radical **11.** Oxidation of compound **11** in aqueous (aq) MeOH with H_2O_2 in the presence of Na_2WO_4 furnished sulfone **12**

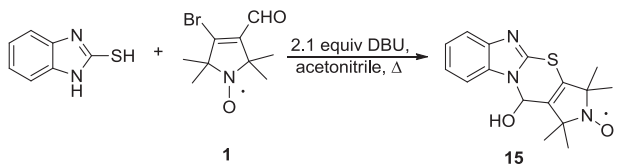
S3 (Scheme 3).

Reaction of compound **6** with 2-aminothiophenol in acetonitrile and 1.1 equiv DBU furnished adduct **13.** The presence of the nitrile band in infrared (IR) at 2210 cm^{-1} indicated that no ring closure occurred, because the nitrile group of compound **6** is a weaker electrophile than the formyl group in compounds **1** and **5**, the latter giving ring closure smoothly with aromatic amines. The thiazepine ring formation can be initiated by refluxing compound **13** in EtOH, saturated with HCl gas. Along with the ring closure, deacetylation also occurred, and hence, after basic work-up followed by oxidation with MnO_2/O_2, we obtained 10-amino-1,1,3,3-tetramethyl-2,3-dihydro-1*H*-pyrrolo[3,4-*b*]benzo[1,5]thiazepin-2-yloxyl

S4 radical **14** (Scheme 4).

Reaction of compound **1** with 2-mercaptobenzimidazole in acetonitrile in the presence of 2.1 equiv DBU with heating provided 11-hydroxy-1,1,3,3-tetramethyl-1,2,3,11-tetrahydro-benzimidazo[2,1-*b*]pyrrolo[3,4-*e*][1,3]

Scheme 5. Reaction of aldehyde **1** with 2-mercaptobenzimidazole.



thiazin-2-yloxyl radical **15** in a (3 + 3) cyclocondensation reaction, in an analogous reaction published earlier by Hungarian researchers [24] (Scheme 5). **S5**

CONCLUSIONS

Reactions of β-bromo-β,γ-unsaturated pyrroline nitroxide aldehyde (**1**) or nitrile (**4**) or their *O*-acetyl derivatives (**5, 6**) with various *N*-binucleophiles and *S*-binucleophiles depending on reaction partners or absence/presence of a base gave structurally diversified paramagnetic polycyclic compounds. We suggested camouflaging of the nitroxide function in the presence of aromatic thiols in most cases to avoid unwanted side reactions. Although reactions of nitroxides have been studied for several decades, there are still many challenges (selectivity problems) that remain to be solved. We believe that the reactions studied in this work are extendable to the reactions of any β-halogen-α,β-unsaturated aldehydes or nitriles, giving a straightforward synthetic access to a number of interesting fused *S*-containing and *N*-containing polyheterocycles.

Experimental. Melting points were determined using Boetius micro melting point apparatus and are Q1 uncorrected. Elemental analyses (C, H, N, S) were performed on Fisons EA 1110 CHNS elemental analyser; bromine determination was carried out titrimetrically by Schöniger's method. Mass spectra were recorded on a Thermoquest Automass Multi. ^1H NMR and ^{13}C NMR spectra were recorded with Bruker Avance 3 Ascend 500 spectrometer. Chemical shifts are referenced to Me_4Si. The paramagnetic compound was reduced with 5 equiv

hydrazobenzene or pentafluorophenyl hydrazine/radical. Measurements were run at 298 K probe temperature in $CDCl_3$ or CD_3OD solution. Electron spin resonance spectra were taken on Miniscope MS 200 in 10^{-4} M $CHCl_3$ solution, and all monoradicals gave triplet line a_N = 14.4 G. The IR spectra were taken with Bruker Alpha FTIR instrument with ATR support (ZnSe plate). Flash column chromatography was performed on Merck Kieselgel 60 (0.040–0.063 mm). Qualitative thin-layer chromatography (TLC) was carried out on commercially available plates (20 × 20 × 0.02 cm) coated with Merck Kieselgel GF254. Compounds **1** [25] and **4** [7] were prepared according to published procedures, and other reagents were purchased from Aldrich or Alfa Aesar.

Synthesis of diamagnetic* O*-acetyl derivatives, general procedure (5, 6). Into a two-necked flask equipped with magnetic stirrer, N_2 inlet, and condenser, we placed the $MgSO_4$ drying agent (10 g) and Et_3N (1.11 g, 11.0 mmol). In another round bottomed flask with two necks, we placed compound **1** or **4** dissolved in dioxane/water (3:1) (32 mL). The mixture was stirred at 35–40°C under N_2, and ascorbic acid (8.80 g, 50.0 mmol) was added in four to five portions. After the solution became colorless or pale yellow, it was extracted in $CHCl_3$ (2 × 20 mL), and the colorless bottom organic phases were sunk down into the $MgSO_4$, Et_3N-containing flask directly. Then, the mixture was cooled to 0°C, and AcCl (863 mg, 11.0 mmol) was added dropwise. After removing the cooling bath, the mixture was allowed to stir at ambient temperature for 1 h under N_2. After quenching with MeOH (1 mL), the mixture was filtered on a glass frit, the filtrate was evaporated, and the residue was partitioned between brine (10 mL) and EtOAc (25 mL). The organic phase was separated, dried ($MgSO_4$), filtered, and evaporated to offer a colorless thick oil, which was further purified by flash column chromatography (hexane/Et_2O).

3-Bromo-4-formyl-2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrol-1-yl acetate (5). white crystal, 1.39 g (48%), mp 71–72°C; R_f: 0.43 (hexane/Et_2O, 2:1); IR: 2937, 2845, 1768, 1676, 1603 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.35 (s, 3*H*), 1.38 (s, 3*H*), 1.41 (s, 6*H*), 2.15 (s, 3*H*), 9.82 (s, 1*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ 19.0, 21.8, 21.9, 27.2, 27.4, 70.8, 72.6, 139.1, 145.6, 170.5, 188.1; MS (70 eV): *m/z* 291/289 (M^+, 14/14), 276/274 (76/76), 249/247 (61/61), 234/232 (98), 43 (100). *Anal*. Calcd. for $C_{11}H_{16}BrNO_3$: C, 45.53; H, 5.56; N, 4.83; Br, 27.54. Found: C, 45.38; H, 5.52; N, 4.76; Br, 27.40.

3-Bromo-4-cyano-2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrol-1-yl acetate (6). white crystalline solid, 1.40 g (57%), mp 60–61°C; R_f: 0.38 (hexane/Et_2O, 2:1); IR: 2982, 2932, 2866, 2225, 1770, 1680, 1623 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.34 (s, 3*H*), 1.37 (s, 3*H*), 1.40 (s, 3*H*), 1.46 (s, 3*H*), 2.15 (s, 3*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ 18.9, 22.6 (2C), 27.5, 27.9, 71.7, 73.9, 113.1, 119.3, 141.6, 169.8; MS (70 eV): *m/z* 288/286 (M^+, 3/3), 273/271 (7/7), 246/244 (20/20), 229/221 (100), 150 (45), 43 (73). *Anal*. Calcd. for $C_{11}H_{15}BrN_2O_2$: C, 46.01; H, 5.27; N, 9.76; Br, 27.83. Found: C, 46.06; H, 5.06; N, 9.94; Br, 27.60.

3-(Benzthiazo-2-yl)-4-bromo-2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrol-1-yloxyl radical (7). A solution of compound **5** (580 mg, 2.0 mmol) and 2-aminothiophenol (250 mg, 2.0 mmol) in dimethyl sulfoxide (5 mL) was heated at 90°C for 2 h. After cooling, the solvent was evaporated off, the residue was dissolved in MeOH (10 mL), and freshly made NaOMe solution was added (5 mL MeOH +5 mg Na metal). After standing at room temperature (RT) for 30 min, the solvent was evaporated off, and the residue was partitioned between saturated aq NH_4Cl solution (10 mL) and $CHCl_3$ (10 mL). The organic phase was extracted with $CHCl_3$ (10 mL) again, and the combined organic phases were dried ($MgSO_4$), activated MnO_2 (43 mg, 0.5 mmol) was added, and O_2 was bubbled through for 10 min. The mixture was filtered, evaporated, and purified by flash column chromatography (hexane/Et_2O) to give compound **7** as a yellow solid, 183 mg (26%), mp 84–85°C; R_f: 0.67 (hexane/Et_2O, 2:1); IR: 3059, 2976, 2929, 2863, 1683, 1610, 1558 cm^{-1}; ^1H NMR (500 MHz, CD_3OD + $C_6F_5N_2H_3$): δ 1.36 (s, 6*H*), 1.55 (s, 6*H*), 7.66–8.17 (m, 4*H*); ^{13}C NMR (125 MHz, CD_3OD + $C_6F_5N_2H_3$): δ 23.8 (2C), 24.0 (2C), 71.3, 71.9, 121.1, 122.8, 125.5, 126.1, 131.7, 134.3, 152.1, 160.24; MS (70 eV): *m/z* 355/353/351 (M^+, 1>, 10/10), 310/308/306 (1>/13/13), 242 (100), 226 (20). *Anal.* Calcd. for $C_{15}H_{16}BrN_2OS$: C, 51.14; H, 4.58; N, 7.95; S, 9.10; Br, 22.68. Found: C, 51.32; H, 4.72; N, 8.04; S, 8.95; Br, 22.50.

1,1,3,3-Tetramethyl-2,3-dihydro-1*H*-pyrrolo-[3,4-b]benzo[1,5]thiazepin-2-acetate (8). To a solution of compound **5** (1.45 g, 5.0 mmol) and 2-aminothiophenol (625 mg, 5.0 mmol) in acetonitrile (10 mL), DBU (836 mg, 5.5 mmol) was added and the mixture was allowed to stir at RT. for 2 h. The acetonitrile was evaporated off, the residue was dissolved in EtOAc (20 mL), the organic phase was washed with water (10 mL), and the organic phase was separated, dried ($MgSO_4$), filtered, and evaporated. The residue was subjected to flash column chromatography to yield compound **8** as white crystals, 1.18 g (75%), mp 70–72°C; R_f: 0.69 ($CHCl_3$/Et_2O, 2:1); IR: 2973, 2929, 1762, 1603 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.30 (s, 6*H*), 1.32 (s, 6*H*), 2.13 (s, 3*H*), 7.15–7.21 (m, 3*H*), 7.32–7.35 (m, 1*H*), 8.22 (s, 1*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ 19.0, 22.3, 23.0, 27.1, 27.6, 69.9, 71.9, 115.2, 118.1, 129.2, 131.5, 138.4, 139.4, 148.7, 150.3, 157.5, 170.7; MS (70 eV): *m/z* 316 (M^+, 4), 301

(10), 259 (63), 227 (100), 211 (42), 43 (24). *Anal*. Calcd. for $C_{17}H_{20}N_2O_2S$: C, 64.53; H, 6.37; N, 8.85; S, 10.13. Found: C, 64.32; H, 6.45; N, 9.01; S, 10.07.

1,1,3,3-Tetramethyl-2,3-dihydro-1H-pyrrolo-[3,4-b]benzo[1,5]thiazepin-2-yloxyl radical (9). To a solution of compound **8** (948 mg, 3.0 mmol) in MeOH (10 mL), freshly made NaOMe (5 mL MeOH +7.5 mg Na) was added. After standing at RT for 30 min, the solvent was evaporated off, and the residue was dissolved in saturated aq NH_4Cl solution (10 mL) and extracted with $CHCl_3$ (2 × 10 mL). The combined organic phase was dried ($MgSO_4$), activated MnO_2 (65 mg, 0.75 mmol) was added to the mixture, and O_2 was bubbled through for 10 min. The mixture was filtered, evaporated, and purified by flash column chromatography (hexane/Et_2O) to give the product as yellow crystals, 417 mg (51%), mp 104–106°C; R_f: 0.45 (hexane/EtOAc, 2:1); IR: 2971, 2926, 2856, 1618, 1596, 1576 cm^{-1}; MS (70 eV): *m/z* 273 (M^+, 38), 259 (20), 243 (74), 136 (51), 108 (100). *Anal*. Calcd. for $C_{15}H_{17}N_2OS$: C, 65.90; H, 6.27; N, 10.25; S, 11.73. Found: C, 65.96; H, 6.00; N, 10.06; S, 11.64.

1,1,3,3-Tetramethyl-9,10-dihydro-1H-pyrrolo-[3,4-b]benzo[1,5]thiazepin-2(3H)-yloxyl radical (10). To a stirred solution of compound **9** (546 mg, 2.0 mmol) in EtOH (15 mL), $NaBH_4$ (76 mg, 2.0 mmol) was added at 0°C. After removing the cooling bath, the mixture was stirred for 2 h. The EtOH was evaporated off, and the residue was partitioned between saturated aq NH_4Cl solution (10 mL) and $CHCl_3$ (15 mL). The phases were separated, the aq phase was re-extracted with $CHCl_3$ (15 mL), and the combined phases were dried ($MgSO_4$), filtered, and evaporated. The residue was purified by flash column chromatography (hexane/EtOAc and $CHCl_3$/Et_2O) to offer compound **10** as a yellow solid, 374 mg (68%), mp 138–139°C; R_f: 0.49 ($CHCl_3$/Et_2O, 2:1); IR: 3250, 2974, 2928, 2864, 1653, 1585 cm^{-1}. For NMR study, the paramagnetic compound **10** was reduced to the diamagnetic secondary amine with Fe/AcOH as published earlier [26]. ^1H NMR (500 MHz, $CDCl_3$): δ 1.206 (s, 6*H*), 1.34 (s, 6*H*), 3.79 (s, 2*H*), 6.93 (d, 1*H*, *J* = 7.5 Hz), 6.98 (t, 1*H*, *J* = 7.5 Hz), 7.19 (t, 1*H*, *J* = 7.5 Hz), 7.38 (d, 1*H*, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 29.1 (2C), 29.4 (2C), 46.4, 65.7, 66.9, 123.0, 123.3, 128.7, 129.3, 130.8, 132.7, 138.1, 150.4; MS (70 eV): *m/z* 275 (M^+, 31), 245 (100), 230 (39), 136 (64). *Anal*. Calcd. for $C_{15}H_{19}N_2OS$: C, 65.42; H, 6.95; N, 10.17; S, 11.64. Found: C, 65.49; H, 6.76; N, 10.06; S, 11.52.

1,1,3,3,9-Pentamethyl-9,10-dihydro-1H-pyrrolo-[3,4-b]benzo[1,5]thiazepin-2(3H)-yloxyl radical (11). To a stirred mixture of compound **10** (275 mg, 1.0 mmol) and powdered K_2CO_3 (138 mg, 1.0 mmol) in acetonitrile (7 mL), CH_3I (426 mg, 3.0 mmol) was added and the mixture was stirred and refluxed. After 5 h, further CH_3I (142 mg, 1.0 mmol) was added, and after the consumption of the starting material (~10 h), the solution was diluted with $CHCl_3$ (10 mL), the reaction mixture was filtered through sintered glass funnel, and the solvents were evaporated off. The residue was dissolved in EtOAc (15 mL) and washed with water (10 mL), and the organic phase was separated, dried ($MgSO_4$), filtered, and evaporated. The crude product was subjected to column chromatography (hexane/EtOAc, then $CHCl_3$/Et_2O) to give compound **11** as yellow crystals, 225 mg (78%), mp 122–124°C; R_f: 0.76 ($CHCl_3$/Et_2O, 2:1); IR: 3055, 2977, 2930, 2816, 2788, 1653, 1579 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$ + $(PhNH)_2$): δ 1.20 (s, 6*H*), 1.36 (s, 6*H*), 3.0 (s, 3*H*), 3.5 (s, 2*H*,); ^{13}C NMR (125 MHz, $CDCl_3$ + $(PhNH)_2$): δ 24.0 (2C), 24.4 (2C), 44.54, 55.1, 69.8, 71.0, 120.2, 123.6, 129.2, 131.3, 134.9, 148.9, 152.7, 153.9; MS (70 eV): *m/z* 289 (M^+, 16), 295 (30), 244 (10), 151 (100). *Anal*. Calcd. for $C_{16}H_{21}N_2OS$: C, 66.40; H, 7.31; N, 9.68; S, 11.08. Found: C, 66.70; H, 7.19; N, 9.68; S 10.95.

2-Oxyl-1,1,3,3,9-pentamethyl-9,10-dihydro-1H-pyrrolo-[3,4-b]benzo[1,5]thiazepin-4,4-dioxide radical (12). To a stirred solution of compound **11** (289 mg, 1.0 mmol) and Na_2WO_4 $2H_2O$ (33 mg, 0.1 mmol) in MeOH (10 mL) and water (3 mL) aq 30%, H_2O_2 (1 mL) was added at 0°C, and the mixture was allowed to stay at RT. After 24 h, further 30% H_2O_2 (0.5 mL) was added, and the mixture was allowed to stay for further 24 h when TLC monitoring showed the consumption of the starting materials and sulfoxide intermediates. The mixture was diluted with brine, extracted with $CHCl_3$ (2 × 20 mL), and the organic phase was dried ($MgSO_4$), filtered, and evaporated. The residue was purified by flash column chromatography to furnish compound **12** as a yellow solid, 176 mg (55%), mp 162–164°C; R_f: 0.48 ($CHCl_3$/Et_2O, 2:1); IR: 2976, 2929, 1590, 1572, 1294, 1132 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$ + $(PhNH)_2$): δ 1.26 (s, 6*H*), 1.63 (s, 6*H*), 3.04 (s, 3*H*), 3.77 (s, 2*H*); ^{13}C NMR (125 MHz, $CDCl_3$ + $(PhNH)_2$): δ 24.0 (2C), 24.8 (2C), 43.5, 55.1, 69.8, 70.8, 119.8, 123.2, 127.1, 134.7, 137.0, 139.9, 148.9, 149.9; MS (70 eV): *m/z* 321 (M^+, 41), 291 (2), 227 (30), 212 (100). *Anal*. Calcd. for $C_{16}H_{21}N_2O_3S$: C, 59.79; H, 6.59; N, 8.72; S, 9.98. Found: C, 59.66; H, 6.51; N, 8.68; S, 9.87.

3-((2-Aminophenyl)thio)-4-cyano-2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-1-yl acetate (13). To a stirred solution of compound **6** (1.43 g, 5.0 mmol) and DBU (836 mg, 5.5 mmol) in acetonitrile (10 mL), 2-aminothiophenol (625 mg, 5.0 mmol) was added and the mixture was stirred at ambient temperature till the consumption of starting materials (~2 h, monitored by TLC). The acetonitrile was evaporated off, the residue was dissolved in EtOAc (20 mL) and washed with water (10 mL), and

the organic phase was separated, dried ($MgSO_4$), filtered, and evaporated. The residue was purified by flash column chromatography (hexane/EtOAc) to offer compound **13** as beige crystals, 1.18 g (75%), mp 122–124°C; R_f: 0.33 (hexane/EtOAc, 2:1); IR: 3452, 3356, 2982, 2931, 2210, 1761, 1629, 1589 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$ + $(PhNH)_2$): δ 1.34 (s, 6*H*), 1.45 (s, 6*H*), 2.16 (s, 3*H*), 4.29 (s, 2*H*), 6.79 (m, 2*H*), 7.32 (m, 1*H*), 7.43 (m, 1*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ 19.0, 22.6 (2C), 23.1 (2C), 27.9, 71.2, 73.5, 108.5, 112.4, 115.5, 118.8, 132.8, 137.8, 149.8, 155.5, 170.3; MS (70 eV): *m/z* 331 (M^+, 12), 316 (19), 289 (24), 274 (100), 215 (42), 142 (94). *Anal*. Calcd. for $C_{17}H_{21}N_3O_2S$: C, 61.61; H, 6.39; N, 12.68; S, 9.67. Found: C, 61.78; H, 6.35; N, 12.94; S, 9.61.

10-Amino-1,1,3,3-tetramethyl-2,3-dihydro-1H-pyrrolo-[3,4-b]benzo[1,5]-thiazepin-2-yloxyl radical (14). A solution of compound **13** (662 mg, 2.0 mmol) in EtOH saturated with HCl gas was heated at reflux temperature for 10 h. After cooling, the solvent was evaporated off, the residue was dissolved in saturated aq $NaHCO_3$ solution (50 mL) (caution, intense foaming!), and this solution was extracted with $CHCl_3$ (2 × 15 mL). The combined organic phases were dried ($MgSO_4$), activated MnO_2 (43 mg, 0.5 mmol) was added, and O_2 was bubbled through for 15 min. After filtering the mixture, the solvent was evaporated off, and the residue was subjected to flash column chromatography ($CHCl_3/Et_2O$) to give the product as a pale yellow solid, 190 mg (30%), mp 155–157°C; R_f: 0.33 ($CHCl_3$/MeOH, 9:1); IR: 3319, 2970, 2924, 2853, 2223, 1653 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$ + $C_6F_5N_2H_3$): δ 1.21 (s, 3*H*), 1.25 (s, 6*H*), 1.34 (s, 3*H*), 6.24 (s, 2*H*), 7.04–7.28 (m, 4*H*); ^{13}C NMR (125 MHz, $CDCl_3$ + $C_6F_5N_2H_3$): δ 23.3, 23.7, 27.0, 27.8, 69.0, 70.9, 124.4, 125.2, 128.2, 128.9, 131.8, 137.4, 147.0, 149.0, 158.0; MS (70 eV): *m/z* 288 (M^+, 10), 258 (100), 226 (62), 215 (62). *Anal*. Calcd. for $C_{15}H_{18}N_3OS$: C, 62.47; H, 6.29; N, 14.57; S, 11.12. Found: C, 62.42; H, 6.35; N, 14.71; S, 11.06.

11-Hydroxy-1,1,3,3-tetramethyl-1,2,3,11-tetrahydrobenzimidazo[2,1-b]pyrrolo[3,4-e][1,3-]thiazin-2-yloxyl radical (15). To a stirred suspension of 2-mercaptobenzimidazole (300 mg, 2.0 mmol) and DBU (638 mg, 4.2 mmol) in acetonitrile (10 mL), compound **1** (494 mg, 2.0 mmol) was added and the mixture was heated at reflux temperature for 30 min, upon which the solid dissolved. After cooling, the acetonitrile was evaporated off, the residue was dissolved in $CHCl_3$ (30 mL) and washed with brine (10 mL), and the organic phase was separated, dried ($MgSO_4$), filtered, and evaporated. The residue was purified by flash column chromatography (hexane/EtOAc, $CHCl_3/Et_2O$) to give the title compound as a yellow solid, 474 mg (75%), mp 219–221°C; R_f: 0.30 ($CHCl_3/Et_2O$, 2:1); IR: 2983, 2924, 2854, 1617 cm^{-1}; ^1H NMR (500 MHz, CD_3OD + $C_6F_5N_2H_3$): δ 1.36 (s, 3*H*), 1.39 (s, 3*H*), 1.40 (s, 3*H*), 1.49 (s, 3*H*), 6.58 (s, 1*H*), 7.31 (m, 2*H*), 7.57 (m, 1*H*), 7.70 (m, 1*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ 23.1, 23.4, 24.0, 24.4, 69.0, 69.7, 73.1, 110.7, 117.0, 122.2, 123.1, 133.5, 142.4, 144.7, 149.7, 152.5; MS (70 eV): *m/z* 316 (M^+, 20), 286 (239), 282 (100), 269 (83), 150 (59). *Anal*. Calcd. for $C_{16}H_{18}N_3O_2S$: C, 60.74; H, 5.73; N, 13.28; S, 10.13. Found: C, 60.58; H, 5.91; N, 13.41; S, 10.01.

DECLARATION OF INTEREST

The authors declare no conflict of interest.

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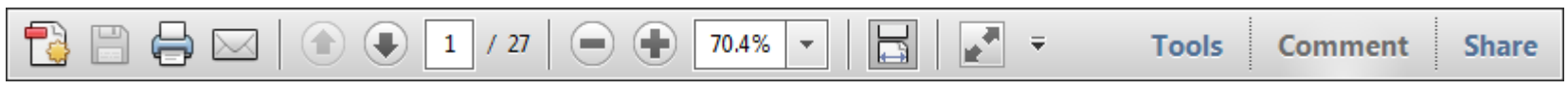

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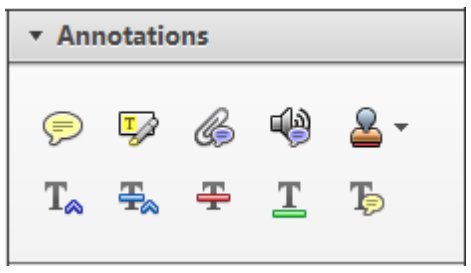

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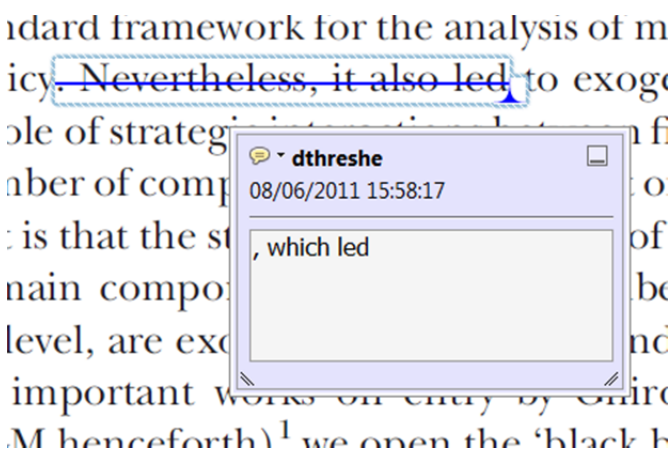

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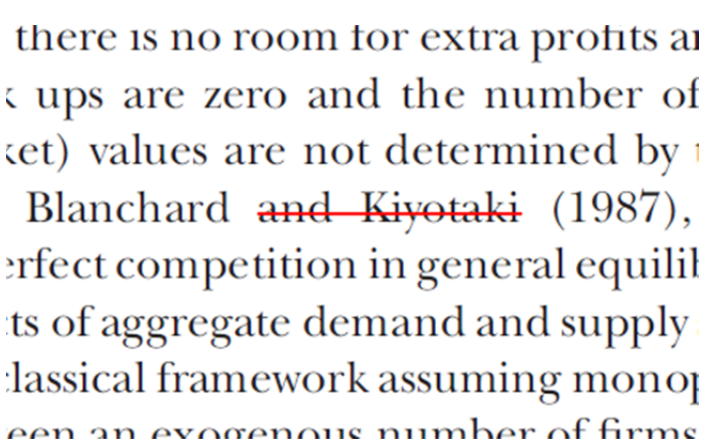

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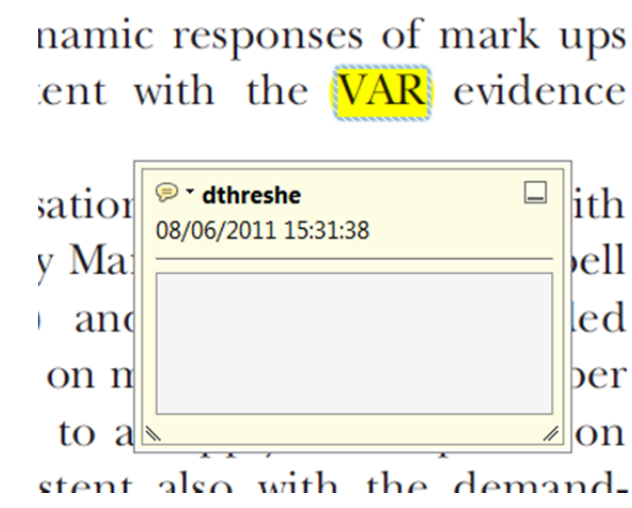

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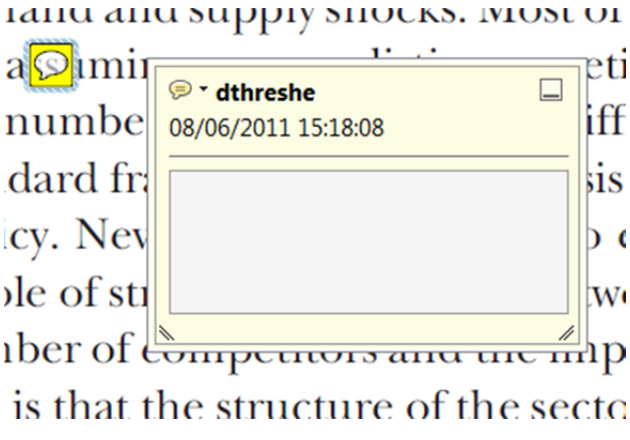

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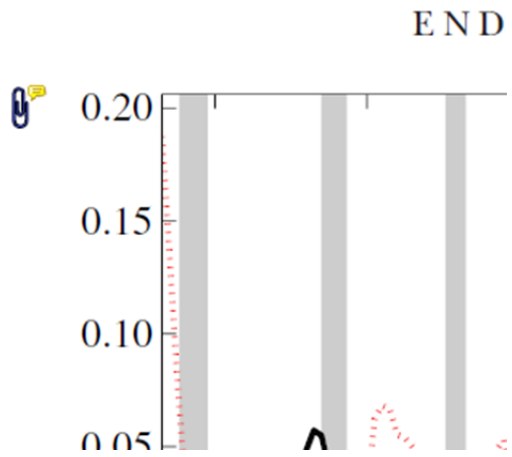

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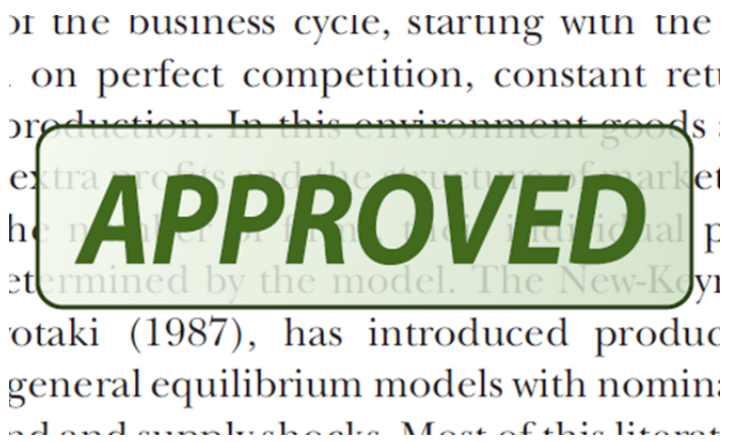

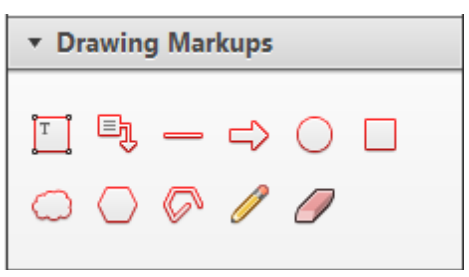

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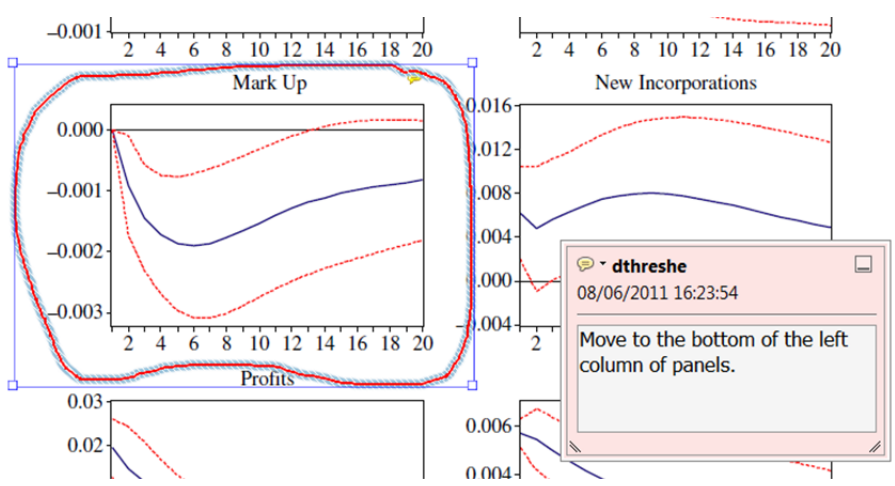

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