NOVEL HETEROCYCLES: A BENZODITHIOLANE *S*-OXIDE AND A BENZOTHIADIAZINANE *S*-OXIDE

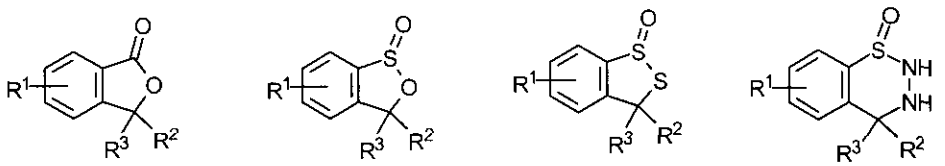
Alan R. Katritzky,*[a] Zhongxing Zhang,[a] Ming Qi,[a] Nusrallah Jubran,[b] and Louis M. Leichter[b]

[a] Center for Heterocyclic Compounds, Department of Chemistry, University of Florida, Gainesville, FL 32611-7200, USA

[b] Imation Corp., Oakdale, Minnesota 55128-3414, USA

Abstract - Synthetic methodology has been developed for the synthesis of novel heterocycles from 3,3-diaryl-3*H*-2,1-benzoxathiole 1-oxides (**2**). Cyclic sulfinates (**2**) were converted directly into 3,3-diaryl-1,2-benzodithiolane 1-oxide (**3**) and 4,4-diaryl-1,2,3-benzothiadiazinane 1-oxide (**4**) which represent a cyclic thiosulfinate and a cyclic sulfinyl hydrazide, respectively. 3,7-Bis(dimethylamino)-10-(*p*-dimethylamino-benzene)thiaxanthene 5,5-dioxide (**8a**) and 3-dimethylamino-10-(*p*-dimethylaminobenzene)thiaxanthene 5,5-dioxide (**8b**) were formed from the reaction of hydrazine and compound(**2**).

Much attention has been recently devoted to the search for new color formers. Benzolactones (**1**, R^2, R^3 = alkylaminophenyl, dialkylaminophenyl, or alkylamino substituted polycycle) are good color formers for carbonless imaging.[1] We recently disclosed 3,3-diaryl-3*H*-2,1-benzoxathiole 1-oxides (**2**) as novel sultine color-formers for carbonless imaging, some of which develop stable dark-blue colors in acidic media.[2] We now report the conversion of 3,3-diaryl-3*H*-2,1-benzoxathiole 1-oxides (**2**) into sultine derivatives(**3**) and(**4**), which represent two novel heterocycles.



1 **2** **3** **4**

1-4: R^1 = H, alkoxyl, amino *etc.*; R^2, R^3 = aminoaryl

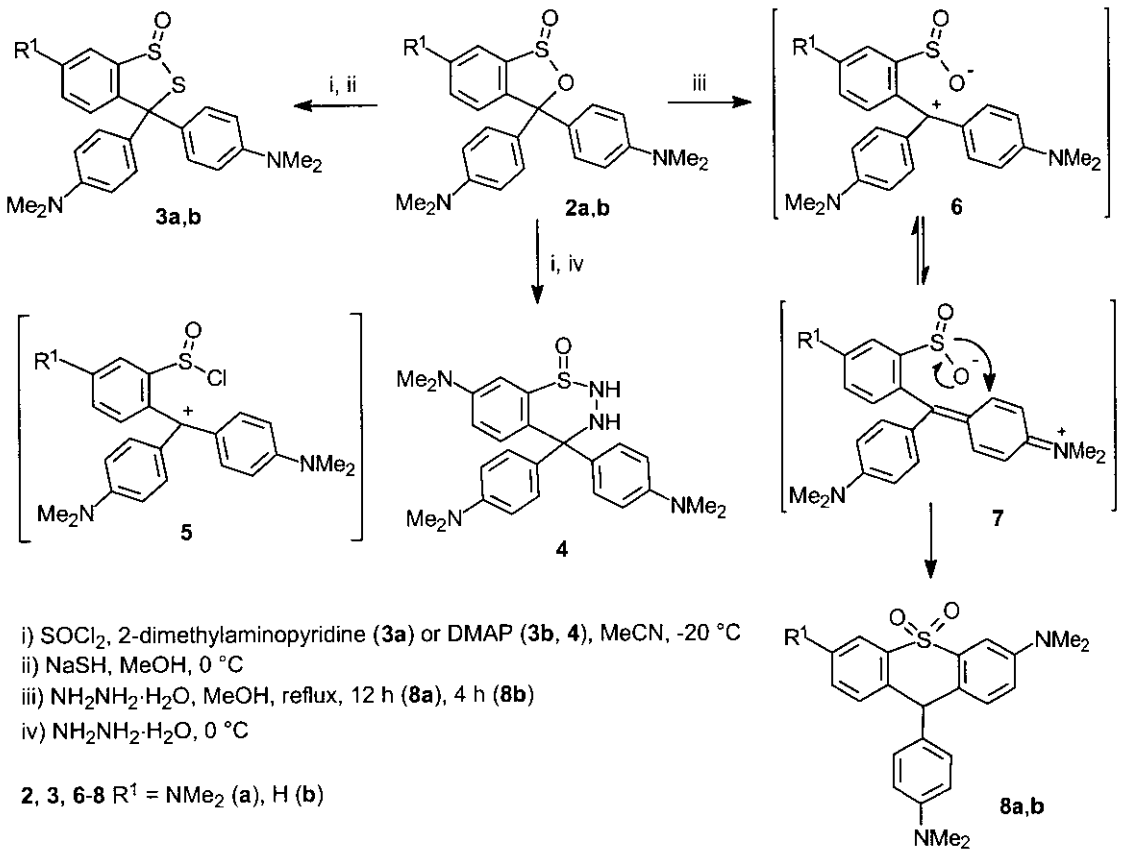
RESULTS AND DISCUSSION

Synthesis of 3,3-Diaryl-1,2-benzodithiolane 1-Oxide (3). Thiosulfinate esters are reported to possess tumor inhibiting,[3] antithrombotic,[4] antifungal and antibacterial[5] properties. Generally, acyclic thiosulfinates are synthesized from sulfinyl chlorides,[6] sulfinamides,[7] or sulfinyl azides.[8] Few methods have been reported for the preparation of cyclic thiosulfinates: i) the oxidation of cyclic 1,2-[9] or 1,3-disulfides;[10] ii) ring forming reactions of disulfur monoxide (S_2O) with dienes[5b] or transition-metal-complexes.[11] There is no previous report of the transformation of cyclic sulfinates into cyclic thiosulfinates. This transformation would involve breaking both the S-O bond and the C-O bond of a C-S(O)-O-C group, and concurrent formation of both an S-S bond and a C-S bond to give a C-S(O)-S-C moiety. Herein, we disclose novel one-pot procedures for converting 3,3-diaryl-3*H*-2,1-benzoxathiole 1-oxides (**2**) into 3,3-diaryl-1,2-benzodithiolane 1-oxides (**3**), which possesses a novel heterocyclic ring system.

3,3-Diaryl-3*H*-2,1-benzoxathiole 1-oxides (**2a,b**) were prepared according to the previous paper.[2] Treatment of 3,3-diaryl-3*H*-2,1-benzoxathiole 1-oxide (**2a**) and 2-dimethylaminopyridine with thionyl chloride followed by sodium hydrogen sulfide (NaSH) gave 6-dimethylamino-3,3-bis[(4-dimethylamino)phenyl]-1,2-benzodithiolane 1-oxide (**3a**) as an off-white solid in 65% yield (Scheme 1).[12] ^{1}H and ^{13}C NMR support the structure assignment: particularly, the ^{13}C chemical shift of C-3, which was identified as a quaternary carbon using APT techniques, shifted upfield from 106 ppm (**2a**) to 77.9 ppm reflecting the change in connection from oxygen (**2a**) to sulfur (**3a**) (Scheme 1). This structure was also supported by satisfactory elemental analysis and HRMS (see Experimental).

Attempted synthesis of compound (**3b**) from 3,3-bis[(4-dimethylamino)phenyl]-3*H*-2,1-benzoxathiole 1-oxide (**2b**) under the same reaction conditions gave an inseparable mixture of **3b** and unknown impurities, according to ^{1}H and ^{13}C NMR spectra of the mixture. These results suggest that all three amino groups in **2a** are necessary for the complete and clean reaction of **2** → **3**.

We believe that these reactions involve cationic sulfinyl chloride intermediates (**5**) (Scheme 1). The C-O bonds in compounds of type (**2**) undergo scission to give carbocations (**6**) and the resulting sulfinate anion is converted into a sulfinyl chloride by thionyl chloride. Intermediates (**5**) then react with sodium hydrogen sulfide to afford the cyclic thiosulfinates (**3**).



Scheme 1

Synthesis of 4,4-Diarylbenzo-1,2,3-thiadiazinane 1-Oxide (4) from 3,3-Diaryl-3*H*-2,1-benzoxathiole 1-Oxide and Hydrazine. Syntheses of unstable acyclic sulfinyl hydrazides[13] and 5-membered heterocyclic sulfinyl hydrazides are documented.[14] However, there is no previous report of the synthesis of 6-membered heterocycles containing a sulfinyl hydrazine moiety [S(O)-NH-NH] in the ring.

The original idea for the synthesis of the desired compound (**4**) comprised the reaction of 3,3-diaryl-3*H*-2,1-benzoxathiole 1-oxides (**2**) and hydrazine, similar to the literature method of Kuzuya *et al.*[15] for the conversion of lactones to cyclic acylhydrazines (Scheme 1). After **2a** and hydrazine hydrate were heated in methanol for 12 h, compound (**8a**) was obtained as a white solid in 90% yield. Elemental analysis and HRMS gave the molecular formula as $C_{25}H_{29}N_3O_2S$ (*m/z*: found 435.2388; calcd 435.1980; for other analysis data, see Experimental). In accordance with NMR analytical data (including APT) and a plausible reaction mechanism (Scheme 1), the structure was assigned as 3,7-bis(dimethylamino)-10-(*p*-dimethylaminophenyl)thiaxanthene 5,5-dioxide (**8a**). Compound (**2b**) reacted under the same conditions to form 3-dimethylamino-10-(*p*-dimethylaminophenyl)thiaxanthene 5,5-dioxide (**8b**) as a white solid in 90%

yield. Compounds (**8a**,**b**) are colorless in acidic media. Surprisingly, compound (**2a**) in the absence of hydrazine was unchanged after refluxing overnight in methanol.

The preparation of compound (**4**) succeeded by using another procedure, which was used for the synthesis of **3** (Scheme 1). Thus, treatment of **2a** with DMAP and thionyl chloride in acetonitrile, followed by hydrazine monohydrate (10 equiv), gave the pure compound 6-dimethylamino-4,4-bis[(4-dimethylamino)phenyl]benzo-1,2,3-thiadiazinane 1-oxide (**4**) in 81% yield with satisfactory ^{1}H and ^{13}C NMR and microanalysis. Compound (**4**) represents a novel example of a rare heterocyclic system.[16]

In conclusion, novel heterocycles, the benzodithiolane *S*-oxide (**3a**) and the benzothiadiazinane *S*-oxide (**4**) were synthesized and characterized. Their potential uses as color formers for carbonless imaging were tested.[17]

EXPERIMENTAL

Melting points were measured on a hot-stage microscope and are uncorrected. ^{1}H and ^{13}C NMR data were collected on a 300 NMR spectrometer (300 MHz and 75 MHz respectively), with TMS or $CDCl_3$ as internal reference in $CDCl_3$. Column chromatography was carried out using 230-400 mesh silica gel.

6-Dimethylamino-3,3-bis[(4-dimethylamino)phenyl]-1,2-benzodithiolane 1-Oxide (3a). Thionyl chloride (0.36 mL, 5 mmol) was added dropwise to a solution of 2-dimethylaminopyridine (0.55 g, 4.5 mmol) in acetonitrile (30 mL) at -20 °C, and the mixture was stirred at -20 °C for 30 min. Compound (**2a**) (0.96 g, 2.2 mmol) was then added, and the mixture was stirred at -20 °C for a further 30 min. The mixture was allowed to warm to 0 °C and then kept at this temperature for 2 h. The above solution was added to a solution of sodium hydrogen sulfide (2.80 g, 50 mmol) in methanol (15 mL) and stirred at 0 °C for 2 h. After the addition of water (80 mL), the resulting precipitate was filtered, and sequentially washed with water and ether and then dried. The crude product was purified by recrystallization from ethyl acetate to obtain product (**3a**) (0.64 g, 65%), an off-white solid, mp 224-225 °C. *Anal.* Calcd for $C_{25}H_{29}N_3OS_2$: C, 66.49; H, 6.48; N, 9.31. Found: C, 66.30; H, 6.63; N, 9.19. ^{1}H NMR (δ, ppm): 2.90 (s, 18H), 6.38 (d, 1H, J = 8.1 Hz), 6.60-6.68 (m, 6H), 7.26 (d, 4H, J = 8.5 Hz). ^{13}C NMR (δ, ppm): 40.3, 40.5, 77.9, 107.0, 108.9, 111.3, 127.3, 130.1, 130.3, 134.3, 143.5, 149.4, 149.6. HRMS (FAB): Calcd for $C_{25}H_{29}N_3OS_2$ + H 452.1830, found 452.1833.

Typical Procedure for the Preparation of 3,7-Bis(dimethylamino)-10-(*p*-dimethylaminophenyl)-thiaxanthene 5,5-Dioxide (8a). A mixture of **2a** (0.65 g, 1.5 mmol) and hydrazine hydrate (1.0 mL, 20 mmol) in ethanol (50 mL) was heated under reflux for 12 h. The precipitated solid was collected and washed with ether three times to give the pure product **(8a)** (0.58 g, 90%), white solid, mp 195-196 °C (ethanol). *Anal.* Calcd for $C_{25}H_{29}N_3O_2S$: C, 68.93; H, 6.72; N, 9.65. Found: C, 68.61; H, 6.79; N, 9.74. ^{1}H NMR (δ, ppm): 2.92 (s, 6H), 2.97 (s, 12H), 5.21 (s, 1H), 6.70 (d, 4H, *J* = 8.1 Hz) 7.01 (d, 2H, *J* = 7.6 Hz), 7.12 (d, 2H, *J* = 7.5 Hz), 7.39 (s, 2H). ^{13}C NMR (δ, ppm): 40.3, 40.5, 46.1, 105.7, 112.7, 115.8, 129.1, 129.3, 130.1, 130.2, 137.3, 149.2, 149.5. HRMS (FAB): Calcd for $C_{25}H_{29}N_3O_2S$ 435.1980, found 435.2388.

3-Dimethylamino-10-(*p*-dimethylaminophenyl)thiaxanthene 5,5-Dioxide (8b). The title compound was prepared as for **8a** from **2b** and hydrazine monohydrate except that the reaction was refluxed for 4 h in 90% yield, white solid, mp 227-228 °C (ethanol). *Anal.* Calcd for $C_{23}H_{24}N_2O_2S$: C, 70.38; H, 6.17; N, 7.14. Found: C, 70.37; H, 6.28; N, 7.20. ^{1}H NMR (δ, ppm): 2.94 (s, 6H), 2.98 (s, 6H), 5.33 (s, 1H), 6.72 (d, 3H, *J* = 8.5 Hz), 7.04 (d, 1H, *J* = 8.8 Hz), 7.14 (d, 2H, *J* = 8.7 Hz), 7.20-7.23 (m, 1H), 7.39-7.42 (m, 3H), 8.12-8.15 (m, 1H). ^{13}C Nmr (δ, ppm): 40.3, 40.4, 47.1, 105.8, 112.7, 115.9, 123.4, 127.1, 127.9, 128.2, 129.2, 130.2, 130.4, 131.9, 137.1, 137.2, 142.5, 149.4.

6-Dimethylamino-4,4-bis[(4-dimethylamino)phenyl]benzo-1,2,3-thiadiazinane 1-Oxide (4). Thionyl chloride (0.32 mL, 4.5 mmol) was added dropwise to a solution of 4-dimethylaminopyridine (DMAP, 0.49 g, 4 mmol) in acetonitrile (30 mL) at -20 °C, and the solution was stirred at -20 °C for 30 min. Compound **(2a)** (0.86 g, 2 mmol) was then added, and the mixture was stirred at -20 °C for 30 min. The mixture was allowed to warm to 0 °C and then kept at this temperature for 2 h. The above mixture was added to hydrazine monohydrate (2.0 mL, 40 mmol) and stirred at 0 °C for 2 h. After the addition of water (80 mL), the resulting precipitate was filtered, sequentially washed with water and ether and then dried to obtain product **(4)** (0.73 g, 81%), blue solid, mp 162-163 °C (ethanol). *Anal.* Calcd for $C_{25}H_{31}N_5OS$: C, 66.78; H, 6.95; N, 15.59. Found: C, 66.84; H, 7.18; N, 15.24. ^{1}H NMR (δ, ppm): 2.92 (s, 6H), 2.94 (s, 6H), 2.97 (s, 6H), 3.59 (s, 2H), 6.64-6.69 (m, 4H), 6.77 (dd, 1H, *J* = 2.4, 8.7 Hz), 6.99 (d, 1H, *J* = 8.7 Hz), 7.05 (d, 1H, *J* = 2.4 Hz), 7.16-7.26 (m, 4H). ^{13}C NMR (δ, ppm): 40.5, 40.6, 82.8, 106.9, 111.9, 112.1, 116.1, 126.2, 129.0, 130.4, 134.5, 149.8, 150.5.

This paper is dedicated to Dr. Bernhard Witkop in the celebration of his 80th birthday.

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17. The color former properties of compounds **3a** and **4** were measured using a HunterLab Lab Scan II Sprectrophotometer, as discussed in detail in our previous paper.[2] Both compounds develop blue color (**3a**: L, 78.62; a, -6.23; b, -12.77. **4**: L, 73.71; a, -6.64; b, -15.54).

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