An Odorless Preparative Method of Sulfides and Thiocarboxylic *S*-Esters Using 3-(Alkylthio)-1,2-benzisothiazole 1,1-Dioxide

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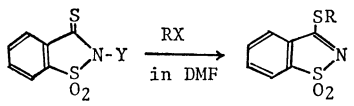
Synopsis. It was found that sodium salt of 1,2-benzisothiazole-3(2*H*)-thione 1,1-dioxide (thiosaccharin) readily reacted with alkyl halide affording 3-(alkylthio)-1,2-benzisothiazole 1,1-dioxide (**3**). Treatment of **3** with piperidine produces the corresponding alkanethiol *in situ* quantitatively and subsequent treatment with various electrophiles gives the corresponding sulfides and thiocarboxylic *S*-esters in good yields.

Recently the herbicidal and fungicidal properties of 3-substituted 1,2-benzisothiazole 1,1-dioxide have been noted,[1,2] and the preparation of such compounds was performed by the reaction of 3-chloro-1,2-benzisothiazole 1,1-dioxide with an alcohol or thiol in the presence of base.[2] Generally, thiols have unpleasant odor, therefore the development of odorless equivalent of thiols would be convenient. We have found that 3-(alkylthio)-1,2-benzisothiazole 1,1-dioxide (**3**), which is prepared from the sodium salt (**2**) of thiosaccharin (**1**) and alkyl halides is an efficient synthetic equivalent of alkanethiols. 3-(Alkylthio)-1,2-benzisothiazole 1,1-dioxide (**3**) was prepared upon treatment of **2** with 1.1 equivalent of halide in excellent yields as shown in Table 1 (Eq. 1). Odorless compounds **3** reacted

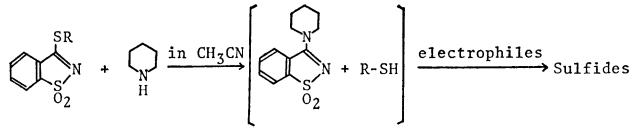


(1)

1 Y=H
2 Y=Na

3(BID-SR)

with secondary amines stoichiometrically. The reaction of **3** with piperidine produces the corresponding alkanethiols smoothly *in situ*. Subsequently treatment with electrophiles gives the corresponding sulfides in one-pot reaction. Treatment with acid chlorides led



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to the corresponding thiocarboxylic *S*-esters in high yields. In the same manner, the reactions with other electrophiles such as α,β-unsaturated carbonyl compounds, alkyl halides and epoxide also give satisfactory results. As mentioned above, it is clear that readily available **3** is a useful equivalent of the corresponding thiol.

Experimental

*Preparation of 3-(Alkylthio)-1,2-benzisothiazole 1,1-Dioxides (**3a—g**).* Typically, to a solution of **2** (663 mg, 3 mmol) in DMF (2 ml) was added a solution of benzyl bromide (564 mg, 3.3 mmol) in DMF (2 ml) at room temperature under nitrogen. After stirring for 3 h, water was added to the reaction mixture. The precipitate was recrystallized from ethanol and dichloromethane to give 3-(benzylthio)-1,2-benzisothiazole-1,1-dioxide (**3a**) (791 mg, 93%), whose structure was established by comparison with the authentic sample prepared by the reaction of 3-(chloro)-1,2-benzisothiazole 1,1-dioxide with benzenemethanethiol in the presence of triethylamine in CH_3CN (Mp, IR). **3a**: Mp 141.0—142.0 °C; IR (KBr) 1587, 1320, 1163 cm^{-1}; Found: C, 57.82; H, 3.94; N, 4.75%. Calcd for $C_{14}H_{11}NO_2S_2$: C, 58.11; H, 3.83; N, 4.85%. **3b**: Mp 144.5—145.5 °C; IR (KBr) 1587, 1312, 1163 cm^{-1}: Found: C, 59.34; H, 4.14, N, 4.75%. Calcd for $C_{15}H_{13}NO_2S_2$: C, 59.40, H, 4.32; N, 4.62%. **3c**: Mp 129.5—130.5 °C; IR (KBr) 1587, 1328, 1166 cm^{-1}; Found: C, 61.12; H, 4.31; N, 4.38%. Calcd for $C_{16}H_{13}NO_2S_2$: C, 60.93; H, 4.15; N, 4.44%. **3d**: Mp 114.0—115.0 °C; IR (KBr) 3067, 1497, 1325, 1235, 1167, 990, 930, 784 cm^{-1}; Found: C, 50.37; H, 3.81; N, 5.82%. Calcd for $C_{10}H_9NO_2S_2$: C, 50.19; H, 3.79; N, 5.86%. **3e**: Mp 168.0—169.0 °C; IR (KBr) 3257, 1493, 1319, 1157 cm^{-1}; Found: C, 50.63; H, 2.85; N, 5.73%. Calcd for $C_{10}H_7NO_2S_2$: C, 50.62; H, 2.97; N, 5.90%. **3f**: Mp 234.5—235.5 °C; IR (KBr) 2247, 1504, 1318, 1163 cm^{-1}; Found: C, 45.47; H, 2.30; N, 11.97%. Calcd for $C_9H_6N_2O_2S_2$: C, 45.39; H, 2.54; N, 11.76%. **3g**: Mp 227.5—228.5 °C; IR (KBr) 1488, 1316, 1170, 1156, cm^{-1}; Found: C, 45.30; H, 3.17; N, 6.53%. Calcd for $C_8H_7NO_2S_2$: C, 45.08; H, 3.31; N, 6.57%.

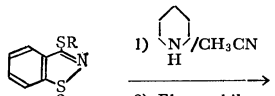
TABLE 1. PREPARATION OF 3-(ALKYLTHIO)-1,2-BENZISOTHIAZOLE 1,1-DIOXIDE (**3**) FROM THE SODIUM SALT (**2**) AND HALIDES

RX	Time/h	**3a—g**	Yield/%
$PhCH_2Br$[b]	3	**3a**	93
$PhCH_2CH_2Br$[c]	11	**3b**	82
$PhCH{=}CHCH_2Cl$[c]	3.5	**3c**	84
$CH_2{=}CHCH_2Br$[b]	3	**3d**	87
$CH{\equiv}CCH_2Br$[b]	4	**3e**	80
$N{\equiv}CCH_2Cl$[b]	3.5	**3f**	85
CH_3I[b]	3	**3g**	89

a) The reactions performed in DMF. b) Room temp. c) 50 °C.

*Preparation of Thiocarboxylic S-Esters (**4a—h**).* Typically, to a solution of 3-(methylthio)-1,2-benzisothiazole 1,1-dioxide (3 g) (211 mg, 1 mmol) in CH_3CN (3 ml) was added an CH_3CN solution of piperidine (85 mg, 1 mmol) at −18 °C under N_2. After 20 min a solution of benzoyl chloride (169 mg, 1.2 mmol) in CH_3CN (1.5 ml) was added followed by the addition of a solution of triethylamine (121 mg, 1.2 mmol) in CH_3CN (1.5 ml). The mixture was kept at −18 °C for 1.5 h and gradually warmed to room temperature. The solvent was removed *in vacuo* to give a residue. A crude material was subjected to preparative TLC (benzene) to give pure **4d** (138 mg, 91%). **4a**: Oil; *m/e* 178 (M^+); IR (neat) 1656, 1200, 901, 673 cm^{-1}; NMR ($CDCl_3$) δ 3.70 (2H, d, J=7.0 Hz), 4.96—5.48 (2H, m), 5.55—6.26 (1H, m), 7.15—8.11 (5H, m). **4b**: Oil; *m/e* 176 (M^+); IR (neat) 3300, 1660, 1205, 911, 680 cm^{-1}; NMR ($CDCl_3$)

Table 2. Preparation of thiocarboxylic *S*-esters (**4**) and sulfides (**5**) from BID-SR (**3**) and electrophiles



BID-SR

BID-SR	Electrophile	Product	Yield/%
3d	PhCOCl	$PhCOSCH_2CH{=}CH_2$[a] **(4a)**	95[a]
3e	PhCOCl	$PhCOSCH_2C{\equiv}CH$[a] **(4b)**	91[a]
3f	PhCOCl	$PhCOSCH_2C{\equiv}N$[a] **(4c)**	89
3g	PhCOCl	$PhCOSCH_2$[a] **(4d)**	91
3a	CH_3COCl	CH_3COSCH_2Ph[b] **(4e)**	94[b]
3a	$PhCH_2COCl$	$PhCH_2COSCH_2Ph$[b] **(4f)**	92[b]
3a	$CH_3(CH_2)_2COCl$	$CH_3(CH_2)_2COSCH_2Ph$[b] **(4g)**	94[b]
3a	$(CH_3)_3CCOCl$	$(CH_3)_3CCOSCH_2Ph$[c] **(4h)**	33[c]
3a	$CH_3COCH{=}CH_2$	$CH_3COCH_2CH_2SCH_2Ph$[d] **(5a)**	quant.[g]
3b	$CH_3COCH{=}CH_2$	$CH_3COCH_2CH_2SCH_2CH_2Ph$[d] **(5b)**	87
3c	$CH_3COCH{=}CH_2$	$CH_3COCH_2CH_2SCH_2CH{=}CHPh$[d] **(5c)**	92
3a	$CH_2{=}CHCHO$	$PhCH_2SCH_2CH_2CHO$[d,g] **(5d)**	92[g]
3a	$CH_3CH{=}CHCHO$	$PhCH_2SCH(CH_3)CH_2CHO$[d,g] **(5e)**	89[g]
3a	$PhCH{=}CHCH_2Cl$	$PhCH_2SCH_2CH{=}CHPh$[e] **(5f)**	88
3a	$(CH_3)_2CHBr$	$PhCH_2SCH(CH_3)_2$[e] **(5g)**	81[11]
3a	$CH_3(CH_2)_3CH_2I$	$PhCH_2S(CH_2)_4CH_3$[e] **(5h)**	89[11]
3a	$PhCH_2Br$	$PhCH_2SCH_2Ph$[e] **(5i)**	90[12]
3a		PhCH-CH(OH)Ph **(5j)** SCH_2Ph (erythro)	quant.

a) Condition: −18 °C—room temp, 90 min. b) Room temp, 5 min. c) Room temp, 1.5 h. d) Room temp, 4.5 h. e) Room temp, 5 h. f) Triethylamine used as a base in **4a—h**, DBU used in **5a—i**, 2.4 equiv. of 1 M NaOH used in **5j**. g) They were isolated as 2,4-dinitrophenylhydrazone derivatives.

δ 2.22 (1H, t, J=2.6 Hz), 3.83 (2H, d, J=2.6 Hz), 7.23—8.17 (5H, m). **4c**: Oil; *m/e* 177 (M^+); IR (neat) 2985, 1667, 1211, 911 cm^{-1}; NMR ($CDCl_3$) δ 3.85 (2H, s), 7.26—8.07 (5H, m). **4d**: Oil; *m/e* 152 (M^+); IR (neat) 1650, 1195, 902, 673 cm^{-1}; NMR ($CDCl_3$) δ 2.45 (3H, s), 7.17—8.07 (5H, m). **4e**: Oil; *m/e* 166 (M^+); IR (neat) 1680, 1126, 697 cm^{-1}; NMR ($CDCl_3$) δ 2.32 (3H, s), 4.10 (2H, s), 7.24 (5H, s). **4f**: Mp 39.5—40.5 °C; *m/e* 242 (M^+); IR (KBr) 1672, 1014, 697 cm^{-1}; NMR ($CDCl_3$) δ 3.71 (2H, s), 3.99 (2H, s), 7.07 (5H, s), 7.14 (5H, s). **4g**: Oil; *m/e* 194 (M^+); IR (neat) 2959, 1680, 982, 697 cm^{-1}; NMR ($CDCl_3$) δ 0.91 (3H, t, J=7.0 Hz), 1.66 (2H, t,q. J=7.2, J=7.0 Hz), 2.49 (2H, t, J=7.2 Hz), 4.03 (2H, s), 7.12 (5H, s). **4h**: Oil; *m/e* 208 (M^+); IR (neat) 2690, 1672, 949, 697 cm^{-1}; NMR ($CDCl_3$) δ 1.24 (9H, s), 4.03 (2H, s), 7.20 (5H, s).

*Addition of Thiols to α,β-Unsaturated Carbonyl Compounds (**5a—e**).* Typically, to a solution of 3-(cinnamylthio)-1,2-benzisothiazole 1,1-dioxide (**3c**) (154 mg, 0.5 mmol) in CH_3CN (1 ml) was added a CH_3CN solution of piperidine (43 mg, 0.5 mmol) under N_2 at room temperature. After 30 min a solution of methyl vinyl ketone (38 mg, 0.5 mmol) in CH_3CN (1.5 ml) was added dropwise and then after 3 h a drop of triethylamine was added. The reaction mixture was stirred for additional 1.5 h and evaporated *in vacuo*. Purification with preparative TLC (benzene–ethyl acetate=10:1 v/v) gave **5a** (101 mg, 92%). **5a**: Oil; *m/e* 194 (M^+); IR (neat) 1700, 1408, 1353, 693 cm^{-1}; NMR ($CDCl_3$) δ 2.09 (3H, s), 2.62 (4H, s), 3.69 (2H, s), 7.26 (5H, s). **5b**: Oil; *m/e* 208 (M^+); IR (neat) 2920, 1709, 1355, 690 cm^{-1}; NMR ($CDCl_3$) δ 2.12 (3H, s), 2.69 (4H, s), 2.80 (4H, s), 7.17 (5H, s). **5c**: Oil; *m/e* 220 (M^+); IR (neat) 3035, 2933, 1712, 1361, 963 cm^{-1}; NMR ($CDCl_3$) δ 2.08 (3H, s), 2.67 (4H, s), 3.25 (2H, d, J=6.0 Hz), 6.12 (1H, t, d, J=6.0, 15.6 Hz), 6.35 (1H, d, J=15.6 Hz),7.03—7.47 (5H, m).

Compounds (**5d—e**) were not stable to silica gel purification and then characterized as 2,4-dinitrophenylhydrazones, respectively. **5d**: Mp 99.0—99.5 °C (from EtOH); Found: C, 53.24; H, 4.42; N, 15.53%. Calcd for $C_{16}H_{16}N_4O_4S$: C, 53.32; H, 4.48; N, 15.55%. **5e**: Mp 65.0—65.5 °C (from EtOH); Found: C, 54.40; H, 4.69; N, 14.94%. Calcd for $C_{17}H_{18}N_4O_4S$: C, 54.43; H, 4.85; N, 14.96%.

*Preparation of the Sulfides (**5f—i**).* Typically, to a suspension of 3-(benzylthio)-1,2-benzisothiazole 1,1-dioxide (**3a**) (142 mg, 0.5 mmol) in CH_3CN (1 ml) was added a solution of piperidine (43 mg, 0.5 mmol) in CH_3CN (1 ml) under N_2. After stirring for 20 min, a solution of DBU (92 mg, 0.6 mmol) in CH_3CN (1 ml) was added followed by the addition of a solution of benzyl bromide (102 mg, 0.6 mmol) in CH_3CN (1 ml). The reaction mixture was stirred for 5 h and worked up in the usual way. Preparative TLC (hexane–benzene=5:2 v/v) gave pure **5i** (96 mg, 90%). **5f**: Oil; *m/e* 240 (M^+); IR (neat) 3049, 1496, 961 cm^{-1}; NMR ($CDCl_3$) δ 3.21 (2H, d, J=6.4 Hz), 3.62 (2H, s), 6.11 (H, t, d, J=6.4, 15.4 Hz), 6.20 (1H, d, J=15.4 Hz), 6.92—7.74 (10H, m). **5g**: Oil; *m/e* 166 (M^+); IR (neat) 2950, 1484, 1443, 1374, 685 cm^{-1}; NMR ($CDCl_3$) δ 1.23 (6H, d, J=6.6 Hz), 2.68 (1H, q, J=6.6 Hz), 3.67 (2H, s), 7.19 (5H, s). **5h**: Oil; *m/e* 194 (M^+); IR (neat) 2920, 1481, 1443, 685 cm^{-1}; NMR ($CDCl_3$) δ 0.63—1.82 (9H, m), 2.37 (2H, t, J=7.0 Hz), 3.63 (2H, s), 7.18 5H, s). **5i**: Oil; *m/e* 214 (M^+); IR (neat) 3012, 1488, 1445, 685 cm^{-1}; NMR ($CDCl_3$) δ 3.53 (4H, s), 7.20 (10H, s). **5j**: Mp 107—108 °C; IR (KBr) 3390, 1595, 1445, 1046 cm^{-1}; NMR ($CDCl_3$) δ 2.31 (1H, bs), 3.29 (2H, s), 3.80 (1H, d, J=6.4 Hz), 4.85 (1H, d, J=6.4 Hz), 6.71—7.61 (15H, m); Found: C, 78.79; H, 6.26%. Calcd for $C_{21}H_{20}OS$: C, 78.71; H, 6.29%.

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