A FACILE ONE-POT PREPARATION OF 2,3-DIHYDRO-1,4-BENZODITHIINS AND 2,3-DIHYDRO-1,4-BENZOXATHIINS

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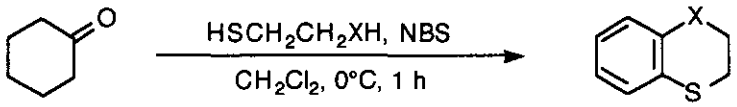
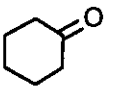
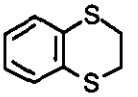
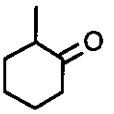
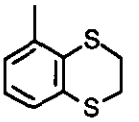
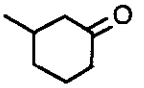
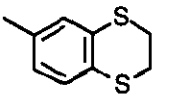
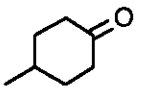
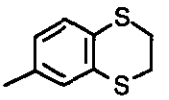
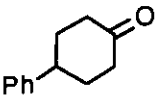
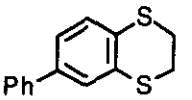
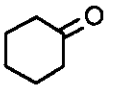
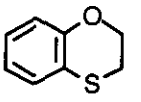
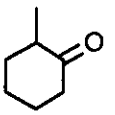
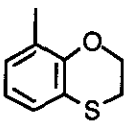
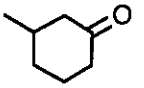
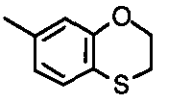
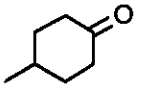
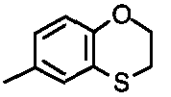
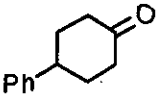
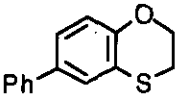
Abstract - 2,3-Dihydro-1,4-benzodithiines and 2,3-dihydro-1,4-benzoxathiines were prepared in good yields by a one-pot procedure from the reaction of cyclohexanone derivatives with ethane-1,2-dithiol or 2-mercaptoethanol using *N*-bromosuccinimide in dichloromethane at 0°C.

The monobenzofused 1,4-dithiin and 1,4-oxathiin derivatives were originally prepared *via* a base-catalyzed nucleophilic substitution reaction of benzene-1,2-dithiol or 2-mercaptophenol with α-haloacetal.[1] Although the improved method starting from more readily available materials such as thiophenol or phenol has been devised,[2] the preparation of these compounds is still not easy. The chemistry of such compounds appears scarcely exploited for the disadvantages of troublesome synthetic methods. In this paper we wish to report a simple method for the preparation of 2,3-dihydro-1,4-benzodithiins, and 2,3-dihydro-1,4-benzoxathiins from easily available cyclohexanones.



1: X=S or O **4**

Table 1. Preparation of 2,3-dihydro-1,4-benzodithiins and 2,3-dihydro-1,4-benzoxathiins

Entry	Substrate(**1**)	Product(**4**)	Yield/%[a]	[mp/°C] or bp/°C/Torr
a			68	102/0.5
b			48	85-90/0.1[d]
c			52[c]	90-95/0.1[d]
d			58	90-95/0.1[d]
e			75	[79-80]
f			82	75/0.7
g			45	70-75/0.1[d]
h			81[c]	75-80/0.1[d]
i			83	95-100/0.1[d]
j			86	140-145/0.1[d]

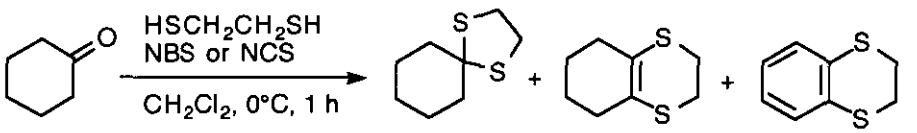
a) Yields were based on the isolated compounds. All compounds were identified by ir, nmr, and ms spectra as well as by direct comparison with authentic specimens.[4]

b) Regioisomer **4b** was also formed. The ratio of **4c/4b** was determined to be 4/1 by ^{1}H-NMR.

c) The content of regioisomer **4g** was negligible.

d) Bps refer to Kugelrohr oven temperatures.

For example, 2,3-dihydro-1,4-benzodithiin (**4a**) was prepared in 68% yield by stirring a mixture of cyclohexanone, ethane-1,2-dithiol and *N*-bromosuccinimide (NBS, 3 equiv.) in dichloromethane at 0 °C for 1 h. When 2-mercaptoethanol was used instead of ethane-1,2-dithiol, 2,3-dihydro-1,4-benzoxathiin (**4f**) was obtained in 82% yield. Thus various cyclohexanones were converted into 2,3-dihydro-1,4-benzodithiins and 2,3-dihydro-1,4-benzoxathiins by this method. Two regioisomers could be formed from 3-methylcyclohexanone, but **4c** and **4h** were formed selectively. The results are summarized in Table 1.



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

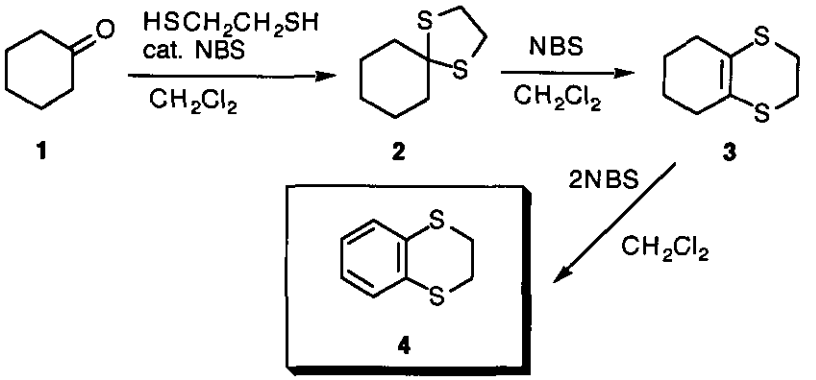
Table 2. The reaction of cyclohexanone with 1,2-ethanedithiol catalyzed by NBS or NCS

Entry	**1** /mmol	Ethanedithiol /mmol	NBS or NCS equiv./mol%	**2** /%[a)]	**3** /%[a)]	**4** /%[a)]
a	1	1	NBS(0.1)	92	0	0
b	1	1	NBS(0.5)	66	10	0
c	1	1	NBS(1.0)	25	40	2
d	1	1	NBS(2.0)	4	23	40
e	1	1	NBS(3.0)	0	0	68
f	1	1	NBS(4.0)	0	0	27[b)]
g	1	1	NCS(0.1)	87	0	0
h	1	1	NCS(0.5)	66	2	1
i	1	1	NCS(1.0)	21	9	9
j	1	1	NCS(2.0)	5	12	5
k	1	1	NCS(3.0)	0	0	3

a) Yields were estimated by glc analysis.

b) Products were obtained together with brominated compounds.

In order to elucidate the mechanism of the present reaction, the reaction of cyclohexanone with ethanedithiol was carried out under various conditions in the presence of various amounts of NBS or *N*-chlorosuccinimide (NCS). The results are summarized in Table 2. When the reaction was carried out in the presence of a catalytic amount of NBS, cyclohexanone ethylenedithioacetal (**2**) was formed in 92% yield. A mixture of **2**, 2,3,5,6,7,8-hexahydro-1,4-benzodithiin (**3**) and **4** was obtained if 0.5-2.0 equivalents of NBS were used. Three equivalents of NBS were required to get **4** as a sole product. NCS was effective for the dithioacetalization of **1**, it was less effective to induce ring expansion[3] and aromatization[3,5] than NBS. Thus NBS catalyzed the dithioacetalization of ketone, ring expansion and aromatization as shown in Scheme 1.



Scheme 1

Although the similar ring expansion and aromatization can be induced by halogens,[3] this method offers a more convenient and versatile pathway for the synthesis of 1,4-benzodithiins and 1,4-benzoxathiins from cyclohexanones by a one-pot procedure. The superiority of the present method over the literature methods[1-3] is evident, because procedures are very simple and the requisite starting materials are readily available.

EXPERIMENTAL

Melting points were obtained on an Yanaco micro melting point apparatus and are uncorrected. Proton and carbon magnetic resonance spectra (^{1}H and ^{13}C nmr) were recorded at 270 MHz on a JEOL JNM-GSX270 FT-NMR

spectrometer. Ir spectra were recorded with a Hitachi 270-30 spectrophotometer. Mass spectra were measured on a Hitachi M-80B instrument operating at 20 eV. Microanalyses were performed on a Perkin-Elmer 240C elemental analyzer. Column chromatography was performed on Alumina, Activated (Wako Pure Chemical Industries, LTD., abt. 200 mesh). Cyclohexanone and substituted cyclohexanones were purchased from Wako Pure Chemical Industries, LTD. All chemicals and solvents were used as purchased without purification.

General Procedure for the Preparation of 2,3-Dihydro-1,4-benzodithiin (**4a**)[2]. To a stirred mixture of cyclohexanone (10 mmol) and ethane-1,2-dithiol (10 mmol) in dry dichloromethane (100 ml), *N*-bromosuccinimide(NBS, 5.34 g, 30 mmol) was added at 0 °C. After 1 h, the reaction mixture was washed with water (100 ml) and extracted with dichloromethane. The organic layer was dried over magnesium sulfate and evaporated under reduced pressure to give the crude product. The obtained product was purified by aluminum chromatography or distilled under reduced pressure to give corresponding pure 2,3-dihydro-1,4-benzodithiin. bp 102°C/0.5 Torr; ^{1}H-nmr($CDCl_3$) δ 3.25(4H, s), 7.0-7.2(4H, m); ^{13}C-nmr($CDCl_3$) δ 29.18, 125.18, 128.81, 131.29; ir(NaCl) 3052, 2916, 1456, 1424, 1290, 1250, 1106, 746 cm^{-1}; ms(20 eV) m/z(rel intensity) 168(M^+, 100), 153(87), 140(40).

Following compounds were prepared by this procedure:

2,3-Dihydro-5-methyl-1,4-benzodithiin (**4b**)[3]: bp 85-90°C/0.1 Torr(Kugelrohr oven temperature); ^{1}H-nmr($CDCl_3$) δ 2.26(3H, s), 3.22(4H, s), 6.8-7.0(4H, m); ^{13}C-nmr($CDCl_3$) δ 20.07, 29.00, 29.39, 124.17, 126.45, 126.73, 130.70, 130.95, 136.46; ir(NaCl) 3048, 2916, 1440, 1290, 1182, 1054, 768 cm^{-1}; ms(20 eV) m/z(rel intensity) 182(M^+, 100), 167(100), 153(65), 121(30).

2,3-Dihydro-6-methyl-1,4-benzodithiin (**4c** and **4d**): bp 90-95°C/0.1 Torr(Kugeorohr oven temperature); ^{1}H-nmr($CDCl_3$) δ 2.21(3H, s), 3.18(4H, s), 6.7-7.0(3H, m); ^{13}C-nmr($CDCl_3$) δ 20.60, 28.96, 29.22, 126.10, 127.58, 128.54, 129.00, 130.91, 134.90; ir(NaCl) 3044, 2916, 1470, 1290, 1116, 808 cm^{-1}; ms(20 eV) m/z(rel intensity) 182(M^+, 100), 167(100), 153(63), 121(25). Anal. Calcd for $C_9H_{10}S_2$: C, 59.30; H, 5.53. Found: C, 58.95; H, 5.57. **4c** was obtained as a mixture of 2,3-dihydro-6-methyl-1,4-benzodithiin and 2,3-dihydro-5-methyl-1,4-benzodithiin (4:1) and the raitio was estimated by ^{1}H-nmr.

2,3-Dihydro-6-phenyl-1,4-benzodithiin (**4e**): mp 79-80°C; ^{1}H-nmr($CDCl_3$) δ 3.20(4H, S), 7.18-7.51(8H, m); ^{13}C-nmr($CDCl_3$) δ 28.98, 29.04, 123.86, 126.57, 127.04, 127.23, 128.64, 128.96, 130.14, 131.42, 138.09,

139.76; ir(KBr) 3024, 2912, 1460, 764, 702 cm^{-1}; ms(20 eV) m/z(rel intensity) 244(M^+, 100), 229(55), 216(17). Anal. Calcd for $C_{14}H_{12}S_2$: C, 68.61; H, 4.95. Found: C, 68.42; H, 4.98.

2,3-Dihydro-1,4-oxathiin (**4f**)[2]: bp 75°C/0.7 Torr; ^{1}H-nmr($CDCl_3$) δ 3.12(2H, t, J=4.6 Hz), 4.40(2H, t, J=4.6 Hz), 6.79-7.05(4H, m); ^{13}C-nmr($CDCl_3$) δ 25.62, 65.22, 117.65, 118.33, 121.48, 125.49, 127.48, 151.63; ir(NaCl) 2928, 1572, 1478, 1442, 1306, 1216, 1060, 752 cm^{-1}; ms(20 eV) m/z(rel intensity) 152(M^+, 100), 137(28), 96(96).

2,3-Dihydro-8-methyl-1,4-oxathiin (**4g**): bp 70-75°C/0.1 Torr(Kugelrohr oven temperature); ^{1}H-nmr($CDCl_3$) δ 2.16(3H, s), 3.05(2H, t, J=4.6 Hz), 4.38(2H, t, J=4.6 Hz), 6.7-6.9(3H, m); ^{13}C-nmr($CDCl_3$) δ 16.10, 25.64, 65.23, 116.93, 120.64, 124.96, 126.82, 127.34, 149.73; ir(NaCl) 2924, 1470, 1306, 1210, 1084, 766 cm^{-1}; ms(20 eV) m/z(rel intensity) 166(M^+, 100), 151(21), 110(84). Anal. Calcd for $C_9H_{10}OS$: C, 65.03; H, 6.06. Found: C, 64.79; H, 5.99.

2,3-Dihydro-7-methyl-1,4-oxathiin (**4h**): bp 75-80°C/0.1 Torr(Kugelrohr oven temperature); ^{1}H-nmr($CDCl_3$) δ 2.22(3H, s), 3.04(2H, t, J=4.6 Hz), 4.34(2H, t, J=4.6 Hz), 6.6-6.7(2H, m), 6.89(1H, d, J=8.5 Hz); ^{13}C-nmr($CDCl_3$) δ 20.74, 25.42, 65.23, 113.78, 118.71, 122.37, 127.12, 135.44, 151.23; ir(NaCl) 2924, 1488, 1306, 1160, 802 cm^{-1}; ms(20 eV) m/z(rel intensity) 166(M^+, 100), 151(28), 110(100). Anal. Calcd for $C_9H_{10}OS$: C, 65.03; H, 6.06. Found: C, 64.73; H, 6.04.

2,3-Dihydro-6-methyl-1,4-oxathiin (**4i**): bp 95-100°C/0.1 Torr(Kugelrohr oven temperature); ^{1}H-nmr($CDCl_3$) δ 2.21(3H, s), 3.09(2H, t, J=4.6 Hz), 4.35(2H, t, J=4.6 Hz), 6.70(1H, d, J=8.2 Hz), 6.77(1H, d, J=8.2 Hz), 6.83(1H, s); ^{13}C-nmr($CDCl_3$) δ 20.37, 25.66, 65.18, 117.12, 118.01, 126.23, 127.50, 130.84, 149.45; ir(NaCl) 2924, 1496, 1304, 1228, 1054, 1018, 812, 740 cm^{-1}; ms(20 eV) m/z(rel intensity) 166(M^+, 100), 110(82). Anal. Calcd for $C_9H_{10}OS$: C, 65.03; H, 6.06. Found: C, 64.86; H, 6.08.

2,3-Dihydro-6-phenyl-1,4-oxathiin (**4j**): bp 140-145°C/0.1 Torr(Kugelrohr oven temperature); ^{1}H-nmr($CDCl_3$) δ 3.11(2H, t, J=4.6 Hz), 4.40(2H, t, J=4.6 Hz), 6.87(1H, d, J=8.2 Hz), 7.2-7.5(7H, m); ^{13}C-nmr($CDCl_3$) δ 25.60, 65.36, 117.92, 118.59, 124.36, 125.92, 126.63, 126.86, 128.65, 134.66, 140.21, 151.11; ir(NaCl) 3056, 3028, 2964, 1480, 1304, 1224, 1058, 1014, 764, 700cm^{-1}; ms(20 eV) m/z(rel intensity) 228(M^+, 100), 172(68), 128(9). Anal. Calcd for $C_{14}H_{12}OS$: C, 73.65; H, 5.30. Found: C, 73.55; H, 5.54.

REFERENCES

1. W. E. Parham, T. M. Roder, and W. R. Hasek, J. Am. Chem. Soc., 1953, **75**, 1647; W. E. Parham, T. M. Roder, and W. R. Hasek, J. Am. Chem. Soc., 1954, **76**, 1068.
2. J. H. Verheijen and H. Klosterziel, Synthesis, 1975, 451.
3. R. Caputo, C. Ferreri, G. Palumbo, and F. Russo, Tetrahedron, 1991, **47**, 4187; R. Caputo, C. Ferreri, and G. Palumbo, Synthesis, 1991, 223; R. Caputo, C. Ferreri, and G. Palumbo, Tetrahedron, 1986, **42**, 2369.
4. E. Wenkert and C. A. Broka, Finn. Chem. Lett., 1984, 126.
5. I. G. Mursakulov, E. A. Ramazanov, F. F. Kerimov, I. M. Abbasov, and N. S. Zefirov, Zh. Org. Khim., 1990, **26**, 134; I. G. Mursakulov, E. A. Ramazanov, F. F. Kerimov, I. M. Abbasov, and N. S. Zefirov, Zh. Org. Khim., 1986, **22**, 448.

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