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SYNTHESIS AND REACTIVITY OF 3-METHYLSULFINYL-2*H*-CYCLOHEPTA[*b*]FURAN-2-ONES

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Abstract – 2*H*-Cyclohepta[*b*]furan-2-ones (**2a**,**b**) reacted with dimethyl sulfide dittiflate to give dimethyl(2-oxo-2*H*-cyclohepta[*b*]furan-3-yl)sulfonium trifluoromethanesulfonates (**3a**,**b**), which were treated with Et_3N to give 3-methylthio-2*H*-cyclohepta[*b*]furan-2-ones (**4a**,**b**). Sulfides **4a** and **4b** were oxidized with *m*-CPBA to give corresponding sulfoxides (**5a**,**b**) and sulfones (**6a**,**b**). The sulfoxides (**5a**,**b**) thermally underwent coupling reaction to give 3,3'-bi-2*H*-cyclohepta[*b*]furan-2-ones (**7a**,**b**). The sulfoxides (**5a**,**b**) reacted with trifluoromethanesulfonic anhydride (Tf_2O) to afford sulfonium ions **8a** and **8b** at lower temperature, which reacted with **2a** or **2b** to give sulfonium ions (**9a-c**). Treatment of compounds **9a-c** with Et_2NH or Et_3N gave corresponding sulfide products (**10a-c**).

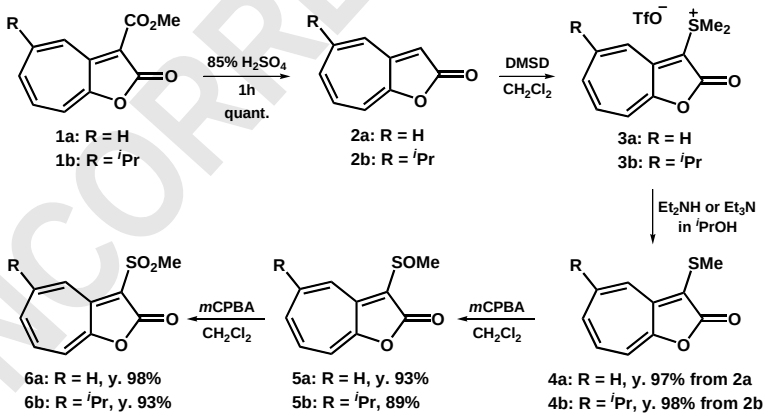
†Dedicated to Prof. Ryoji Noyori on the occasion of his 70th birthday.

INTRODUCTION

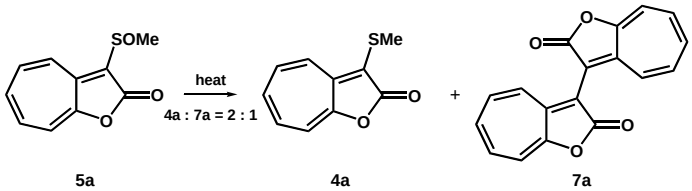
Dimethyl sulfide ditriflate (DMSD)[1] is a good electrophile, which is useful for introduction of methylthio group in aromatic compounds. 2*H*-Cyclohepta[*b*]furan-2-ones,[2] which have heptafulven and heteroazulene structures,[3] react with electrophiles such as arylaldehydes[4] and 1-trifuruoromethane-sulfonylpyridinium trifluoromethanesulfonate[5] to afford triarylmethanes and dihydropyridinyl-substituted products, respectively. During the investigation of electrophilic substitution using Tf_2O in 2*H*-cyclo-hepta[*b*]furan-2-ones, we found new coupling reactions of 2*H*-cyclohepta[*b*]furan-2-one rings.[6]

RESULTS AND DISCUSSION

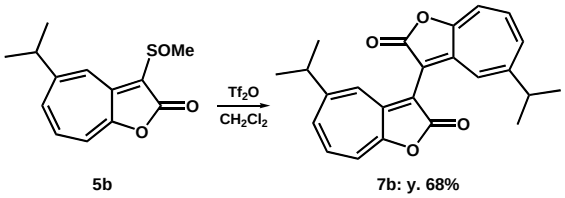
Methyl 2-oxo-2*H*-cyclohepta[*b*]furan-3-carboxylates (**1a**,**b**) were selected as starting materials. Methoxycarbonyl group was easily removed with 85% H_2SO_4 to afford 2*H*-cyclohepta[*b*]furan-2-ones (**2a**,**b**).[2] **2a** could be recrystallized from EtOH, but **2b** was oil at room temperature. **2a** and **2b** reacted with DMSD to afford aryl dimethyl sulfoniumu trifluoromethanesulfonate derivatives (**3a**,**b**) as greenish crystals. Although **3a** was recrystallized from MeOH, **3b** couldn't because of its high solubility. These sulfonium compounds (**3a**,**b**) dissolved in ^{i}PrOH were treated with Et_2NH or Et_3N at 100 °C to give **4a** and **4b**, respectively.[7] These sulfides (**4a**,**b**) were easily oxidized with *m*-CPBA to give 3-methylsulfinyl-2*H*-cyclohepta[*b*]furan-2-ones (**5a**,**b**) as yellow crystals. Furthermore **5a** and **5b** were oxidized with anther *m*-CPBA to afford **6a** and **6b** within 2h, respectively.



Scheme 1



Scheme 2

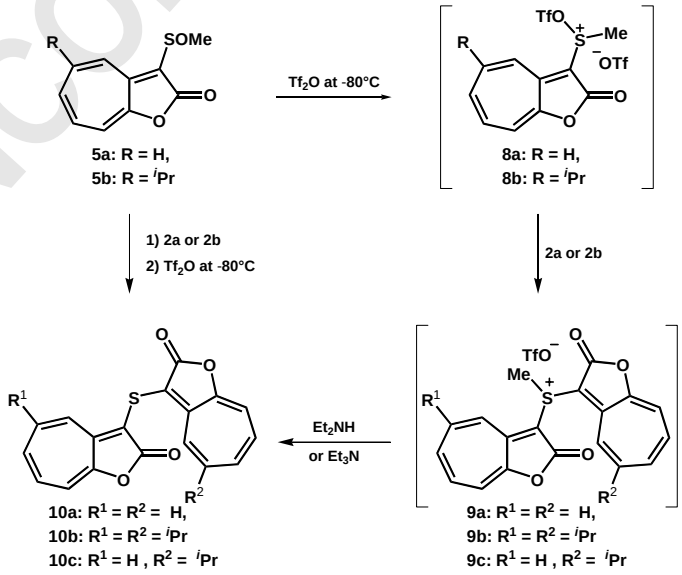


5b 7b: y. 68%

Scheme 3

We thought that diaryl sulfides (**10a**-**c**) can be obtained from sulfoxides (**5a**,**b**) similarly. Sulfoxide **5b** dissolved in CH_2Cl_2 was reacted with Tf_2O. When Tf_2O was dropped into the solution, the solution turned from yellow to dark brown. After the purification, unexpected product (**7b**) was obtained as brown plates (Scheme 3). The structure of **7b** was determined by spectral data. Similarly **5a** was treated with Tf_2O. However, only unidentified products were obtained. Product **7a** was prepared by heating **5a** at 40 °C under reduced pressure (Scheme 2), along with **4a** (**4a** : **7a** = 2 : 1). Although the mechanism is not clear, we supposed that the reaction was taken place by heat and/or in the presence of small amount of acid. There are few reports concerning aryl-aryl coupling of aromatic compounds with sulfur as far as we know. Although it is necessary to optimize their condition, this reaction will be applicable for preparing electron rich bi-aryl compounds.

Sulfoxide **5a**, sulfonium **8a** and **8b** might be unstable at even room temperature, therefore the reaction was carried out at -80 °C in the presence of **2b**. As diaryl methyl sulfonium ion **9b** was considered stable compound compared with **8a** and **8b**, **2b** was reacted immediately with aryl methyl sulfoniumu ditrifulate **8b** to give **9b** (Scheme 4). The reaction mixture was treated with Et_3N to afford bis(5-isopropyl-2-oxo-2*H*-cyclohepta[*b*]furan-3-yl) sulfide (**10b**) as orange needles. In addition, the other sulfides (**10a**,**c**) were prepared via diaryl methyl sulfonium cation (**9a**,**c**) under the same condition. Although **10b** and **10c** dissolve in various solvents due to isopropyl group, **10a** dose not.



Scheme 4

Spectral properties of 2*H*-cyclohepta[*b*]furan-2-ones

The chemical shifts of the ring protons in 2*H*-cyclohepta[*b*]furan-2-ones are determined on the basis of H-H COSY as shown in Table1.

Table 1. Chemical Shifts of ring proton (ppm)

Compound	Position				
	4	5	7	8	6
2a	7.32	7.05	7.03	6.97	6.84
3a*	8.09	8.01	7.89	7.86	7.72
4a	7.51	7.13	7.02	6.95	6.86
5a	8.35	7.45	7.36	7.35	7.22
6a	8.73	7.69	7.58	7.62	7.44
7a	7.45	7.17	7.12	7.11	6.96
10a	8.21	7.36	7.13	7.08	7.01

Compound	Position			
	4	7	8	6
2b	7.21	6.97	6.87	6.77
3b*	8.13	7.71	7.66	7.57
4b	7.44	7.00	6.88	6.81
5b	8.20	7.32	7.27	7.16
6b	8.70	7.55	7.52	7.40
7b	7.31	7.05	7.01	6.87
10b	8.20	7.07	6.97	6.94

* : Messured in CD_3CN

Table 2. Δδ values of ring proton: Δδ = δ (products) - δ (2a,b)

Compound	Position				
	4	5	7	8	6
3a*	0.77	0.96	0.86	0.89	0.88
4a	0.19	0.08	-0.01	-0.02	0.02
5a	1.03	0.40	0.33	0.38	0.38
6a	1.41	0.64	0.55	0.65	0.60
7a	0.13	0.12	0.09	0.14	0.12
10a	0.89	0.31	0.10	0.11	0.17

Compound	Position			
	4	7	8	6
3b*	0.92	0.74	0.79	0.80
4b	0.23	0.03	0.01	0.04
5b	0.99	0.35	0.40	0.39
6b	1.49	0.58	0.65	0.63
7b	0.10	0.08	0.14	0.10
10b	0.99	0.10	0.10	0.17

* : Messured in CD_3CN

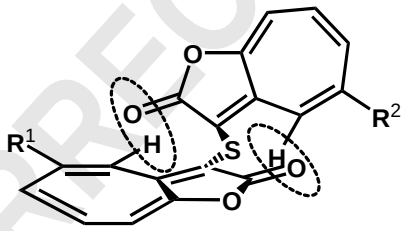


Chart 1

The Δδ values of products are shown Table 2. Dimethylsulfonium, methylsulfinyl and methylsulfonyl groups behave as electron-withdrawing group (EWG). In sulfonium cations (**3a**,**b**), the chemical shifts of all ring protons shifted to downfield by 1.0-0.7 ppm compared with **2a** and **2b**. In sulfoxides (**5a**,**b**) and sulfones (**6a**,**b**), the chemical shifts at the 4-position only shifted to downfield more by 0.86-0.63 ppm. It was caused by the anithotropy of sulfinyl or sulfonyl group. The Δδ values of sulfides (**4a**,**b**) are very small, but the shift at the 4-position is larger than any other position. It is caused by the interaction (ex. hydrogen bond) of lone pair electrons on sulfur. Similar tendency was observed in 3,3'-bi(2*H*-cyclohepta[*b*]furan-2-one-3-yl)s (**7a**,**b**). In **7a** and **7b**, the conjugation caused downfield shift. However diaryl sulfides (**10a**-**c**) showed suspicious behavior. The chemical shifts at the 4 and 5-position extraordinarily shifted to downfield. Such phenomena are caused by the anisotropy of its carbonyl group through space (Chart 1).

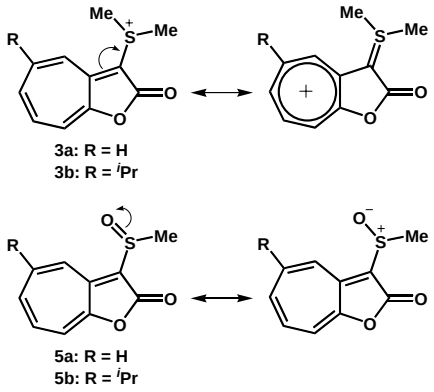


Chart 2

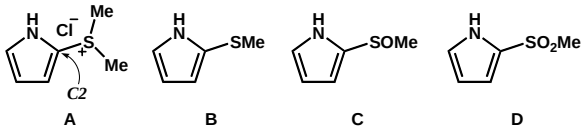


Chart 3

Table 3. ^{13}C NMR Chemical Shifts in CD_3Cl (ppm)

Position	A	B	C	D	Position	3a*	4a	5a	6a	Position	3b	4b	5b	6b
C2	103.6	121.3	128.1	127.1	*C3*	82.77	104.72	107.02	104.25	*C3*	-	103.29	105.38	102.45
CH_3	31.0	21.9	49.0	45.6	CH_3	26.62	16.17	38.43	43.20	CH_3	-	16.30	37.83	43.17

* : Messured in CD_3CN

In also ^{13}C NMR spectra, interesting phenomena were observed (Table 3). In general, the chemical shift of carbon substituted with EWG appears in downfield. Interestingly however, the chemical shifts at 3-pisition increased in following order: (ppm); **3a** (82.77)<**6a** (104.25)<**4a** (104.72)<**5a** (107.02), and **6b** (102.45)<**4b** (103.29)<**5b** (105.38). It seems that dimethylsulfonium group is electron-donating group, and sulfinyl group is EWG. This observation is explained as follows. The 3-carbon in **3a** would be sealed magnetically to cause upper field shift because of the contribution of ylene form (Chart 2). Sulfinyl groups can polarize, and then those groups inductively withdrew electrons to deshield the carbons. The similar phenomena were observed in pyrrole derivertives (**A-D**, shown in Chart 3).[8] The chemical shifts at the 2-pisition are 103.6, 121.3, 128.1 and 127.1 ppm, respectively in this order (Table 3). In contrast, the chemical shifts of methyl group in our compounds increased in following order: (ppm); **4a** (16.17)<**3a** (26.62)<**5a** (38.42)<**6a** (43.20) and **4b** (16.30)<**5b** (37.83)<**6b** (43.17). In the pyrrole derivatives, the chemical shifts of methyl group are 31.0, 21.9, 49.0 and 45.6 ppm, respectively. These data suggest that both sulfinyl and sulfonyl group are EWG. Such a significant difference in NMR spectra might be caused by the difference of alkyl and aryl group.

2*H*-Cyclohepta[*b*]furan-2-ones (**2a** and **2b**) have tow absorptions at 374 and 389 nm, respectively (Table 4). Introduction of methylthio, methylsulfinyl and methylsulfonyl groups caused redshift slightly. Absorption maximum of diaryl sulfides (**10a**-**c**) shifted from 374 nm to about 420 nm by 22-46 nm. These red-shifts might be caused by the intramolecular interaction. In 3,3'-bi(2-oxo-2*H*-cyclohepta-[*b*]furan-2-one-3-yl)s (**7a** and **7b**), λ_{max} appeared around 450 nm due to an expansion of the π-conjugation. This suggests that the dihedral angels in **7a** or **7b** are small.

Table 4. Absorption maximum in CH_2Cl_2 (nm)

Compound	λ_{max}		Compound	λ_{max}	
2a	253	374, 389	2b	258	374, 389
3a*	256	393	3b	-	-
4a	254	402	4b	261	403
5a	258	399	5b	263	400
6a	258	396	6b	266	398
7a	253	452	7b	256	457
10a	258	417	10b	265	420
			10c	262	419

* : Messured in CH_3CN

EXPERIMENTAL

General: Melting points were determined with a Yanagimoto MPS3 micro melting apparatus and are uncorrected. Mass spectra were obtained with a JEOL HX-110, a Hitachi M-2500, or a Bruker APEX II instrument, usually at 70 eV. IR and UV spectra were measured with a Shimadzu FTIR-8100M and a Hitachi U-3410 spectrophotometer, respectively. ^{1}H and ^{13}C NMR spectra were recorded with a JEOL GSX 400 (400 and 100 MHz), or a Bruker AM 600 spectrometer (600 and 150 MHz). Elemental analyses were performed at the Research and Analytical Center for Giant Molecules, Graduate School of Science, Tohoku University.

Synthesis of (2-oxo-2*H*-cyclohepta[*b*]furan-3-yl)dimethylsulfonium trifluoromethanesulfonate (3a): The solution of Tf_2O (2.13 g, 7.50 mmol) dissolved in CH_2Cl_2 (20 mL) was added dropwise to a solution of **2a** (742 mg, 5.08 mmol) dissolved in CH_2Cl_2 (40 mL). The solvent was removed under reduced pressure. The residue was purified by recrystallization from MeOH. **3a** (1.27 g, 3.56 mmol, 70 %) was obtained as green needle crystals.

mp 150-152 °C; HRMS (ESI): Calcd for $C_{11}H_{11}O_2S^+$ $[M]^+$ 207.0474. Found: 207.0473; IR (KBr disk): ν_{max} 3042 (m), 3001 (w), 2970 (w), 2943 (w), 2889 (w), 1859 (w), 1782 (m), 1742 (s, C=O), 1692 (m), 1616 (w), 1597 (m), 1541 (m), 1481 (s), 1466 (s), 1431 (s), 1404 (m), 1327 (m), 1281 (s), 1258 (s), 1223 (s), 1159 (s), 1065 (m), 1053 (m), 1028 (s), 997 (s), 955 (m), 937 (m), 891 (w), 868 (w), 768 (s), 718 (m), 629 (s), 573 (m), 517 (m), 486 (w), 426 (w), 411 (w) cm^{-1}; UV/Vis (CH_3CN): λ_{max}, nm (logε) 219 (4.31), 256 (4.41), 260 sh (4.39), 393 (4.35); ^{1}H NMR (600 MHz, CD_3CN): δ 8.09 (d, J = 11.0 Hz, 1H, H-4), 8.01 (ddd, J = 11.0, 9.5, 2.0 ,1H, H-5), 7.89 (dd, J = 9.5, 2.0 Hz, 1H, H-8), 7.86 (t, J = 9.5 Hz, 1H, H-7), 7.72(ddt, J = 9.5, 2.0, 0.7 Hz, 1H, H-6), 3.24 (s, 6H, -S^+($C\underline{H}_3$)$_2$); ^{13}C NMR (150 MHz, CD_3CN): δ 164.61 (C-2), 158.67 (C-8a or 3a), 156.08 (C-8a or 3a), 142.66 (C-5), 139.20 (C-8), 137.68 (C-6), 130.61 (C-4), 123.01 (C-7), 121.95 (q, J = 318 Hz, -CF_3), 82.77 (C-3), 26.62 (-CH_3); Anal. Calcd for $C_{12}H_{11}F_3O_5S_2$: C, 40.45; H, 3.11. Found: C, 40.386; H, 3.214.

Synthesis of (5-isopropyl-2oxo-2*H*-cyclohepta[*b*]furan-3-yl)dimethylsulfonium trifluoromethane-sulfonate (3b): The solution of Tf_2O (883 mg, 3.11 mmol) dissolved in CH_2Cl_2 (10 mL) was added dropwise to a solution of **2b** (391 mg, 2.08 mmol) dissolved in CH_2Cl_2 (10 mL). The solvent was removed under reduced pressure. **3b** was obtained as green needle crystals.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, J = 1.2 Hz, 1H, H-4), 7.71 (d, J = 9.6, 9.6 Hz, 1H, H-7), 7.66 (dd,

J = 9.6, 1.2 Hz, 1H, H-8), 7.57 (ddd, *J* = 9.6, 1.2, 1.2 Hz, 1H, H-6), 3.35 (s, 6H, -$S^+(CH_3)_2$), 3.25 (sept, *J* = 6.8, 1H, -C<u>H</u>$(CH_3)_2$), 1.39 (d, *J* = 6.8 Hz, 6H, -CH(C<u>H</u>$_3)_2$)

Synthesis of 3-methylthio-2*H*-cyclohepta[*b*]furan-2-one (4a): The solution of Tf_2O (4.39 g, 15.5 mmol) dissolved in CH_2Cl_2 (40 mL) was added dropwise to a solution of **2a** (1.50 g, 10.3 mmol) and DMSO (1.61 g, 20.6 mmol) dissolved in CH_2Cl_2 (40 mL) at 0 °C follwed by stirring for 10 min. Et_3N (40 mL) was added to the solution and refluxed at 70 °C for 20 min. The solvent was removed under reduced pressure. The residue was extracted with CH_2Cl_2/H_2O, dried over $MgSO_4$ and purified on silica gel column chromatography with CH_2Cl_2. **4a** (1.91 g, 9.95 mmol, 97 %) was obtained as red crystals.

mp 68-69 °C; HRMS (ESI): Calcd for $C_{10}H_8O_2S$ + Na $[M + Na]^+$ 215.0137. Found: 215.0137; IR (KBr disk): ν_{max} 3069 (w), 3049 (w), 3038 (w), 3018(w), 2997 (w), 2922 (m), 2862 (w), 2818 (w), 1779 (w), 2764 (w), 1767 (m), 1728 (s, C=O), 1678 (m), 1595 (s), 1528 (s), 1504 (s), 1464 (m), 1412 (m), 1308 (m), 1294 (m), 1265 (s), 1232 (s), 1148 (m), 1049 (m), 1003 (w), 989 (w), 978 (m), 959 (m), 947 (m), 891 (m), 864 (m), 843 (w), 758 (s), 737 (m), 702 (m), 629 (m), 611 (w), 581 (w), 486 (w), 449 (w) cm^{-1}; UV/Vis (CH_2Cl_2): λ_{max}, nm (logε) 254 (4.26), 402 (4.20); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.51 (bd, 1H, *J* = 11.2 Hz, H-4), 7.13 (ddd, 1H, *J* = 11.2, 8.5, 0.8 Hz, H-5), 7.02 (ddd, 1H, *J* = 11.0, 9.0, 0.8 Hz, H-7), 6.95 (dd, *J* = 9.0, 0.9 Hz, 1H, H-8), 6.86 (dddd, 1H, *J* = 11.0, 8.5, 0.9, 0.7 Hz,H-6), 2.42 (s, 3H, -SMe); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.50 (C-2), 157.45 (C-8a), 151.27 (C-3a), 135.29 (C-5), 132.74 (C-7), 130.89 (C-6), 128.02 (C-4), 113.68 (C-8), 104.72 (C-3), 16.17 (-SMe); Anal. Calcd for $C_{10}H_8O_2S$: C, 62.48; H, 4.19. Found: C, 62.661; H, 4.321.

Synthesis of 5-isopropyl-3-methylthio-2*H*-cyclohepta[*b*]furan-2-one (4b): The solution of Tf_2O (4.25 g, 15.0 mmol) dissolved in CH_2Cl_2 (25 mL) was added dropwise to a solution of **2b** (1.53 g, 8.13 mmol) and DMSO (1.17 g, 15.0 mmol) dissolved in CH_2Cl_2 (40 mL). The solvent was removed under reduced pressure. CH_2Cl_2 (30 mL) and Et_2NH (15 mL) was added to the residue followed by stirring for a few minutes. The solvent was removed under reduced pressure. The residue was purified on silica gel chromatography with CH_2Cl_2. **4b** (1.87 g, 7.97 mmol, 98 %) was obtained as orange oil.

HRMS (ESI): Calcd for $C_{13}H_{14}O_2S$ + Na $[M + Na]^+$ 257.0607. Found: 257.0607; IR (KBr disk): ν_{max} 3034 (w), 2961 (m), 2926 (m), 2872 (m), 1987 (w), 1858 (w), 1736 (s), 1628 (w), 1595 (s), 1507 (s), 1495 (s), 1420 (s), 1381 (w), 1364 (w), 1296 (m), 1271 (s), 1237 (s), 1129 (w), 1073 (w), 1053 (m), 1040 (m), 1019 (w), 968 (w), 947 (w), 928 (w), 909 (m), 862 (w), 799 (m), 756 (m), 718 (w), 696 (w), 652 (w), 627 (w), 455 (w) cm^{-1}; UV/Vis (CH_2Cl_2): λ_{max}, nm (logε) 240 sh (4.22), 261 (4.33), 403 (4.23); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.44 (dd, 1H, *J* = 1.4, 0.7 Hz, H-4), 7.00 (ddd, 1H, *J* = 11.5, 9.0, 0.5 Hz, H-7), 6.88 (dd, 1H, *J* = 9.0, 0.9 Hz, H-8), 6.81 (ddd, 1H, *J* = 11.5, 1.4, 0.7 Hz, H-6), 2.89 (sept, 1H, *J* = 6.8, -C<u>H</u>$(CH_3)_2$), 2.41 (s, 3H, -SMe), 1.29 (d, 6H, *J* = 6.8 Hz, -CH(C<u>H</u>$_3)_2$); ^{13}C NMR (150 MHz, $CDCl_3$): δ 167.78 (C-2), 157.10 (C-5), 156.77 (C-8a), 151.21 (C-3a), 132.17 (C-7 or 6), 132.04 (C-7 or 6), 124.66

(C-4), 112.78 (C-8), 103.29 (C-3), 38.97 (-CH(CH_3)$_2$), 23.05 (-CH(CH_3)$_2$), 16.30 (-SMe); Anal. Calcd for $C_{13}H_{14}O_2S$: C, 66.64; H, 6.02. Found: C, 66.644; H, 6.033.

Synthesis of 3-methylsulfinyl-2*H*-cyclohepta[*b*]furan-2-one (5a): *m*-CPBA (212 mg, 1.23 mmol) was added to the solution of **4a** (214 mg, 1.11 mmol) dissolved in $CHCl_3$ (10 mL) followed by stirring for a few minutes. The solution was extracted with 10 % K_2CO_3 solution, dried over $MgSO_4$ and evaporated under reduced pressure. **5a** (214 mg, 1.03 mmol, 93 %) was obtained as yellow crystals.

mp 117-119 °C; HRMS (ESI): Calcd for $C_{10}H_8O_3S$ + Na $[M + Na]^+$ 231.086. Found: 231.0085; IR (KBr disk): ν_{max} 3056 (w), 3029 (w), 3015 (w), 3004 (w), 2923 (w), 1775 (m), 1740 (s), 1532 (m), 1493 (m), 1483 (m), 1462 (m), 1422 (m), 1404 (m), 1294 (w), 1271 (m), 1242 (m), 1229 (m), 1146 (w), 1057 (w), 1028 (s), 953 (m), 943 (m), 887 (w), 860 (w), 768 (m), 749 (m), 716 (m), 687 (w), 629 (m), 612 (w), 482 (w), 459 (w), 430 (w), 419 (w), 403 (w) cm^{-1}; UV/Vis (CH_2Cl_2): λ_{max}, nm (logε) 258 (4.34), 399 (4.26); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.35 (bd, 1H, *J* = 11.2 Hz, H-4), 7.45 (ddd, 1H, *J* = 11.2, 8.8, 0.5 Hz, H-5), 7.36 (dd, 1H, *J* = 11.2, 9.2 Hz, H-7), 7.35 (bd, 1H,*J* = 9.2 Hz, H-8), 7.22 (dddd, 1H, *J* = 11.2, 8.8, 1.3, 0.9, H-6), 3.14 (s, 3H, -SOMe); ^{13}C NMR (150 MHz, $CDCl_3$): δ 163.53 (C-2), 157.41 (C-8a), 152.59 (C-3a), 138.15 (C-5), 134.84 (C-7), 133.39 (C-6), 127.42 (C-4), 118.20 (C-8), 107.02 (C-3), 38.43 (-SOMe); Anal. Calcd for $C_{10}H_8O_3S$: C, 57.68; H, 3.87. Found: C, 57.290; H, 4.047.

Synthesis of 5-isopropyl-3-methylsulfinyl-2*H*-cyclohepta[*b*]furan-2-one (5b): *m*-CPBA (95.7 mg, 0.553 mmol) was added to the solution of **4b** (118 mg, 0.504 mmol) dissolved in CH_2Cl_2 (8 mL) followed by stirring for a few minutes. The solution was extracted with 10 % NaOH solution, dried over K_2CO_3 and evaporated under reduced pressure. The residue was purified on silica gel column chromatography with EtOAc. **5b** (108 mg, 0.449 mmol, 89 %) was obtained as yellow crystals.

m.p. 88.5-90 °C; HRMS (ESI): Calcd for $C_{13}H_{14}O_3S$ + Na $[M + Na]^+$ 273.0556. Found: 273.0554; IR (KBr disk): ν_{max} 3011 (w), 2965 (w), 2915 (w), 2870 (w), 1869 (w), 1794 (w), 1736 (s, C=O), 1628 (m), 1593 (m), 1512 (m), 1489 (m), 1466 (m), 1458 (m), 1429 (w), 1414 (w), 1381 (w), 1364 (w), 1321 (w), 1294 (w), 1277 (m), 1192 (w), 1167 (w), 1103 (w), 1063 (w), 1044 (w), 1019 (w), 1005 (w), 999 (w), 968 (w), 947 (w), 901 (w), 864 (w), 806 (w), 754 (w), 735 (w), 722 (w), 695 (w), 650 (w), 627 (m), 515 (w), 463 (w), 448 (w), 419 (w), 407 (w) cm^{-1}; UV/Vis (CH_2Cl_2): λ_{max}, nm (logε) 263 (4.32), 400 (4.20); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.20 (d, 1H, *J* = 1.4 Hz, H-4), 7.32 (dd, 1H, *J* = 11.2, 9.2 Hz, H-7), 7.27 (dd, 1H, *J* = 9.2, 1.1 Hz, H-8), 7.16 (ddd, 1H, *J* = 11.2, 1.4, 1.1 Hz, H-6), 3.15 (s, 3H, -SOMe), 3.00 (sept, 1H, *J* = 6.8, -CH(CH_3)$_2$), , 1.31 (d, 6H, *J* = 6.8 Hz, -CH(CH_3)$_2$); ^{13}C NMR (150 MHz, $CDCl_3$): δ 163.73 (C-2), 160.80 (C-5), 156.91 (C-8a), 152.49 (C-3a), 134.33 (C-7 or 6), 134.28 (C-7 or 6), 124.54 (C-4), 117.29 (C-8), 105.38 (C-3), 39.51 (-CH(CH_3)$_2$), 37.83 (-SOMe), 23.20 (-CH(CH_3)$_2$); Anal. Calcd for $C_{13}H_{14}O_3S \cdot 0.2H_2O$: C, 61.49; H, 5.72. Found: C, 61.355; H, 5.830

Synthesis of 3-methylsulfonyl-2*H*-cyclohepta[*b*]furan-2-one (6a): *m*-CPBA (394 mg, 2.28 mmol) was

added to the solution of **4a** (393 mg, 2.05 mmol) dissolved in $CHCl_3$ (20 mL). The solution was extracted with 10 % K_2CO_3 solution, dried over $MgSO_4$ and evaporated under reduced pressure. Another *m*-CPBA (477 mg, 2.76 mmol) was added to the solution of the residue dissolved in $CHCl_3$ (15 mL) followed by stirring for 1h. Et_2NH (2 mL) was added to the solution followed by evaporation. The residue was purified on silica gel column chromatography with $CHCl_3$/EtOAc (10:1). **6a** (451 mg, 2.01 mmol, 98 %) was obtained as yellow crystals.

mp 219-221 °C; HRMS (ESI): Calcd for $C_{10}H_8O_4S$ + Na $[M + Na]^+$ 247.0036. Found: 247.0037; IR (KBr disk): ν_{max} 3065 (w), 3015 (w), 3006 (w), 2921 (w), 1782 (w), 1736 (s, C=O), 1686 (w), 1619 (w), 1595 (w), 1570 (m), 1536 (m), 1485 (s), 1460 (s), 1428 (w), 1406 (s), 1327 (w), 1316 (m), 1296 (s), 1266 (s), 1227 (m),1159 (m), 1134 (m), 1123 (s), 1063 (w), 1001 (w), 982 (w), 968 (m), 943 (w), 926 (w), 895 (w), 876 (w), 864 (w), 797 (w), 777 (m), 754 (m), 741 (w), 714 (w), 625 (m), 615 (w), 552 (s), 521 (w), 475 (w), 426 (w) cm^{-1}; UV/Vis (CH_2Cl_2): λ_{max}, nm (logε) 258 (4.37), 264 sh (4.34), 396 (4.26); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.73 (bd, 1H, *J* = 11.2 Hz, H-4), 7.69 (ddd, 1H, *J* = 11.2, 9.0, 0.5 Hz, H-5), 7.62 (dd, 1H, *J* = 9.0, 1.3 Hz, H-8), 7.58 (dddd, 1H, *J* = 11.2, 9.0, 1.1, 0.5 Hz, H-7), 7.44 (dddd, *J* = 11.2, 9.0, 1.1, 0.9 1H, H-6), 3.32 (s, 3H, -SO_2<u>Me</u>); ^{13}C NMR (150 MHz, $CDCl_3$): δ 163.59 (C-2), 157.47 (C-8a), 151.64 (C-3a), 1040.18 (C-5), 136.34 (C-7), 134.91 (C-6), 129.15 (C-4), 121.01 (C-8), 104.25 (C-3), 43.20 (-SO_2<u>Me</u>); Anal. Calcd for $C_{10}H_8O_4S$: C, 53.56; H, 3.60. Found: C, 53.525; H, 3.759.

Synthesis of 5-isopropyl-3-methylsulfonyl-2*H*-cyclohepta[*b*]furan-2-one (6b): *m*-CPBA (213 mg, 1.23 mmol) was added to the solution of **5b** (257 mg, 1.03 mmol) dissolved in $CHCl_3$ (10 mL) followed by stirring for 2h. The solution was extracted with 10% K_2CO_3 solution, dried over $MgSO_4$ and evaporated under reduced pressure. **6b** (254 mg, 0.955 mmol, y. 93 %) was obtained as yellow crystals.

mp 111-112 °C; HRMS (ESI): Calcd for $C_{13}H_{14}O_4S$ + Na $[M + Na]^+$ 289.0505. Found: 289.0504; IR (KBr disk): ν_{max} 3021 (w), 3006 (w), 2977 (w), 2924 (m), 2869 (w), 1860 (w), 1744 (s, C=O), 1626 (m) 1595 (s), 1518 (s), 1509 (s), 1491 (s), 1472 (s), 1431 (m), 1426 (m), 1412 (m), 1389 (m), 1363 (m), 1331 (s), 1321 (m), 1300 (s), 1294 (s), 1271 (s), 1240 (s), 1194 (m), 1167 (m), 1132 (s), 1061 (m), 1042 (m), 970, (s), 943 (m), 936 (m), 914 (m), 874 (m), 814 (m), 801 (m), 801 (m), 777 (m), 772 (m), 760 (m), 752 (m), 720 (w), 660 (w), 623 (w), 596 (m), 552 (s), 527 (m), 498 (w), 419 (w), 403 (w) cm^{-1}; UV/Vis (CH_2Cl_2): λ_{max}, nm (logε) 266 (4.47), 398 (4.35); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.70 (d, 1H, *J* = 1.4 Hz, H-4), 7.55 (dd, 1H, *J* = 10.3, 9.5 Hz, H-7), 7.52 (dd, 1H, *J* = 9.5, 2.0 Hz, H-8), 7.40 (ddd, 1H, *J* = 10.3, 2.0, 1.4 Hz, H-6), 3.31 (s, 3H, -SO_2C<u>H_3</u>), 3.09 (sept, *J* = 6.8, 1H, -C<u>H</u>$(CH_3)_2$), 1.35 (d, *J* = 6.8 Hz, 6H, -CH(C<u>H_3</u>$)_2$); ^{13}C NMR (150 MHz, $CDCl_3$): δ 163.86 (C-2), 163.43 (C-3a), 156.88 (C-8a), 151.17 (C-5), 135.88 (C-6), 135.74 (C-7), 126.55 (C-4), 119.88 (C-8), 102.45 (C-3), 43.17 (-SO_2Me), 39.88 (-<u>C</u>H$(CH_3)_2$), 23.41 (-CH(<u>C</u>$H_3)_2$); Anal. Calcd for $C_{13}H_{14}O_4S$: C, 58.63; H, 5.30. Found: C, 58.483; H, 5.300.

Synthesis of 3,3'-bi(2-oxo-2*H*-cyclohepta[*b*]furan) (7a): 7a (16.5 mg, 0.0569 mmol) and **4a** (26.9 mg, 0.140 mmol) were accidentally obtained by heating **5a** at 40 °C under reduced pressure.

Reddish brown powder; HRMS (ESI): Calcd for $C_{18}H_{10}O_4$ + Na $[M + Na]^+$ 313.0471. Found: 313.0470; UV/Vis (CH_2Cl_2): λ_{max}, nm 253, 452; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, 2H, *J* = 11.2 Hz, H-4, 4'), 7.17 (d, 2H, *J* = 11.2, 8,8 Hz, H-5, 5'), 7.12 (dd, 2H, *J* = 8.8 Hz, H-7, 7'), 7.11 (d, 2H, *J* = 8.8 Hz, H-8, 8'), 6.96 (dd, 2H, *J* = 8.8, 8.8 Hz, H-6, 6')

Synthesis of 3,3'-bi(5-isopropyl-2*H*-cyclohepta[*b*]furan-2-one) (7b): The solution of Tf_2O (174 mg, 0.612 mmol) dissolved in CH_2Cl_2 (10 mL) was added dropwise to a solution of **5b** (125 mg, 0.499 mmol) dissolved in CH_2Cl_2 (10 mL) at 0 °C. The solvent was removed under reduced pressure. The residue was extracted with CH_2Cl_2. **7b** (63.8 mg, 0.170 mmol, 68 %) was obtained red crystals.

mp 218-219 °C; HRMS (ESI): Calcd for $C_{24}H_{22}O_4$ + Na $[M + Na]^+$ 397.1410. Found: 397.1411; IR (KBr disk): ν_{max} 3017 (w), 2953 (w), 2930 (w), 2903 (w), 2868 (w), 1803 (w), 1746 (s, C=O), 1722 (s), 1665 (w), 1655 (w), 1638 (w), 1597 (w), 1514 (s), 1464 (m), 1420 (w), 1389 (w), 1364 (w), 1344 (w), 1321 (w), 1281 (w), 1265 (m), 1248 (w), 1230 (m), 1202 (w), 1186 (w), 1049 (w), 1034 (w), 937 (w), 914 (w), 901 (w), 878 (m), 831 (w), 791 (m), 783 (w), 754 (m), 710 (w), 644 (w) cm^{-1}; UV/Vis (CH_2Cl_2): λ_{max}, nm (logε) 256 (4.66), 263 sh (4.64), 366 sh (3.90), 457 (4.44); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.31 (d, *J* = 1.3 Hz, 2H, H-4, 4'), 7.05 (dd, *J* = 11.0, 9.2 Hz, 2H, H-7, 7'), 7.01 (dd, *J* = 9.2, 1.1 Hz, 2H, H-8, 8'), 6.87 (ddd, *J* = 11.0, 1.3, 1.1 Hz, 2H, H-6, 6'), 2.85 (sept, *J* = 6.8 Hz, 2H, -C<u>H</u>$(CH_3)_2$), 1.26 (d, *J* = 6.8 Hz, 12H, -CH(C<u>H</u>$_3)_2$); ^{13}C NMR (150 MHz, $CDCl_3$): δ 167.19 (C-2), 158.04, 156.52, 148.00, 132.77 (C-6), 132.26 (C-7), 126.48 (C-4), 113.99 (C-8), 99.66 (C-3), 39.07 (-<u>C</u>H$(CH_3)_2$), 23.2 (-CH(<u>C</u>H$_3)_2$); Anal. Calcd for $C_{24}H_{22}O_4 \cdot 0.5H_2O$: C, 75.18; H, 6.05. Found: C, 75.018; H, 5.929.

Synthesis of bis(2-oxo-2*H*-cyclohepta[*b*]furan-3-yl)sulfide (10a): The solution of Tf_2O (166 mg, 0.585 mmol) dissolved in CH_2Cl_2 (8 mL) was added dropwise to a solution of **2a** (78.9 mg, 0.540 mmol) and **5a** (110 mg, 0.529 mmol) dissolved in CH_2Cl_2 (8 mL) at –80 °C. The suspension was warmed up to room temperature. Et_2NH (4 mL) was added to the solution and solvent was removed under reduced pressure. The residue was purified on silica gel column chromatography with $CHCl_3$/EtOAc (1:1) followed by GPC with CH_2Cl_2. Mixture of compound **10a** and **4a** (21.1 mg, 4.8 : 1, measured by ^{1}H NMR) was obtained.

HRMS (ESI): Calcd for $C_{18}H_{10}O_4S$ + Na $[M + Na]^+$ 345.0192. Found: 345.0191; UV/Vis (CH_2Cl_2): λ_{max}, nm 258, 417; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21 (bd, 1H, *J* = 10.8 Hz, H-4), 7.36 (ddd, 1H, *J* = 10.8, 9.2, 0.8 Hz, H-5), 7.13 (dd, 1H, *J* = 10.8, 9.2 Hz, H-7), 7.08 (dd, 1H, *J* = 9.2, 1.2 Hz, H-8), 7.01 (dddd, 1H, *J* = 10.8, 9.2, 1.2, 0.8 Hz, H-6)

Synthesis of bis(2-oxo-5-isopropyl-2*H*-cyclohepta[*b*]furan-3-yl)sulfide (10b): The solution of Tf_2O (290 mg, 1.02 mmol) dissolved in CH_2Cl_2 (10 mL) was added dropwise to a solution of **2b** (185 mg, 0.983 mmol) and **5b** (251 mg, 1.00 mmol) dissolved in CH_2Cl_2 (10 mL) at -80 °C. The suspension was

warmed up to room temperature. Et_3N (4 mL) was added to the solution and solvent was removed under reduced pressure. The residue was purified on Al_2O_3 column chromatography with CH_2Cl_2 followed by GPC with CH_2Cl_2. **10b** (250 mg, 0.615 mmol, 62 %) was obtained as yellow needle crystals.

mp 212-216 °C; HRMS (ESI): Calcd for $C_{24}H_{22}O_4S$ + Na $[M + Na]^+$ 429.1131. Found: 429.1130; IR (KBr disk): ν_{max} 3061 (w), 2973 (w), 2955 (m), 2930 (w), 2869 (w), 1740 (s, C=O), 1593 (s), 1505 (s), 1470 (s), 1458 (s), 1420 (s), 1385 (m), 1375 (m), 1358 (m), 1320 (m), 1306 (m), 1273 (s), 1231 (s), 1115 (w), 1073 (w), 1055 (m), 1034 (m), 1005 (w), 941 (w), 920 (m), 901 (w), 882 (w), 860 (w), 801 (s), 764 (m), 756 (m), 729 (w), 718 (w), 650 (m), 625 (m), 592 (w), 523 (w), 511 (w), 482 (w), 455 (w), 442 (w), 423 (w) cm^{-1}; UV/Vis (CH_2Cl_2): λ_{max}, nm (logε) 265 (4.67), 420 (4.55); ^1H NMR (400 MHz, $CDCl_3$): δ 8.20 (d, *J* = 1.2 Hz, 2H, H-4, 4'), 7.07 (dd, *J* = 11.2, 9.2 Hz, 2H, H-7, 7'), 6.97 (dd, *J* = 9.2, 1.2 Hz, 2H, H-8, 8'), 6.94 (ddd, *J* = 11.2, 1.2, 1.2 Hz, 2H, H-6, 6'), 3.01 (sept, *J* = 6.8 Hz, 2H, -C<u>H</u>$(CH_3)_2$), 1.35 (d, *J* = 6.8 Hz, 12H, -CH(C<u>H</u>$_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.29 (C-2), 159.28, 158.03, 154.84, 133.88, 133.23, 127.15, 115.04, 39.73 (-<u>C</u>H$(CH_3)_2$), 23.71 (-CH(<u>C</u>H$_3)_2$); Anal. Calcd for $C_{24}H_{22}O_4S$: C, 70.91; H, 5.46. Found: C, 70.802; H, 5.529.

Synthesis of (2-oxo-2*H*-cyclohepta[b]furan-3-yl) (5-isopropyl-2-oxo-2*H*-cyclohepta[b]furan-3-yl) sulfide (10c): The solution of Tf_2O (175 mg, 0.616 mmol) dissolved in CH_2Cl_2 (15 mL) was added dropwise to a solution of **2a** (74.0 mg, 0.506 mmol) and **5b** (126 mg, 0.503 mmol) dissolved in CH_2Cl_2 (10 mL) at -80 °C. The suspension was warmed up to rt. Et_2NH (4 mL) was added to the solution and solvent was removed under reduced pressure. The residue was purified on silica gel column chromatography with EtOAc followed by GPC with CH_2Cl_2. **10c** (124 mg, 0.340 mmol, 68 %) was obtained as yellow needle crystals.

mp 138-140 °C; HRMS (ESI): Calcd for $C_{21}H_{16}O_4S$ + Na $[M + Na]^+$ 387.0662. Found: 387.0661; IR (KBr disk): ν_{max} 3065 (w), 3015 (w), 2961 (w), 2874 (w), 1856 (w), 1775 (s), 1752 (s), 1738 (s), 1597 (s), 1526 (m), 1507 (s), 1493 (s), 1460 (m), 1426 (w), 1412 (m), 1306 (w), 1294 (w), 1264 (m), 1231 (m), 1217 (n), 1057 (w), 1048 (w), 945 (w), 928 (w), 905 (w), 885 (w), 864 (w), 855 (w), 804 (m), 768 (m), 754 (m), 737 (w), 718 (w), 702 (m), 652 (w), 625 (m), 486 (w), 450 (w), 438 (w) cm^{-1}; UV/Vis (CH_2Cl_2): λ_{max}, nm (logε) 262 (4.64), 419 (4.55); ^1H NMR (400 MHz, $CDCl_3$): δ 8.22 (dd, *J* = 11.2, 1.2 Hz, 1H, H-4'), 8.19 (d, *J* = 1.2 Hz, 1H, H-4), 7.34 (ddd, *J* = 11.2, 8.8, 1.2 Hz, 1H, H-5'), 7.12 (dd, *J* = 10.0, 9.2 Hz, 1H, H-7'), 7.10 (dd, *J* = 11.2, 9.2 Hz, 1H, H-7), 7.06 (dd, *J* = 9.2, 1.2 Hz, 1H, H-8'), 7.00 (dd, *J* = 9.2, 0.8 Hz, 1H, H-8), 7.00 (dddd, *J* = 10.0, 8.8, 1.2, 1.2 Hz, 1H, H-6'), 6.97 (ddd, *J* =11.2, 1.2, 0.8 Hz, 1H, H-6), 3.02 (sept, *J* = 6.8 Hz, 1H, -C<u>H</u>$(CH_3)_2$), 1.36 (d, *J* = 6.8 Hz, 6H, -CH(C<u>H</u>$_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.23, 168.94, 159.32, 158.31, 157.94, 155.03, 154.88, 137.19, 134.00, 133.79, 133.30, 132.48, 130.04, 127.17, 116.00, 115.24, 101.24, 98.99, 39.73 (-<u>C</u>H$(CH_3)_2$), 23.71 (-CH(<u>C</u>H$_3)_2$); Anal. Calcd for $C_{21}H_{16}O_4S \cdot 0.25H_2O$: C, 68.37; H, 4.51. Found: C, 68.552; H, 4.663.

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