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AN EFFICIENT PREPARATION OF 2*H*-CYCLOHEPTA[*b*]FURAN-2-ONES[!]

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Abstract- 2*H*-cyclohepta[*b*]furan-2-one (**3**) was prepared in high yield from a [2+2] cycloadduct between cycloheptatriene and dichloroketene by Baeyer–Villiger oxidation followed by dehydrochlorination. 3-Chloro- (**8**) and 6-chloro-2*H*-cyclohepta[*b*]furan-2-one (**9**) were obtained from the [2+2] cycloadduct by adding an epoxidation step to the above synthetic way in moderate yields.

INTRODUCTION

Since the pioneering work of troponoid compounds by Seto and Nozoe 2*H*-cyclohepta[*b*]furan-2-one (**3**) and its derivatives, e. g., 3-ethoxycarbonyl-2*H*-cyclohepta[*b*]furan-2-one, were considered as intermediates of preparation of azulene from active troponoid compounds with malonic acid derivatives. These compounds were isolated and their physical and chemical properties have been clarified.[1,2] Especially, this parent molecule is planer and exhibits a small bond alternation in the seven-membered ring on the basis of single-crystal X-Ray analysis.[3] Its large dipole moment exhibits the contribution of dipolar structures.[4] The synthetic procedures for 3-ethoxycarbonyl-2*H*-cyclohepta[*b*]furan-2-one (Scheme 3) and related compounds have been improved. Other synthetic ways of 2*H*-cyclohepta[*b*]furan-2-one derivatives have been developed.[5-7] Reactions of **3** and its derivatives with enamines or enol ethers are well known as a synthetic method of azulene derivatives.[8] In chemistry of natural product bioactive 2*H*-cyclohepta[*b*]furan-2-one derivatives were found from plants.[9] Recently, some 2*H*-cyclohepta[*b*]furan-2-one derivatives were used as synthons of biologically active natural products.[10]

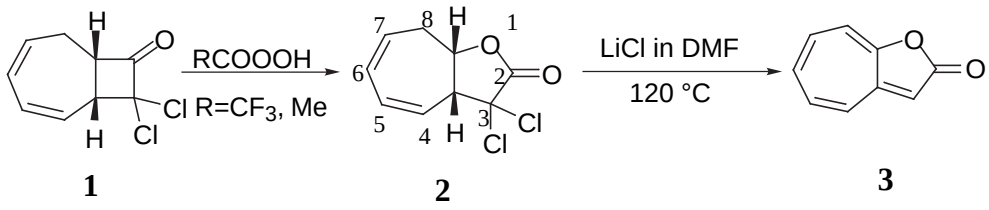
As described above, 2*H*-cyclohepta[*b*]furan-2-one and its derivatives are very important compounds in physical organic chemistry and chemistry of natural product. We have studied about reactivities of π-conjugated compounds with dichloroketene.[11] In these works, we found that cycloheptatriene reacted with dichloroketene by [2+2] cycloaddition to give 2,2-dichloro-2,2a,7,7a-tetrahydro-1*H*-cycloheptabuten-1-

[!] Dedicated to Professor Shô Ito on the occasion of his 77th birthday.

one (**1**) in a good yield.[12] We investigated the reactivities of **1** to prepare several types of π-conjugated compounds. Consistently, here we report a new and efficient preparation of 2*H*-cyclohepta[*b*]furan-2-one (**3**) and its derivatives from this cycloadduct.

RESULTS AND DISCUSSION

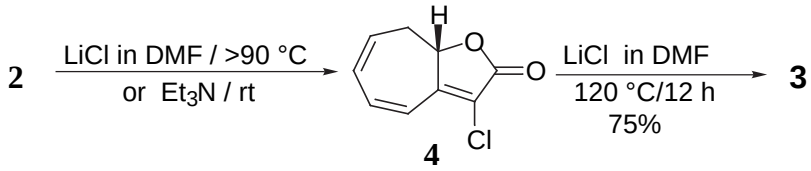
Synthesis of 2*H*-cyclobuta[*b*]furan-2-one (3). Reaction of **1** with trifluoroperacetic acid or peracetic acid at room temperature for 7 h resulted in selective Baeyer–Villiger oxidation to form only 3,3-dichloro-3,3a,8,8a-tetrahydro-2*H*-cyclohepta[*b*]furan-2-one (*cis*-fused) (**2**) in 73% yield. The lactone (**2**) was treated with lithium chloride in dimethylformamide (DMF) at 120 °C for 12 h to give **3** in 72% yield in one pot (Scheme 1).



1 **2** **3**

Scheme 1

3-Chloro-8,8a-dihydro-2*H*-cyclohepta[*b*]furan-2-one (**4**) is expected to be an intermediate of this reaction. When the reaction was stopped for 20 min., compound (**4**) was obtained in 65% yield. The dehydrochlorination of **2** takes place more easily at room temperature for 2 h by triethylamine to give compound **4** in 95% yield. Under the similar conditions, **4** was converted to **3** in 75% yield (Scheme 2).

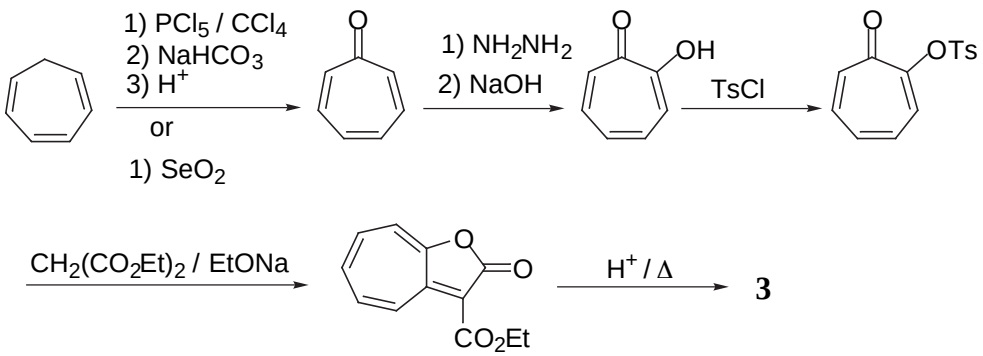


4

Scheme 2

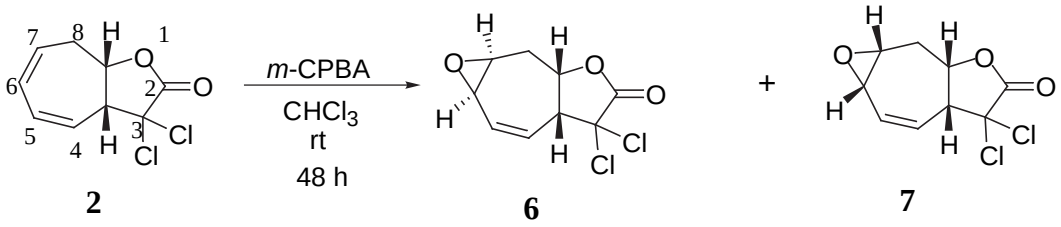
Although **3** has so far been prepared from commercially available cycloheptatriene with six or more steps (Scheme 3),[13] by using developed our method **3** can be obtained from the same compound in three steps. There are toxic waste problems to use selenium oxide or carbon tetrachloride in conventional synthetic ways from cycloheptatriene. These problems will be solved by the use of our procedure, while there are no toxic waste problems in the preparation of tropolone from cyclopentadiene and dichloroketene.[14]

Synthesis of chloro-2*H*-cyclohepra[*b*]furan-2-one. We extended our procedure to a simple, straight



Scheme 3

forward synthesis of substituted 2*H*-cyclohepta[*b*]furan-2-ones. The lactone (**2**) was reacted with *m*-chloroperbenzoic acid (*m*-CPBA) to give *anti*-3,3-dichloro-6,7-epoxy-3,3a,6,7,8,8a-hexahydro-2*H*-cyclohepta[*b*]furan-2-one (**6**) and *syn*-6,7-epoxy-3,3-dichloro-3,3a,6,7,8,8a-hexahydro-2*H*-cyclohepta-[*b*]furan-2-one (**7**) in 74 and 11% yields, respectively. These structures were established on the basis of ^{1}H NMR. NOE was observed between H-8a and H-6 in compound (**7**). NOE was not observed between H-6



2 **6** **7**

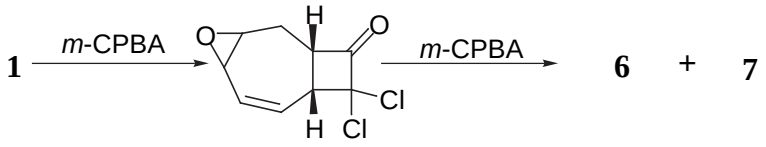
Scheme 4

and H-8a in compound (**6**). Therefore, **7** was assigned to the *syn* configuration. 4,5-Epoxy compounds were not found in this reaction. Although the direction of epoxidation of 3,3a,6,6a-tetrahydro-2*H*-cyclopenta[*b*]furan-2-one with *m*-CPBA depends on solvent to give preferably *syn*-4,5-epoxy-3,3a,6,6a-tetrahydro-2*H*-cyclopenta[*b*]furan-2-one,[15] the lactone (**2**) did not exhibit solvents effect (Table 1).

Table 1. Epoxidation of lactone (**2**) with *m*-CPBA

entry	solvent	**2** (%)	**6** (%)	**7** (%)
1	Et_2O	21	42	5
2	CH_2Cl_2	4	65	12
3	$CHCl_3$	6	74	11
4	Toluene	8	73	6

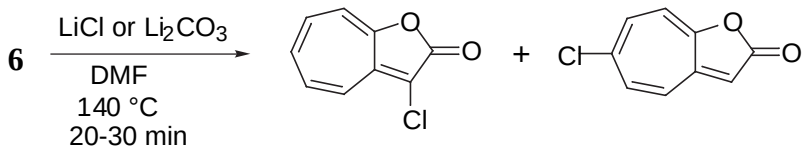
Compound (**1**) was oxidized with *m*-CPBA (1.2 eq.) at room temperature for 13 h to give 5,6-epoxy-2,2-dichloro-1,2,5,6,7,7a-hexahydro-1*H*-cycloheptabuten-1-one (**5**) in 74% yield, regioselectively. No formation of 3,4-epoxy derivative was observed. When 2.5 eq. of *m*-CPBA was used, a mixture of **6** and **7** (74:11) was obtained in 85% yield after 48 h.



5

Scheme 5

Dehydrochlorination of epoxides (**6**) by lithium chloride at high temperature (140 °C) with short reaction time (20 min) gave 3-chloro-2*H*-cyclohepta[*b*]furan-2-one (**8**) and 6-chloro-2*H*-cyclohepta-



8 **9**

Scheme 6

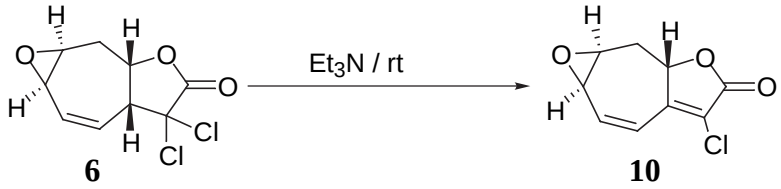
[*b*]furan-2-one (**9**) in 47 and 18% yields, respectively. Using lithium carbonate instead of lithium chloride, a mixture of **8** and **9** (60:11) was obtained in 71% yield. Prolonged heating tends to increase polymerization.

Epoxidation and Baeyer–Villiger oxidation undergoes in one pot using *m*-CPBA. Thus, the synthetic way from cycloheptatriene to **8** and **9** in three steps has been achieved. This is a better synthetic way comparing with Ciabattoni's method.[5] In this reaction, there are some intermediates. 3-Chloro-6,7-epoxy-6,7,8,8a-tetrahydro-2*H*-cyclohepta[*b*]furan-2-one (**10**) is the initial intermediate (see Table 2, entry 5).

Table 2. Reaction of epoxide (**6**) with LiCl or Li_2CO_3

entry	reagent	Temp. (°C)	time	**10** (%)	**8** (%)	**9** (%)
1	LiCl	120	4 h	0	15	9
2	LiCl	120	1 h	0	26	13
3	LiCl	140	30 min	0	32	17
4	LiCl	140	20 min	0	47	18
5	Li_2CO_3	120	5 min	70	9	trace
6	Li_2CO_3	120	4 h	0	28	4
7	Li_2CO_3	120	1 h	0	47	10
8	Li_2CO_3	140	30 min	0	50	8
9	Li_2CO_3	140	20 min	0	60	11

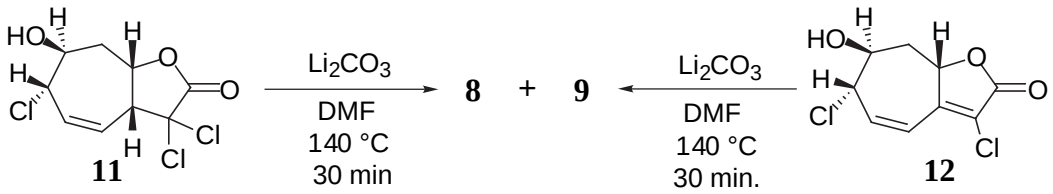
Compound (**10**) was also obtained by treatment of **6** with triethylamine in 97% yield. Compounds **6** and



6 **10**

Scheme 7

10 reacted with 2M HCl to give selectively ring opening products, 3,3,6-trichloro-7-hydroxy-3,3a,6,7,7,8,8a-hexahydro-2*H*-cyclohepta[*b*]furan-2-one (**11**) and 3,6-dichloro-7-hydroxy-3,3a,6,7,8,8a-hexaahydro-2*H*-cyclohepta[*b*]furan-2-one (**12**), in 83 and 96% yields, respectively. The chlorohydroxyl compound (**11**) was treated with lithium carbonate at 140°C for 30 min to give compounds (**8** and **9**) in 26 and 7% yields, respectively. Compound (**12**) also reacted with lithium carbonate at 140°C for 30 min to give compounds (**8** and **9**) in 36 and 5% yields, respectively. These results suggest that **12** plays a role as an intermediate in the reaction of **6** with LiCl or lithium carbonate.



11 **12**

Scheme 8

CONCLUSION

A new and efficient method for the preparation of **3** and its chloro derivatives (**8** and **9**) from the cycloadduct (**1**) of dichloroketene to cycloheptatriene in two steps have been developed.

EXPERIMENTAL

General Information. Melting points were determined on a Yanaco micro melting point apparatus and are uncorrected. IR spectra were taken on a Shimazu FTIR-8100M or a Hitachi 270-30 spectrophotometer and UV spectra were measured on a Hitachi U-3410 spectrophotometer. ^{1}H NMR spectra (^{13}C NMR spectra) were recorded on a JEOL GSX 400 at 400 MHz (100 MHz) or a Bruker AM 600 spectrometer at 600 MHz (150 MHz). MS spectra were measured on a JEOL HX-110 or a Hitachi M-2500 instrument usually at 70 eV. Elemental analyses were performed at the Instrumental Analysis Center of Chemistry, Faculty of Science, Tohoku University.

3,3-Dichloro-3,3a,8,8a-tetrahydro-2*H*-cyclohepta[*b*]furan-2-one (2). An aqueous solution of 34% hydrogen peroxide (2.23 g, 22.3 mmol) was added at 0 °C in the period of 10 min under nitrogen atmosphere to a solution of 2,2-dichloro-2,2a,7,7a-tetrahydro-1*H*-cycloheptacyclobuten-1-one (**1**) (3.1 g, 15 mmol) and acetic acid (1.37 g, 22.8 mmol) in dichroromethane (15 mL). The solution was stirred for 10 h at rt. Reaction mixture was diluted with dichloromethane (100 mL), washed with 5% of $NaHCO_3$ and then water, and dried over anhydrous magnesium sulfate, filtered, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to give 2.408 g (73%) of 3,3-dichloro3,3a,8,8a-tetrahydro-2*H*-cyclohepta[*b*]furan-2-one (**2**). colorless crystals; mp 85.5-86.0 ^{o}C (ether); IR (KBr) ν_{max} 3021 (w), 1792 (s), 1771 (m), 1437 (w), 1352 (m), 1294 (m), 1200 (m), 1146 (m), 1024 (m), 997 (m), 968 (m), 874 (m), 843 (m), 777 (w), 749 (m), 716 (m), 681 (m), 639 (m), 596 (m), 579 (m) cm^{-1}; UV (CH_2Cl_2) λ_{max} 235 (ε 9598), 303 sh (1692) nm; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.21 (ddd, *J* = 11.6, 5.8, 2.6 Hz, H-5), 6.07 (ddd, *J* = 10.6, 5.8, 1.8 Hz, H-6), 5.96 (dd, *J* = 11.6, 3.0Hz, H-4), 5.91 (ddd, *J* = 10.6, 8.6, 4.0 Hz, H-7), 4.77 (ddd, *J* = 11.2, 8.0, 3.0 Hz, H-8a), 3.88 (ddd, *J* = 8.0, 3.0, 2.6 Hz, H-3a), 2.88 (dddd, *J* = 14.6, 11.2, 4.0, 1.8 Hz, H-8), 2.69 (ddd, *J* =14.6, 8.6, 3.0 Hz, H-8); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.22 (C-9), 129.09 (C-4), 129.03 (C-3), 126.36 (C-5), 122.93 (C-4), 81.61 (C-8a), 79.76 (C-3), 55.45 (C-3a), 30.61 (C-8); MS (70 eV) m/z 222 (M^++4, 7%), 220 (M^++2, 39), 218 (M^+, 60), 183 (8), 163 (7), 159 (25), 155 (8), 146 (8), 139 (97), 125 (25), 119 (9), 112 (6), 108 (12), 103 (58), 99 (6), 91 (100), 78 (42), 73 (7), 65 (22), 51 (23).; Anal. Calcd for $C_9H_8O_2Cl_2$: C, 49.34; H, 3.68.; Cl, 32.37. Found: C, 49.14; H, 3.79; Cl, 32.34.

2*H*-Cyclohepta[*b*]furan-2-one (3). A solution of **2** (155 mg, 0.71 mmol) and lithium carbonate (155 mg, 3.65 mmol) in DMF (15 mL) was heated at 120 °C for 6.5 h under nitrogene atmosphere. Reaction mixture was poured into ether (40 mL). The solution was washed with water, dried over magnesium

sulfate, and filtered. After the solvent was removed under reduced pressure. The product was purified by silica gel column chromatography using hexane/ethyl acetate (4:1) as eluants to give 2*H*-cyclohepa[*b*]fuan-2-one (**3**) (74 mg, 72%). orange needles; mp 67.5-68.0 ˚C (ethyl acetate) (lit.,[1] 69-70 °C); IR (KBr) ν_{max} 3121 (w), 1748 (s), 1605 (m), 1541 (m), 1509 (m), 1420 (w), 1404 (w), 1298 (w), 1264 (m), 1235 (w), 1213 (m), 1186 (w), 1022 (w), 932 (w), 911 (w), 887 (w), 839 (m), 799 (m), 747 (w), 727 (w), 702 (m), 615 (w), 424 (w) cm^{-1}; UV (MeOH) λ_{max} 223 (ε 14278), 251 (22927), 374 (14647), 388 (14682) nm; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29 (dd, *J* = 11.2, 1.1 Hz, H-4), 7.03 (ddd, *J* = 11.2, 8.6, 0.7 Hz, H-5), 6.99 (ddd, *J* = 10.8, 9.1, 0.7 Hz, H-7), 6.94 (ddd, *J* = 9.1, 1.3, 1.1 Hz, H-8), 6.81 (dddd, *J* = 10.8, 8.6, 1.1, 1.1 Hz, H-6), 5.75 (d, *J* = 1.3 Hz, H-3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.44 (C-2), 158.27, 153.10, 135.31 (C-5), 132.44 (C-7), 130.40 (C-6), 127.78 (C-4), 113.75 (C-8), 98.64 (C-3); MS(70 eV) m/z 146(M^+, 100%), 118 (17), 90 (51), 63 (12), 51 (4).

3-Chloro-8,8a-dihydro-2*H*-cyclohepta[*b*]furan-2-one (4). Triethylamine (405 mg, 4.00 mmol) was added to a solution of **2** (448 mg, 2.04 mmol) in ether (20 mL). The solution was stirred for 2 h. Occurring triethylammonium chloride was removed by filtration. After the solvent was removed under reduced pressure, 3-chroro-8,8a-dihydro-2*H*-cyclohepta[*b*]furan-2-one (**4**) (353 mg, 95%) was obtained. colorless crystals; mp 122.0-122.5 °C (ether); IR (KBr) ν_{max} 3038 (w), 2950 (w), 1750 (s), 1632 (m), 1595 (m), 1568 (m), 1431 (w), 1399 (w), 1360 (w), 1347 (m), 1300 (m), 1248 (w), 1229 (m), 1163 (m), 1111 (m), 1038 (m), 1005 (m), 968 (w), 862 (m), 826 (w), 760 (w), 698 (m), 669 (m), 606 (w), 498 (w), 446 (w) cm^{-1}; UV (MeOH) λ_{max} 220 (ε, 11191), 327 (111297) nm; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.48 (d, *J* = 11.6 Hz, H-4), 6.32 (ddt, *J* = 11.6, 6.8, 1.0 Hz, H-5), 6.05-6.12 (m, H-6,7), 5.21 (dd, *J* = 13.3, 3.7 Hz, H-8a), 2.98 (ddd, *J* = 16.5, 8.7, 3.7 Hz, H-8), 2.61 (dd, *J* = 16.5, 13.3 Hz, H-8); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.60 (C-2), 155.39 (C-3a), 134.21 (C-5), 129.38 (C-7), 127.61 (C-6), 117.82 (C-4), 117.20 (C-3), 77.87 (C-8a), 31.39 (C-8); MS (70 eV) m/z 184 (M^++2, 31%), 182 (M^+, 100), 167 (12), 154 (41), 147 (15), 140 (3), 125 (85), 119 (41), 112 (7), 103 (4), 99 (12), 91 (92), 85 (4), 77 (14), 73 (11), 63 (25), 51 (19).; Anal. Calcd for $C_9H_7O_2Cl$: C, 59.20; H, 3.86; Cl, 19.42. Found: C, 58.93; H, 3.92; Cl, 19.63.

2,2-Dichloro-5,6-epoxy-2,2a,5,6,7,7a-hexahydrocycloheptabuten-1-one (5). *m*-Chloroper-benzoic acid (70%, 2.115 g, 123 mmol) was added to a solution of **1** (216 mg, 1.06 mmol) in dichloromethane (19 mL) under nitrogen atmosphere. It was stirred for 13 h. Dichloromethane (40 mL) was added. The solution was washed with 5% sodium hydrogen carbonate. It was dried over magnesium sulfate and filtered. After the solvent was removed under reduced pressure, residue was passed through silica gel column using hexane / ethyl acetate (4:1) as eluants to give recovered **1** (48 mg, 23%) and 2,2-dichloro-5,6-epoxy-2,2a,7,7a-tetrahydro-1*H*-cycloheptabuten-1-one (**5**) (172 mg, 74%). colorless crystals; mp 70 °C; IR (neat) ν_{max} 3004 (w), 2944 (w), 1867 (w), 1806 (s), 1445 (w), 1294 (w), 1266 (w), 1237 (w), 1208 (w),

1134 (m), 1117 (m), 1100 (m), 1051 (m), 1103 (m), 970 (m), 911(m), 837 (m), 808 (m), 754 (m), 689 (m), 664 (m), 615 (w), 559 (w), 525 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.02 (ddd, *J*= 11.6, 2.8, 0.4 Hz, H-3), 5.87 (ddd, *J* = 11.6, 4.0, 2.8 Hz, H-4), 3.97 (ddd, *J* = 12.0, 11.2, 4.8 Hz, H-5), 3.89 (ddd, *J*= 11.2, 2.8, 2.8 Hz, H-2a), 3.42 (ddd, *J* = 6.4, 4.0, 1.2 Hz, H-6), 3.34 (ddd, *J* = 4.4, 4.4, 0.4 Hz, H-5), 2.55 (ddd, *J* = 14.0, 6.0, 4.8 Hz, H-7), 2.34 (ddd, *J* = 14.0, 12.0, 1.2 Hz, H-7); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.58 (C-1), 127.94 (C-3), 125.33 (C-4), 87.72 (C-2), 54.93 (C-6a), 53.11 (C-4), 52.08 (C-5), 49.22 (C-2a), 24.91 (C-7); MS (CI) m/z 223 ($M+H^++4$, 13%), 221 ($M+H^++2$, 65), 219 ($M+H^+$, 100), 207 (4), 201 (16), 191 (6), 183 (27), 173 (6), 165 (11), 155 (7), 147 (14), 139 (5), 127 (4), 107 (4).; Anal. Calcd for $C_9H_8O_2Cl_2$: C, 49.34; H, 3.68. Found: C, 44.25; H, 3.96.

***anti*-3,3-Dichloro-6,7-epoxy-3,3a,6,7,8,8a-hexahydro-2*H*-cyclohepta[*b*]furan-2-one (6) and *syn*-3,3-dichloro-6,7-epoxy-3,3a,6,7,8,8a-hexahydro-2*H*-cyclohepta[*b*]furan-2-one (7).** *m*-CPBA (70%, 442 mg, 2.20 mmol) was added to a stirred solution of compound (**2**) (442 mg, 2.02 mmol) in chloroform (20 mL) under nitrogen atmosphere at rt. It was stirred for 48 h. Chloroform (20 mL) was added to the reaction mixture. The organic layer was washed with aqueous 5% sodium hydrogene carbonate solution and dried over magnesium sulfate, filtered, and evaporated. The residue was passed through silica gel column with toluene as eluant to give compounds, *anti*-3,3-dichloro-6,7-epoxy-3,3a,6,7,8,8a-hexahydro-2*H*-cyclohepta[*b*]furan-2-one (**6)** (350 mg, 74%) and *syn*-3,3-dichloro-6,7-epoxy-3,3a,6,7,8,8a-hexahydro-2*H*-cyclohepta[*b*]furan-2-one (**7**) (52 mg, 11%).

6: colorless crystals; mp 146.5-147.0 ^oC (ether); IR (KBr) ν_{max} 3036 (w), 2992 (w), 1786 (s), 1669 (w), 1443 (w), 1362 (m), 1308 (m), 1277 (m), 1194 (s), 1157 (m), 1144 (w), 1078 (w), 1048 (w), 1013 (s), 1001 (s), 986 (m), 974 (m), 938 (m), 912 (m), 866 (m), 847 (m), 810 (s), 766 (m), 725 (m), 691 (m), 633 (m), 602 (m), 565 (m), 544 (w), 484 (m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.11 (ddd, *J* = 12.3, 5.1, 2.7 Hz, H-5), 5.87 (ddd, *J* = 12.3, 3.3, 0.7 Hz, H-4), 5.10 (ddd, *J* = 11.8, 8.0, 3.6 Hz, H-8a), 3.94 (dddd, *J* = 8.0, 3.3, 2.7, 0.9 Hz, H-3a), 3.48 (ddd, *J* = 6.5, 4.8, 0.7 Hz, H-7), 3.35 (ddd, *J* = 5.1, 4.8, 0.7 Hz, H-6), 2.72 (dddd, *J* = 14.4, 6.5, 3.6, 0.9 Hz, H-8), 2.62 (ddd, *J* = 14.4, 11.8, 0.7 Hz, H-8); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.04 (C-2), 127.02 (C-5), 124.14 (C-4), 79.60 (C-3), 76.53 (C-8a), 54.15 (C-7), 54.06 (C-3a), 50.66 (C-6), 28.44 (C-8); MS (70 eV) m/z 199 (M^+-Cl, 27%), 181 (5), 155 (5), 125 (10), 117 (9), 99 (6), 91 (9), 81 (100), 77 (6), 73 (4), 68 (5), 63 (5), 51 (7); MS (CI) m/z 235 ($M+H^+$, 100%), 199 (100), 183 (15), 171 (19), 165 (25), 157 (6), 149 (5), 135 (6), 121 (5), 107 (65); Anal. Calcd for $C_9H_8O_3Cl_2$: C, 45.99; H, 3.43; Cl, 30.16. Found: C, 45.95; H, 3.48; Cl, 30.18.

7: colorless crystals; mp 168.0-168.5 ^oC (ether); IR (KBr) ν_{max} 3007 (w), 2951 (w), 2913 (w), 1802 (s), 1447 (m), 1383 (w), 1352 (m), 1329 (w), 1294 (m), 1235 (w), 1188 (s), 1167 (m), 1136 (m), 1055 (m), 1013 (s), 990 (s), 957 (m), 928 (m), 853 (s), 824 (m), 781 (s), 685 (m), 621 (w), 590 (m), 561 (w), 515 (m), 450 (w); ^1H NMR (600 MHz, $CDCl_3$) δ 6.19 (dtd, *J* = 11.5, 2.0, 1.1 Hz, H-5), 5.83 (dd, *J* = 11.5, 3.0

Hz, H-4), 5.00 (ddd, *J* = 13.2, 7.7, 2.8 Hz, H-8a), 3.99 (ddt, *J* = 7.7, 3.0, 2.0 Hz, H-3a), 3.36 (dt, *J* = 3.8, 2.0 Hz, H-6), 3.31 (dddd, *J* = 7.3, 6.4, 3.8, 1.1 Hz, H-7), 2.69 (ddd, *J* = 13.2, 6.4, 2.8 Hz, H-8), 2.14 (td, *J* = 13.2, 7.3 Hz, H-8); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.71 (C-2), 127.73 (C-5), 123.48 (C-4), 79.30 (C-3), 75.21 (C-8a), 54.71 (C-3a), 50.92 (C-7), 50.11 (C-6), 31.03 (C-8); MS (70 eV) m/z 199 (M^+-Cl, 19%), 181 (6), 161 (6), 155 (4), 125 (10), 117 (8), 111 (4), 99 (8), 91 (15), 87 (3), 81 (100), 77 (7), 73 (6), 65 (5), 51 (7); MS (CI) m/z 235 ($M+H^+$, 100%), 199 (15), 171 (10); Anal. Calcd for $C_9H_8O_3Cl_2$: C, 45.99; H, 3.43; Cl, 30.16. Found: C, 45.85; H, 3.64; Cl, 30.14.

3-Chloro-2*H*-cyclohepta[*b*]furan-2-one (8) and 6-chloro-2*H*-cyclohepta[*b*]furan-2-one (9). A dispersed solution of **6** (213.4 mg, 0.91 mmol) and lithium carbonate (249.2 mg, 3.37 mmol) in DMF (10 mL) was heated at 140 °C for 20 min. with stirring under nitrogen atmosphere. Toluene (100 mL) was added to the reaction mixture and then it was passed through cellulose powder. The solution was washed with water, dried over magnesium sulfate, and filtered. After the solvent was removed under reduced pressure, the residue was purified by silica gel column chromatography with hexane / ethyl acetate (7:3) as eluant to afford 3-chloro-2*H*-cyclohepa[*b*]furan-2-one (**8**) (98.6 mg, 60%) and 6-chloro-2*H*-cyclohepa[*b*]furan-2-one (**9**) (18.1 mg, 11%).

8: orange needles;[5] mp 178.5-179.0 °C (ethyl acetate); IR (KBr) ν_{max} 3027 (w), 1750 (s), 1605 (m), 1541 (m), 1512 (m), 1466 (w), 1414 (m), 1294 (m), 1267 (m), 1250 (m), 1240 (m), 1215 (m), 1146 (w), 1049 (m), 953 (w), 941 (m), 916 (m), 749 (m), 698 (m), 631 (w), 613 (w), 434 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 11.2 Hz, 1H), 7.15 (dd, *J* = 11.2, 8.4 Hz, 1H), 6.97-7.06 (m, 2H), 6.88 (dd, *J* = 9.6, 9.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.25 (C-2), 155.87, 145.94, 135.90, 132.71, 130.98, 125.63, 114.46, 102.68 (C-3); MS (70 eV) m/z 182 (M^++2, 32%), 180 (M^+, 100), 124 (33), 89 (53), 63 (12), 50 (3).

9: orange crystals; mp 178.5-179.0 °C (ethyl acetate); IR (KBr) ν_{max} 3121 (w), 1755 (s), 1603 (m), 1539 (m), 1501 (m), 1437 (m), 1354 (w), 1240 (m), 997 (w), 893 (w), 831 (m), 793 (w), 567 (m) cm^{-1}; UV (MeOH) λ_{max} 230 sh (ε 15373), 255 (19928), 268 sh (18139), 378 (14864), 394 (13988) nm; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 12.0 Hz, H-4), 7.14 (dd, *J* = 10.0, 1.6 Hz, H-7), 7.06 (dd, *J* = 12.0, 1.6 Hz, H-5), 6.76 (dd, *J* = 10.0, 1.2 Hz, H-8), 5.85 (d, *J* = 1.2 Hz, H-3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.53 (C-2), 157.30 (C-8a), 151.07 (C-3a), 136.99 (C-5), 136.29 (C-6), 130.67 (C-7), 127.00 (C-4), 110.97 (C-8), 101.14 (C-3); MS (70 eV) m/z 182 (M^++2, 33%), 180 (M^+, 100), 152 (13), 124 (34), 89 (54), 76 (3), 73 (3), 63 (16), 50 (5); Anal. Calcd for $C_9H_5O_2Cl$: C, 59.86; H, 2.79. Found: C, 59.09; H, 3.99.

3-Chloro-6,7-epoxy-6,7,8,8a-tetrahydro-2*H*-cyclohepta[*b*]furan-2-one (10). Triethylamine (450 mg, 4.0 mmol) was added to a solution of **6** (448 mg, 2.0 mmol) in 20 mL of ether. The solution was stirred for 2 h. Precipitated triethylammonium chloride was removed by filtration. After the solvent was removed,

3-chroro-6,7-epoxy-8,8a-dihydro-2*H*-cyclohepta[*b*]furan-2-one (**10**) (353 mg, 95%) was obtained. colorless crystals; mp 140.0-140.5 ^{o}C (ether); IR (KBr) ν_{max} 3033 (w), 2953 (w), 1761 (s), 1642 (w), 1590 (m), 1443 (w), 1364 (w), 1354 (w), 1312 (w), 1291 (w), 1279 (w), 1227 (w), 1200 (w), 1169 (m), 1111 (w), 1100 (w), 1040 (s), 1017 (m), 905 (m), 882 (w), 860 (m), 801 (m), 764 (w), 752 (w), 729 (w), 644 (m), 606 (w), 534 (w), 492 (w) cm^{-1}; UV (MeOH) λ_{max} 283 (ε 15190) nm; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.67 (d, *J* = 12.0 Hz, H-4,), 6.46 (dd, *J* = 12.0, 5.9 Hz, H-5), 5.27 (dd, *J* = 12.3, 3.9 Hz, H-8a), 3.55 (dd, *J* = 4.6, 4.5 Hz, H-7), 3.44 (dd, *J* = 5.9, 4.6 Hz, H-6,), 3.17 (ddd, *J* = 14.6, 4.5, 3.9 Hz, H-8), 2.09 (dd, *J* = 14.6, 12.3 Hz, H-8); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.43 (C-2), 153.44 (C-3a), 134.55 (C-5), 122.74 (C-4), 119.77 (C-3), 77.33 (C-8a), 54.03 (C-7), 50.84 (C-6), 30.00 (C-8); MS (70 eV) m/z 200 (M^{+}+2, 4.2%), 198 (M^{+}, 12.5), 169 (18), 155 (100), 141 (21), 135 (12), 127 (9), 113 (6), 107 (8), 99 (21), 91 (5), 87 (5), 81 (5), 77 (29), 73 (7), 68 (4), 63 (11), 55 (4), 51 (16).; Anal. Calcd for $C_9H_7O_3Cl$: C, 54.43; H, 3.55. Found: C, 52.79; H, 3.68.

3,3,6-Trichloro-7-hydroxy-3,3a,6,7,7,8,8a-hexahydro-2*H*-cyclohepta[*b*]furan-2-one (11).

Hydrochloric acid (2M, 0.8 mml, 1.6mmol) was added under nitrogen atmosphere to a solution of **6** (245 mg, 1.0 mmol) in tetrahydrofuran (5 mL). The solution was stirred for 1 h at room temperature. The reaction mixture was poured into ethyl acetate (30 mL). The organic layer was washed with 5% sodium hydrogen carbonate and saturated aqueous sodium chlorid, dried over magnesium sulfate, filtered, and removed the solvents to give 3,3,6-trichloro-7-hydroxy-3,3a,6,7,7,8,8a-hexahydro-2*H*-cyclohepta-[*b*]furan-2-one (**11**) (234 mg, 83%). colorless crystals**;** mp 159.5-160.0 ^{o}C (ethyl acetate); IR (KBr) ν_{max} 3509 (s), 3044 (w), 2953 (w), 1790 (s), 1445 (w), 1348 (m), 1314 (w), 1267 (m), 1242 (m), 1210 (s), 1140 (m), 1075 (s), 1013 (m), 995 (m), 972 (s), 936 (m), 897 (w), 860 (s), 750 (m), 689 (m), 673 (s), 617 (m), 558 (m), 484 (w) cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) δ 6.05 (dddd, *J* = 11.6, 5.6, 2.8, 0.4 Hz, H-5,), 5.83 (ddd, *J* = 11.6, 3.6, 1.6 Hz, H-4), 5.33 (ddd, *J* = 12.4, 8.4, 3.2 Hz, H-8a), 4.67 (dddd, *J* = 6.8, 5.6, 1.6, 1.6 Hz, H-6), 4.37 (dddd, *J* = 8.4, 3.6, 2.8, 1.6 Hz, H-3a), 4.20 (dddd, *J* = 6.8, 4.4, 3.2, 0.4 Hz, H-7), 2.65 (ddd, *J* = 14.0, 12.4, 3.2 Hz, H-8), 2.23 (ddd, *J* = 14.0, 4.4, 3.2 Hz, H-8); ^{13}C NMR (100 MHz, acetone-d_6) δ 167.78 (C-2), 133.20 (C-5), 122.67 (C-4), 80.95 (C-3), 76.76 (C-8a), 71.21 (C-7), 61.95 (C-6), 54.63 (C-3a), 34.29 (C-8); MS (70 eV) m/z 274 (M^{+}+4, 0.3%), 272 (M^{+}+2, 0.6), 270 (M^{+}, 0.6), 235 (50), 217 (40), 207 (5), 199 (46), 191 (31), 181 (27), 173 (96), 163 (38), 155 (71), 147 (57), 137 (54), 127 (66), 119 (15), 113 (49), 107 (38), 99 (95), 91 (82), 85 (14), 79 (100), 73 (45), 65 (41), 57 (15), 51 (43); MS (CI) m/z 277 ($M+H^{+}$+6, 4%), 275 ($M+H^{+}$+4, 32), 273 ($M+H^{+}$+2, 98), 271 ($M+H^{+}$, 100), 237 (20), 219 (10), 201 (50), 183 (30), 165 (29), 149 (10), 107 (5).; Anal. Calcd for $C_9H_9O_3Cl_3$: C, 39.81; H, 3.34; Cl, 39.17. Found: C, 40.06; H, 3.49.

3,6-Dichloro-7-hydroxy-3,3a,6,7,8,8a-hexaahydro-2*H*-cyclohepta[*b*]furan-2-one (12).

Hydrochloric acid (2M, 0.7 mL) was added to a solution of **10** (211 mg, 1.06 mmol) in tetrahydrofuran (5 mL). The solution was stirred for 1 h at rt. The reaction mixture was poured into ethyl acetate (30 mL). The organic layer was washed with 5% sodium hydrogen carbonate and saturated aqueous sodium chlorid, dried over magnesium sulfate, filtered, and removed the solvent to give 3,6-dichloro-7-hydroxy-6,7,7,8,8a-tetrahydro-2*H*-cyclohepta [*b*]furan-2-one (**12**) (239 mg, 96%).

12: colorless crystals; mp 155.5-156.0 ˚C (ethyl acetate); IR (KBr) ν_{max} 3486 (s), 2940 (w), 1752 (s), 1647 (m), 1590 (m), 1439 (m), 1360 (m), 1335 (m), 1316 (w), 1300 (m), 1252 (m), 1186 (m), 1123 (m), 1078 (m), 1048 (s), 1013 (m), 968 (m), 926 (w), 893 (m), 857 (m), 814 (s), 783 (w), 760 (w), 720 (m), 668 (m), 615 (w), 571 (w), 515 (m), 502 (m), 438 (w), 413 (w) cm^{-1}; UV (MeOH) λ_{max} 270 (ε 18681) nm; ^{1}H NMR (400 MHz, acetone-d_6) δ 6.56 (d, *J* = 12.0 Hz, H-4), 6.42 (ddd, *J* = 12.0, 6.4, 0.8 Hz, H-5), 5.56 (dd, *J* = 12.0, 4.0 Hz, H-8a), 4.89 (ddd, *J* = 6.4, 5.0, 0.8 Hz, H-6), 4.42 (dddd, *J* = 6.0, 5.0, 1.2, 0.8 Hz, H-7), 2.58 (dddd, *J* = 13.6, 6.0, 4.0, 0.8 Hz, H-8), 2.29 (ddd, *J* = 13.6, 12.0, 1.2 Hz, H-8); ^{13}C NMR (100 MHz, acetone-d_6) δ 167.75 (C-2), 156.61 (C-3), 137.84 (C-5), 120.15 (C-4), 119.66 (C-3a), 77.80 (C-8a), 70.30 (C-7), 59.16 (C-6), 33.60 (C-8); MS (70 eV) m/z 238 (M^++4, 3%), 236 (M^++2, 17), 234 (M^+, 25), 205 (7), 190 (39), 181 (8), 155 (100), 135 (7), 125 (11), 99 (22), 91 (5), 77 (8), 73 (7), 63 (10), 51 (6).; Anal. Calcd for $C_9H_8O_3Cl_2$: C, 45.99; H, 3.43; Cl, 30.16. Found: C, 46.08; H, 3.46; Cl, 30.02.

Reactions of 11 and 12 with Li_2CO_3 in DMF . Reactions of **11** and **12** with Li_2CO_3 in DMF was carried out at 140 °C for 30 min similarly to compound (**6**).After usual work up, compounds (**8**) and (**9**) from **11** were obtained in 26 and 7% yields, respectively. From **12**, compounds (**8**) and (**9**) were obtained in 36 and 5% yields, respectively.

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