THE CHEMISTRY OF 2H-CYCLOHEPTA[b]FURAN-2-ONE: SYNTHESIS, TRANSFORMATION AND SPECTRAL PROPERTIES

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Abstract – Overview of data, obtained in the last 60 years, concerning the synthetic methodology for 2H-cyclohepta[b]furan-2-one, their reactivity and mechanistic aspects, the synthetic potential for the extended π-electronic systems, and their spectral properties, are described.

1. INTRODUCTION

The chemistry of 2H-cyclohepta[b]furan-2-one (1a) is important in connection with troponoid chemistry, fulvenoid chemistry and azulenoid chemistry. Since the first synthesis of 2H-cyclohepta[b]furan-2-ones by Nozoe and Seto was reported at 19531 during the investigation of reactivities in troponoid compounds, a lot of interesting discoveries about 2H-cyclohepta[b]furan-2-one have been reported. Therefore, we will described here about the synthetic methodology for 2H-cyclohepta[b]furan-2-ones, their reactivity, mechanistic aspects, and the other properties about synthetic potential for new extended π-electronic systems.

2. THE FIRST SYNTHESIS OF 2H-CYCLOHEPTA[b]FURAN-2-ONES

\[
\begin{align*}
\text{Cl} & \quad \text{CH}_2\text{(CO}_2\text{Et})_2 / \text{EtOH-NaOEt} \\
2a & \quad 1b \\
\text{CH}_2\text{(COMe)CO}_2\text{Et} / \text{EtOH-NaOEt} & \quad 1c \\
\text{H}_2\text{SO}_4 & \quad 1a \\
\end{align*}
\]

Scheme 1

DOI: 10.3987/REV-09-654
Nozoe and Seto and their co-workers found the first synthetic way of $2H$-cyclohepta[$b$]furan-2-one (1a) which is a key precursor to azulenes starting from troponoids, during studying reactivity of the reactive troponoids (which we call for 2-chlorotropone (2a), 2-methoxytropone (2b), and 2-tosyloxytropone (2c)) with active methylene compounds. To be concrete, 3-ethoxycarbonyl-$2H$-cyclohepta[$b$]furan-2-one (1b) and 3-acyl-$2H$-cyclohepta[$b$]furan-2-one (1c) were prepared by the reaction of 2-chlorotropone with corresponding sodium salts of diethyl malonate and sodium ethyl acetoacetate, respectively. Therefore, these derivatives could be converted to unsubstituted $2H$-cyclohepta[$b$]furan-2-one (1a) itself by hydrolysis and decarboxylation or deacetylation with concentrated sulfuric acid.

3. MECHANISTIC DETAILS IN REACTION OF TROPONOID WITH ACTIVE METHYLENE COMPOUNDS

The mechanism of these reactions may be similar. But there are some differences among the reactive troponoids. In case of the reaction of 2-chlorotropone with diethyl malonate, the reaction proceed according to path a (Scheme 2). The carbanion of the active methylene attacks at C-7. The hydrogen at C-7 shifts to C-2 in the initial intermediate. Then the oxygen of tropone attacks at ester carbonyl carbon and the elimination of ethanol gives $2H$-cyclohepta[$b$]furan-2-one (1).

However, when malononitrile was used as an active methylene reagent, 3-cyano-$2H$-cyclohepta[$b$]furan-2-imine (3d, X=H) is obtained initially by according to a similar mechanism (path a). Imine group easily converts to carbonyl group by hydrolysis during treatment of the product. If 5-substituted 2-chlorotropone is used, either 5-substituted 3-cyano-$2H$-cyclohepta[$b$]furan-2-imine (3e) or the corresponding $2H$-cyclohepta[$b$]furan-2-one is obtained.
If 5-substituted 2-methoxytropone is used as a substrate instead of 2-chlorotropone, diethyl malonate anion attacks at 2-position to give 6-substituted 3-ethoxycabonyl-2H-cyclohepta[b]furan-2-one as shown in Scheme 4 (path b).

In case of 2-tosyloxytropone (2d), the distribution of products are little complicated depend on the reaction conditions. Usually the reactions proceed as similar to those of 2-chlorotopone (path a). When sodium ethoxide is used as a base, the reaction of 2d with diethyl malonate gives 8-hydroxy-2H-cyclohepta[b]furan-2-one (1d) or furotropones (7). These products react with diazomethane to give both corresponding O-methylated products. The mechanism can be considered as follows. After nucleophilic attack of diethyl malonate anion, toluenesulfinate anion dissociates according to path c to give intermediate 4 as shown in Scheme 5. Compound 4 cyclized by dissociation of ethanol to give a mixture of 1d and 7. When malononitrile was used as a reagent, products 3f and 8 were obtained similarly.
Thus, a variety of 2\(H\)-cyclohepta[\(b\)]furan-2-ones can be prepared by the reaction of active troponoid compounds with active methylene reagents, although there are some troubles in case of 3- or 7-substituted troponoid compounds due to steric hindrance. For examples, by using this procedure, Sato prepared methyl derivatives except 3-methyl-2\(H\)-cyclohepta[\(b\)]furan-2-one (13) and 8-methyl-2\(H\)-cyclohepta[\(b\)]furan-2-one (14) and their properties were made clear.\(^3\)

![Scheme 5](image)

Figure 1

4. SYNTHETIC WAY FOR 2\(H\)-CYCLOHEPTA [\(b\)]FURAN-2-ONES BY NUCLEOPHILIC ATTACK

Several other preparing methods for preparation of 2\(H\)-cyclohepta[\(b\)]furan-2-one and its derivatives were reported. The lithium salt of ethyl acetate also reacts with 2-chlorotropone to give ethyl 2-troponylacetate which is easily cyclized to 2\(H\)-cyclohepta[\(b\)]furan-2-one according to eliminate alcohol.\(^4\)
Tropone itself is also shown to be useful in the preparation of 3-cyano-2H-cyclohepta[\textit{b}]furan-2-imine (3d). Tropone undergoes nucleophilic attack at 2-position by anion of malononitrile. The oxygen of tropone attack to carbon of nitrile and subsequent hydrogen shifts to give 2-amino-3-cyano-8H-cyclohepta[\textit{b}]furan (15). It undergoes dehydrogenation with tetrachloro-1,2-benzoquinone to give ionic complex (16). The complex 16 is hydrolyzed to give 3-cyano-2H-cyclohepta[\textit{b}]furan-2-imine (3d) [orange crystals, mp 143 °C (decomp.)].

5. SYNTHETIC WAY FOR 2H-CYCLOHEPTA \textit{b}]FURAN-2-ONE AND 2H-CYCLOHEPTA-\textit{b}]THIOPHEN-2-ONE BY USING CYCLOADDITIONS OF SEVEN-MEMBERED RINGS

In 1967, Ciabattoni and Anderson reported the reaction of tropone with dichloroketene as follows. Tropone reacts with dichloroketene which comes from the reaction of dichloroacetyl chloride with triethylamine to give a [2+8]\textpi cycloadduct. But it cannot be isolated. It undergoes further elimination of hydrogen chloride with triethylamine to give 3-chloro-2H-cyclohepta[\textit{b}]furan-2-one (1f) as yellow-orange needles of mp 179 – 180 °C. However, the yield was not so good (Scheme 8).
Machiguchi reported\(^7\) the reaction of tropothione (2’a) with chloroketene which is generated in situ from chloroacetyl chloride and triethylamine, in benzene at room temperature affords only a 1:2 adduct 17b in 68 \% yield (deep orange leaflets, mp 226 °C). The formation of the adduct 17b is interpreted by three steps, initially [2+8] \(\pi\) cycloaddition, then dehydrohalogenation, to give 2\(H\)-cyclohepta[b]thiophen-2-one (17a). Finally, the compound 17a underwent electrophilic substitution to give 3-chloroacetyl-2\(H\)-cyclohepta[b]thiophen-2-one (17b). The expected initial product 17a can be obtained in 72\% yield as red needles (mp 88 °C) when the reaction temperature is below -60 °C.

\[
\text{CH}_2\text{ClCOCl} + \text{C}_6\text{H}_5\text{C} = \text{O} + \text{Et}_3\text{N} \rightarrow \text{S} + \text{HCl} \\
\text{Scheme 9}
\]

It is well known that tropylcarbonyl chloride (18) undergoes elimination of hydrogen chloride with triethylamine to produce 8-oxoheptafulvene (19).\(^8\)

\[
\text{Scheme 10}
\]

When 8-oxoheptafulvene occurred in the presence of tropone in refluxing benzene, a [2+8] \(\pi\) cycloadduct 20a is obtained as main product along with small amount of heptafulvalene (21a).\(^9\)

\[
\text{Scheme 11}
\]

The [2+8] \(\pi\) cycloadduct 20a converts to 3-cyclohexa-1,4-dienyl-2\(H\)-cyclohepta[b]-furan-2-one (1g) under the conditions by heating in DMSO. The methyne proton in seven-membered ring shifts to six-membered ring by 1,5-hydrogen shift. The dihydrobenzene can be oxidized with DDQ to give3-phenyl-2\(H\)-cyclohepta[b]furan-2-one (1h).\(^10\)
Initially, we thought that the structure of thermal product was 1,3-cyclohexadiene derivative on the basis of 100 MHz NMR data. Coupling constant between methine and methylene proton is large. But recently, on the basis of X-ray analysis, the structure of thermal product is established as 1,4-cyclohexadiene derivative 1g as shown in Figure 2. Both planes of 2H-cyclohepta[b]furan-2-one ring and cyclohexadiene ring are flat and intersect orthogonally each other. There are some difference among single bonds and double bonds in the 2H-cyclohepta[b]furan-2-one ring of 1g. Observed bond distances (Å) are O1-C2 1.407(2), C2-C3 1.431(2), C3-C10 1.374(2), C10-C4 1.43082), C4-C5 1.359(2), C5-C6 1.425(3), C6-C7 1.352 (3), C7-C8 1.424(3), C8-C9 1.351(2), C9-C10 1.443(2), C9-O1 1.369(2).

The similar products are obtained in the reactions of 2-methyltropone, 2-chlorotropone, and 2-acetoxy tropone with 8-oxoheptafulvene. But in the case of 2-methoxytropone very different reactivity is observed. 2-Methoxytropone reacts with 8-oxoheptafulvene to give 4 products (18’, 20 – 22). The products 20c and 21c are similar to those of previous experiments. The other products are very different.
Reaction mechanism of 2-methoxytropone with 8-oxoheptafulvene is considered as follows. 1-Methoxyheptafulvalene (21c) is produced by [2+2]π cycloaddition and subsequent decarboxylation of β-lactone 23c. Norcaradiene type adduct 20c is produced by 1,7-shift of C-C bond in β-lactone 23c although there is a possibility of direct [2+8]π cycloaddition of 2-methoxytropone with 8-oxoheptafulvene (Scheme 14).

Especially the structure and occurring mechanism of bridged 2H-cylohepta[b]furan-2-one 22 are very interesting. The structure of bridged 6-bromo-2H-cylohepta[b]furan-2-one which is produced from 5-bromo-2-methoxytropone (2g) is firmly established on the basis of X-ray analysis (Figure 3).13 There are also some differences between single and double bond length in 2H-cylohepta[b]furan-2-one moiety which is flat.

On the basis of experimental observation using duterated 2-methoxytropons and some other substituted 2-methoxytropons, the mechanism of its formation is hypothesized to involve the [2+2]π cycloaddition, 1,7-shift of C-O bond of β-lactone, Cope rearrangement, and final elimination of methanol (Scheme 15).13
Furthermore, the reaction of 2-N,N-dimethyaminotropone (2h) with 8-oxoheptafulven also gives bridged 2H-cyclohepta[b]furan-2-one as a minor product. The main product is 3-phenyl-2H-cyclohepta[b]furan-2-one (1h) although the yield is low.\textsuperscript{14}

However, if 2,7-dibromotropone (2i) is used as a substrate, 8-bromo-3-phenyl-2H-cyclohepta[b]furan-2-one (1i) can be obtained in good yield. The reaction of troponoid compounds with 8-oxoheptafulvene afford a variety of 2H-cyclohepta[b]furan-2-ones.\textsuperscript{14}

TroponeFe(CO)\textsubscript{3} 24a (R=H) can be easily prepared by the reaction of tropone with ironcarbonyl reagents such as Fe\textsubscript{2}(CO)\textsubscript{9}, Fe\textsubscript{3}(CO)\textsubscript{12}, Fe(CO)\textsubscript{5}, benzalacetoneFe(CO)\textsubscript{3}, etc.\textsuperscript{15} TroponeFe(CO)\textsubscript{3} itself reacts with
8-oxoheptafulvene to give heptafulvaleneFe(CO)₃ as a single product.¹⁵ If there is a substituent at 2-position of tropone, its reactivity changes to give a [2+8]π cycloadduct. In case of complex 2₄f (R=Me), two [2+8]π cycloadducts such as 2₆f and 2₇f can be obtained.¹⁶

[2+8]π cycloadduct 2₆f of 8-oxoheptafulvene (1₉) to 2-methyltroponeFe(CO)₃ 2₄f is treated with ceric ammonium nitrate (CAN) in acetonitrile to give norcaradiene derivative 2₀f in 45% yield and 8-methyl-3-phenyl-2H-cyclohepta[b]furan-2-one (1j) in 11% yield. In the case of 2₆g, norcaradiene derivative 2₀g and 8-t-butyl-3-phenyl-2H-cyclohepta[b]furan-2-one (1k) in 63% and 36% yields, respectively.¹⁷

TroponeFe(CO)₃ reacts with concentrated sulfuric acid to give a dienonium cation (2₇). Treatment of the cation with potassium carbonate and water give a hydroxyl compound 2₈ which is oxidized with the complex of chromium trioxide and pyridine to give 2,4-cyclohexadiene-1,6-dioneFe(CO)₃ (2₉).¹⁸,¹⁹ It is iron tricarbonyl complex of a keto form of β-tropolone. It can be also prepared directly by reaction of 3-hydroxytropone with Fe₂(CO)₉. This complex exhibits a variety of reactivities. It is very interesting that chloroacetate of 2,4-cyclohexa-1,6-dioneFe(CO)₃ (3₀) easily reacts with 8-oxoheptafulvene to give a product 3₁ as a keto form of 2-hydroxyheptafulvaleneFe(CO)₃ by one pot reaction. Because the haloacetate, is susceptible to hydrolysis, chloroacetyl group easily eliminates from chloroacetyloxyheptafulvaleneFe(CO)₃. 5- Cycloheptatrienlidene-cycloheptadiene-1-one (3₁) is treated with trimethylamine N-oxide followed by separation with silica gel column using dichloromethane as an eluent to give 3-chloro-2H-cyclohepta[b]furan-2-one (1f) (about 30% yield).²⁰

![Scheme 19](image1)

![Scheme 20](image2)
Recently, we have also found other new synthetic method for $2H$-cyclohepta[b]furan-2-one, 3- and 6-chloro-$2H$-cyclohepta[b]furan-2-one during the investigation for cycloadducts of cycloheptatriene with dichloroketene as follows. Dichloroketene which was prepared by the reaction of trichloroacetyl chloride with activated zinc, undergoes $[2+2] \pi$ cycloaddition to cycloheptatriene. The $[2+2] \pi$ cyclobutanone adduct could be converted to $\gamma$-lactone by Baeyer–Villiger oxidation. Dehydrogen chloride with lithium chloride at ca. 120 °C in DMF easily converts to $2H$-cyclohepta[b]furan-2-one (Scheme 21).

The $\gamma$-lactone 34 undergoes epoxidation with $m$-CPBA to give 35 which was directly obtained from $[2+2] \pi$ cycloadduct 33 by oxidation with $m$-CPBA. The epoxide 35 is treated with LiCl at 140 °C to give a mixture of 3-chloro-$2H$-cyclohepta[b]furan-2-one (1f) and 6-chloro-$2H$-cyclohepta[b]furan-2-one (1l). Chloro-$2H$-cyclohepta[b]furan-2ones could be obtained by three steps from cycloheptatriene (Scheme 22).

**6. SYNTHETIC WAY FOR 2H-CYCLOHEPTA [b]FURAN-2-ONE FROM HEPTAFULVENE AND CYCLOHEPTATRIENES BY PHOTO-OXYGENATION**

Next method for preparation of $2H$-cyclohepta[b]furan-2-ones is photo-sensitized oxygenation of heptafulvenes or cycloheptatrienes. When a solution of 8-cyanoheptafulvene (36) in acetone is irradiated in the presence of a sensitizer (Rose bengal) with a 100 W high-pressure mercury lamp through a water cooled pyrex filter under oxygen, it absorbed one mole of oxygen within two hours to give a (1:1) mixture of epidioxide 37 and 38 in 85% yield as colorless crystals which detonates at 106 °C in a capillary tube. These epidioxides are treated with triethylamine to give 6-hydroxy-3-cyano-$2H$-cyclohepta[b]furan-2-imine (3e) in 90% yield.
This reaction is applicable to 8-methoxycarbonylheptafulvene (39) and 8,8-dimethoxycarbonylheptafulvene (40) to give corresponding 2H-cyclohepta[b]furan-2-one 1a and 1b’. Epidioxide is converted to 2H-cyclohepta[b]furan-2-one derivatives without hydroxyl group at C-6 using thiourea instead of triethylamine.

These photo-sensitized reactions are utilized to the synthesis of 1a and 3d from cycloheptatriene derivatives 41 and 42 as shown in Scheme 25.

7. SYNTHETIC WAY FOR 2H-CYCLOHEPTA [b]FURAN-2-ONE FROM PHENYL PROPARGYL ETHER BY THE FLASH VACUUM PYROLYSIS

Trahanovsky has found general synthetic way for 2H-cyclohepta[b]furan-2-ones by the flash vacuum pyrolysis (FVP) of phenyl propargyl ethers at 650 °C and ~10^-4 Torr. This method is applicable for methyl substituted phenyl propargyl ethers. On the basis of methyl groups position of starting phenylpropiolate and product 2H-cyclohepta[b]furan-2-ones the FVP mechanism is shown in Scheme 26.
The acetylenic hydrogen of 45 undergoes 1,2-hydrogen shift to give intermediate methylenecarbene 46. The methylenecarbene 46 undergoes intramolecular cycloaddition to give norcaradine intermediate 47. It undergoes valence bond isomerization to give \( \text{2H-cyclohepta}\[b\]furan-2-one}^{22d}

By this FVP method, 8-methyl-\(\text{2H-cyclohepta}\[b\]furan-2-one\) (mp 116 – 117 °C), which cannot be prepared by Nozoe and Seto’s synthetic way, can be obtained as a main product (38 – 45%) along with 4-methyl-\(\text{2H-cyclohepta}\[b\]furan-2-one\) (13 – 15%). The isomeric lactones are separated by column chromatography.

4,8-Dimethyl-\(\text{2H-cyclohepta}\[b\]furan-2-one\) (49) is prepared by the FVP of 2,6-dimethylphenylpropiolate. 2,4,6-Trimethyl-phenylpropiolate gives 4,6,8-trimethyl-\(\text{2H-cyclohepta}\[b\]furan-2-one\) (50) by the FVP.

Indane derivative also underwent pyrolysis to give a mixture of \(\text{2H-cyclohepta}\[b\]furan-2ones\) condensed with five-membered ring in the same 20% yields, respectively. This observation also is consistent with the mechanism shown in Scheme 26.
More polymethylated 2H-cyclohepta[b]furan-2-ones (54 – 56) have also been prepared from corresponding polymethyl phenylpropionate by dynamic gas phase thermo-isomerization. 4,5,6,7,8-Pentamethyl-2H-cyclohepta[b]furan-2-one reveals a slight deviation from planarity on the basis of X-ray analysis and calculation.22bd

8. SYNTHETIC WAY FOR 2H-CYCLOHEPTA[b]FURAN-2-ONE BY WAY OF CYCLOHEPTAOXAPHOSPHOLE

Active troponoid reacts with a variety of ylids to give cycloheptaoxaphosphole. Kawamoto and co-workers characterized a “bonding betaines” as the most serious resonance hybrid forms as shown in Scheme 29.23

In the reaction with phenyl isocyanate the cycloheptaoxaphospholes act as an ylide to give corresponding 2H-cyclohepta[b]furan-2-ones (1a, 1b, and 1d) and 2H-cyclohepta[b]furan-2-imines (3e, 3f, and 3g) accompanied by the liberation of triphenylphosphine N-phenylimine and triphenylphosphorine oxide. The product 3e is a mixture of (E) and (Z). Products 3f and 3g are (Z). The cycloheptaoxaphosphole 57a reacts with phenyl isothiocyanate to give 2-(N-phenylamino)cyclohepta[b]thiophen-4- one (59) and a mixture (E)-3e and (Z)-3e.
The cycloheptaoxaphosphole 57b reacts with phenyl isothiocyanate to give ethoxycarbonylcyclohepta[b]furan-2-thione (58b) and (Z)-imine 3f in 12% and 4% yield, respectively. In the case of 57d, imine 3g is a main product and a small amount of cyclohepta[b]furan-2-thione 58d produced as a by-product. Furthermore, cycloheptaoxaphospholes 57 react with N-methoxyphenylsuccinimide to give [2+8]π adduct (60) and [2+4]π cycloaduct (60') similar to 2H-cyclohepta[b]furan-2-one.

9. ORGANOMETALLIC COMPOUNDS RELATE TO 2H-CYCLOHEPTA [b]FURAN-2-ONE
There is not an organometallic compound in which 2H-cyclohepta[b]furan-2-one moiety coordinates to metal until now. But two unique organometallic compounds \(^{24,25}\) are reported. Tropone reacts with metal carbonyl reagents to give corresponding troponeiron carbonyls. However, tropone reacts with decacarbonyl dimanganese to give tricarbonyl-1-syn-(1',2'-dihydro-2'-oxo-1'-oxa-azulen-3'-yl)\(\eta^5\)-pentadienylmanganese as a main product.\(^{24}\)
It is a purple crystalline solid whose structure is determined by X-ray analysis as shown in Figure 6. Mangane coordinates dienyl part. It is interesting that this 2H-cyclohepta[b]furan-2-one portion exhibits characteristic bond alternation although bond lengths of dienyl portion is almost same.\textsuperscript{24}

The other example is a compound which is replaced carbonyl group of 2H-cyclohepta[b]furan-2-one with metalcarbonyl group. The anions derived from methylmethoxycarbene complexes of chromium and tungsten as nucleophiles react with tropone and 2-substituted tropones to give corresponding oxaazulenylidene complexes,\textsuperscript{25} although their yields are very low as shown in Scheme 32.

On the basis of spectral data, these oxaazulenylidene metal complexes 64 and 65 undergo the perturbation of the canonical formulas B and C similar to 2H-cyclohepta[b]furan-2-one.
Pentacarbonyl(1-oxazulen-2-ylidene)chromium (64a) reacts with \( S_8 \) in refluxing THF to give 1-oxa-2-azulenethione (58a) as a red crystals (mp 181 – 182 °C) in 82% yield.

10. Structural and Spectroscopic Properties of 2\( H \)-cyclohepta[\( b \)]furan-2-one

2\( H \)-Cyclohepta[\( b \)]furan-2-one is obtained as orange needle crystals (mp 69 – 70 °C). Molecular Structure of 2\( H \)-cyclohepta[\( b \)]furan-2-one is investigated by X-ray analysis.\(^{26}\) As a result, 2\( H \)-cyclohepta[\( b \)]furan-2-ones possess an almost planar structure.

It is recognized clearly that a larger and a shorter C-C bonds are disposed alternately. The mean values for the larger and shorter C-C bonds are 1.409 and 1.357 Å with standard deviations of 0.010 Å respectively. The difference between these two values is highly significant, and this fact favors the conventional chemical formula I shown in Fig. 9. However, the mean value of the larger C-C bonds and those of two C-O bonds in the five-membered ring (with standard deviation of 0.010 Å) are significantly different from their pure single bond lengths respectively. Thus, in order to interpret the bond distances more quantitatively, it is necessary to take into account the many resonance structures as shown in Figure 9.
Considering the resonance structures given above, it seems that the seven-membered ring itself is somewhat positively charged. $2H$-Cyclohepta[b]furan-2-one is expected to undergo nucleophilic attack of active methylene at C8a, regiospecifically due to the contribution of 1D. This is justified by the large dipole moment (5.64 D) of this molecule and by some chemical evidences.\textsuperscript{27}

The most intense bands for carbonyl region in the IR spectrum (KBr) appears at 1748 cm\textsuperscript{-1}. Absorptions of the longest wave length (MeOH) appear at 427 nm (sh, $\varepsilon$ = 1980), 453 nm (sh, 780), and 488 nm (sh, 190), assigned as $n\rightarrow\pi^*$ transition. The peaks at 373 nm (14660) and 387 nm (14700) are assigned as $\pi\rightarrow\pi^*$ (2). The peaks at 223 nm (14350) and 251 nm (23150) are assigned as $\pi\rightarrow\pi^*$ (1).\textsuperscript{22b} The hydrogen chemical shifts of $2H$-cyclohepta[b]furan-2-one by using $^1$H (600 MHz) and $^{13}$C (150 MHz) NMR spectrum (CDCl\textsubscript{3}) can be assigned completely as follows. $\delta$ 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 (ddt, $J$=10.8, 8.6, 1.1 Hz, H-6), 5.75 (d, $J$=1.3 Hz, H-3).\textsuperscript{13}C NMR (CDCl\textsubscript{3}), $\delta$ 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).\textsuperscript{22b} These data are very useful when we will investigate the substitution effects for new $2H$-cyclohepta[b]furan-2-one derivatives.

11. THE FORMATION OF AZULENES BY NUCLEOPHILIC ADDITION OF $2H$-CYCLOHEPTA[b]FURAN-2-ONE

$2H$-Cyclohepta[b]furan-2-ones, such as 3-ethoxycarbonyl-$2H$-cyclohepta[b]furan-2-one and 3-aceyl-$2H$-cyclohepta[b]furan-2-one reacted easily with malononitrile, cyanoacetamide, ethyl cyanoacetate, and diethyl malonate in the presence of NaOEt or t-butyamine at room temperature or under cooling with ice-water, giving the corresponding 1,2,3-trisubstituted azulene derivatives, respectively.\textsuperscript{28}

\begin{center}
\includegraphics[width=\textwidth]{scheme35.png}
\end{center}

\textbf{Scheme 35}

The carbanions, $\text{R}_2^-\text{CH}-\text{R}_3$, being produced from malononitrile, cyanoacetamide, ethyl cyanoacetate or diethylmalonate, attack $2H$-cyclohepta[b]furan-2-one at the 8a-position, regioselectively and the lactone ring opens to give a heptafulvene-type intermediate which should exist in the tautomers 62 and 63. The position at which the carbanions attack is confirmed from the observation on the formation of azulene derivatives from $2H$-cyclohepta[b]furan-2-ones bearing the substituent at the seven-membered ring.
12. REACTION OF 2H-CYCLOHEPTA[b]FULAN-2-ONE WITH ENAMINES, EThERS, OTHER ALKENE, AND ALKyne

Yasunami and Takase found 2H-cyclohepta[b]furan-2-one reacts with enamines to give azulenes by the [8+2]π cycloaddition, removable of carbon dioxide and deamination. By this procedure, it is possible to introduce regiospecifically a expected functional group in five membered ring of azulene.²⁹

![Scheme 36](image)

As there is the review of this reaction in 1981 by Yasunami,³⁰ the preparation of new azulenes condensed with π-electronic systems by using this procedure will be described. as shown in Scheme 37-39. 1-Pyrrolidylacenaphtylene (73a) or its derivative (73b) reacts with 1a to give corresponding azuleno[4,5-α]acenaphthylene 74a or 74b. Compound 74a reacts further with dimethyl acetylenedicarboxylate (77b) to give dimethyl acenaphthyleneo[1,2- d]heptalene-8,9-dicarboxylate (76).³¹

![Scheme 37](image)

The compound 80 is prepared by the reaction of 2H-cyclohepta[b]furan-2-one with the enamine 79 as a key compound. Compound 80 undergoes trifluoroacetylation and bromination to give 81. After the reaction of 80 with KOH, methylation with diazomethane was carried out to give 82. Oxidation of 82 with DDQ and hydrolysis with KOH and decarboxylation in CF₃CO₂H gave 2,7-methanocyclodeca[α]azulene (83). The NMR spectrum of 2,7-methanocyclodeca[α]azulene (83).³² Its NMR spectrum revealed that the double bond of methano[10]annulene moiety are delocalized and azulene moiety indicate a bond-length alternation.
The condensed nonalternant hydrocarbon of new azulenazulenes \(89a\) and \(89b\) have been synthesized by combination of the reaction of \(2H\)-cyclohepta\([b]\)furan-2-one with enamines \(84\) and the reaction of acetylene derivatives (\(77a\) and \(77b\)) with enamines \(86\) according to Scheme 39. Methyl azuleno[1,2-\(b\)]azulene-2-carboxylate during the reaction of \(88b\), methoxy carbonyl group shifted to \(89b\). Dimethyl azuleno[1,2-\(b\)]azulene-2,4-dicarboxylate.\(^{33}\)

Nozoe, Wakabayashi and co-workers found that \(2H\)-cyclohepta\([b]\)furan-2-one reacts with enol ethers instead of enamines to give corresponding azulens by \([2+8]\) cycloaddition and followed by decarboxylation and elimination of alcohol. Sometimes, during this reaction, \([2+4]\) cycloaddition as a side reaction is observed. This experiments carried out as follows, a mixture of \(2H\)-cyclohepta\([b]\)furan-2-one and 3 – 5 equivalent of enol ethers are heated in aprotic solvents such as THF, acetonitrile, or toluene at 160 – 190 °C in a Pyrex sealed tube for 20 – 40 h to give deep-colored azulene \(72\) as a main product as shown in Scheme 40.\(^{34}\)
Instead of enolethers, trialkyl orthoformates can be applicable for preparation of 2-alkyloxyazulenes \( \text{93} \), because it can be converted to ketene acetal \( \text{92} \) by heating. The ketene acetal \( \text{92} \) react with 1 to give 2-alchoxyazulene \( \text{93} \) (Scheme 41).

2\(H\)-Cyclohepta[\(b\)]furan-2-one reacts with electron deficient olefins such as 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) and dimethyl acetylenedicarboxylate (DMAD) to give a \([4+2]\)\(\pi\) cycloadduct and/or a \([8+2]\)\(\pi\) cycloadduct.

2\(H\)-Cyclohepta[\(b\)]furan-2-one reacts with PTAD at room temperature to give \([4+2]\)\(\pi\) cycloadduct \( \text{95} \) in a 66% yield as a single product. On the other hand, reaction of 2\(H\)-cyclohepta[\(b\)]furan-2-one with excess amount of dimethyl acetylenedicarboxylate (DMAD) is carried out under reflux in o-xylene to give a \([4+2]\)\(\pi\) cycloadduct \( \text{96} \) (71%) and azulene derivative \( \text{98} \) (9%) in a ratio of 7:1. The azulene derivative is probably derived from \([8+2]\)\(\pi\) cycloaddition followed by decarboxylation as in the enamine reaction.\(^{35}\)

\[ 
\begin{align*}
\text{(Scheme 41)}
\end{align*}
\]
1,3-Butadiene derivatives which are nonpolar olefins react with 2\(H\)-cyclohepta\([h]\)furan-2-one under similar reaction condition to enamines to give heptafulvene (or dihydroazulene) derivatives in good yields.\(^{36}\)

\[
\begin{array}{c}
\text{CO}_2\text{Et} \\
\text{CO}_2\text{Me}
\end{array}
\] + \[\text{Ar, 150 °C, 14h} \]
\[
\begin{array}{c}
\text{CO}_2\text{Et}
\end{array}
\]
\[
\text{Schem 43}
\]

Methyl 2\(H\)-cycloheptan-2-one-3-carboxylate reacts with 6,6-dimethylfulvene by [4+2]\(\pi\) cycloaddition in ethanol refluxed preferably. In refluxing xylene, product 103 is obtained as a sole product. It is produced by [8+2]\(\pi\) cycloaddition and decarboxylation. The adduct 102 is heating to give a mixture of retro Diels-Alder reaction product 1b’ and 101 along with 103.\(^{37}\)

\[
\begin{array}{c}
\text{CO}_2\text{Me}
\end{array}
\] + \[\text{Scheme 44}
\]

<table>
<thead>
<tr>
<th>Solvent (reflux)</th>
<th>Reaction time (h)</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>xylene</td>
<td>25.5</td>
<td>102</td>
<td>35.0</td>
</tr>
<tr>
<td>benzene</td>
<td>24.0</td>
<td>103</td>
<td>35.0</td>
</tr>
<tr>
<td>ethanol</td>
<td>27.0</td>
<td>1b’</td>
<td>38.0</td>
</tr>
</tbody>
</table>

When the complex 103 is treated with phosphoric acid, it underwent proton shift to give azulene derivative 105.

\[
\begin{array}{c}
\text{CO}_2\text{Me}
\end{array}
\] + \[\text{Scheme 45}
\]

Coefficients and energy levels of molecular orbitals (NHOMO, HOMO, LUMO, and NLUMO) of 2\(H\)-cyclohepta\([h]\)furan-2-one are as follows (Figure 10). The periselectivity of [2+8]\(\pi\) and [2+4]\(\pi\) cycloadditions is discussed on the basis of these data.\(^{22c, 37a, 38, 39}\)
13. ELECTROPHILIC SUBSTITUTION OF 2H-CYCLOHEPTA[b]FURAN-2-ONE

Because 2H-cyclohepta[b]furan-2-one is one of aromatic compounds, there is a possibility to undergo electrophilic aromatic substitution. Initially, bromination with bromine, nitration with fuming nitric acid in concentrated sulfuric acid, and acylation with acetic anhydride in the presence of tin tetrachloride are explored.

\[
\begin{array}{cccc}
\text{Br}_2/\text{CH}_3\text{CO}_2\text{H} & \text{80}\% & \text{Ac}_2\text{O}/\text{SnCl}_4 & \text{85}\% \\
\text{fum. HNO}_3/\text{conc. H}_2\text{SO}_4 & \text{80}\% & \text{POCl}_3/\text{DMF} & \text{105}\%
\end{array}
\]

These reactions occur at 3-position of 1a regiospecifically, in good yields. After them, Nozoe and co-worker have investigated the reaction of tropyl ethers with various 1-oxaazulan-2-one to give corresponding 3-tropyl-2H-cyclohepta[b]furan-2-ones. 3-Formyl-2H-cyclohepta[b]furan-2-one is obtained in 63% yield by Vilsmeier reaction of 1a.

It is well known that pyridine react with trifluoromethanesulfonic anhydride to give 1-trifluoromethanesulfonylpyridinium trifluoromethanesulfonate (TPT) which is used as a reagent for trifluoromethanesulfonation of hydroxyl group such as phenol. Recently we found this reagent acts as an electrophile in the reaction of azulene to give 1-(N-trifluoromethanesulfonyl-dihydropyridyl)azulene. It
is easily remove trifluoromethanesulfinic acid by potassium hydroxide to give 1-pyridyl-azulene. This reaction is applicable for $2H$-cyclohepta[b]furan-2-one to give 3-(4-pyridyl)-$2H$-cyclohepta[b]furan-2-one.$^{43}$

![Scheme 47](image)

The reaction of triflic anhydride with dimethylsulfoxide leads to formation of dimethyl (trifluoromethanesulfonyloxy)sulfonium trifluoromethanesulfonate, “dimethyl sulfide ditriflate” (DMSD). It is also a good electrophile for benzenoid compound to give aryldimethylsulfonium trifluoromethanesulfonate.$^{44}$ In case of $2H$-cyclohepta[b]furan-2-one and 5-isopropyl derivative 1u, corresponding (2-oxo-$2H$-cyclohepta[b]furan-3-yl)dimethylsulfonium trifluoromethanesulfonates (1s and 1v) are obtained.$^{45}$ They are treated with diethylamine to give 3-methylthio-$2H$-cyclohepta[b]furan-2-one (1w) and 5-isopropyl-3-methylthio-$2H$-cyclohepta[b]furan-2-one (1x).

![Scheme 48](image)

These methylthio derivatives 1w and 1x are oxidized with $m$-CPBA to give 3-methylsulfinyl-$2H$-cyclohepta[b]furan-2-one (1y) and isopropyl derivative 1z.

3-Methylsulfinyl-$2H$-cyclohepta[b]furan-2-one (1y) is heated at ca. 40 °C to give 3,3’-bi(2-oxo-$2H$-cyclohepta[b]furanyl) (107). Its reaction is carried out -80 °C to give bis(2-oxo-$2H$-cyclohepta[b]furan-3-yl)sulfide (108).
Recently, we reported 2-hydroxyazulene reacts with trifluoromethanesulphonyl chloride in the presence of pyridine to give 1,3-dichloro-2-hydroxyazulene. On the basis of this observation, we found new halogenation with trifluoromethanesulphonyl chloride and halogenide ion. For example, azulene reacts with tetrabuthylammonium bromide and trifluoromethanesulphonyl chloride to give 1-bromoazulene and/or 1,3-dibromoazulene. Under similar conditions, 2H-cyclohepta[b]furan-2-one gives 3-bromo-2H-cyclohepta[b]furan-2-one (1n) (Scheme 50). By the combination of trifluoromethanesulphonyl chloride and potassium iodide, 3-iodo-2H-cyclohepta[b]furan-2-ones (1o) is obtained in 88% yield. 2H-Cyclohepta[b]furan-2-one also undergoes halogenations with halosuccinimide.

![Scheme 49](image)

Scheme 49


The chlorine of 110 can be removed by the treatment of NaI in the trifluoroacetic acid.

Furthermore, they can convert them to azulene analogous 114 by the [2+12]π cycloaddition with dimethyl acetylendicarboxylate.

8H-Cyclohepta[c]tropolone (115) which is prepared from azulene48 reacts with tosyl chloride and dimethyl malonate in the presence of sodium methoxide by Nozoe’s method (70%), to give 8H-heptaleno[b]furan-2-one (117) as orange crystals.49 This derivative will have potentiality as a synthetic key intermediate for a lot of compounds containing 2H-cyclohepta[b]furan-2-one skeleton.

15. THE ROLE OF 2H-CYCLOHEPTA[b]FURAN-2-ONE IN THE CHEMISTRY OF NATURAL PRODUCTS
Two derivatives (Lettucenine A. and Malophylidin) of 2H-cyclohepta[b]furan-2-one are found in plant.\textsuperscript{50} Named lettucenin A has been isolated from leaves of the lettus (Lactuca sativa var. capitata, compositae). Isolated yield from the dried leaves is 0.00084% yields. Lettucenine A is the first guaianolide phytoalexin containing a unique 2H-cyclohepta[b]furan-2-one ring system. Lettucenine A completely inhibits spore germination of Ceratocystis fimbriata at concentrations of 2 \( \mu \text{g/ml} \).

![Image of molecular structures](image)

An isomeric extended azulenequinone malophylidin (119) is isolated from the root of Ferula Malacophylla by Baginov \textit{et al.}\textsuperscript{51} During the isolation of violet pigment linderaazulene from gorgonian Paramuricea Chamaeleon, Alpertunga \textit{et al.}\textsuperscript{52} detected a small amount of yellow pigment, which was a photo oxidation product 121 formed by exposing an ethanol solution of linderaazulene to direct sunlight for six days which is an isomer of malophylidin.\textsuperscript{51}

The 2H-cyclohepta[b]furan derivative 123 have been synthesized from the antimitotic agent colchicines (122) which is one of well-known natural products, by Nozoe’s method as shown in the Scheme 56.\textsuperscript{53}

![Image of synthesis scheme](image)
Ando and co-workers reported synthesis of bioactive molecules Hymenolin and Parthenin used for 8-hydroxy-6-methyl-2-oxo-2\textH-cyclohepta[\textb]furan-3-carboxylate (124) as a key intermediate (Scheme 57).54

Wakabayashi and co-workers have been investigating on cytotoxic activity against human oral tumor cell lines and inhibition of LPS-stimulated NO production in mouse macrophage-like cells by some 2\textH-cyclohepta[\textb]furan-2-ones such as 1b, 1d, and 1d'. However, they cannot get a good result until now.55

\[
\begin{align*}
1b: & \quad R_1=\text{CO}_2\text{Me}, R_2=\text{H} \\
1d: & \quad R_1=\text{CO}_2\text{Et}, R_2=\text{OH} \\
1d': & \quad R_1=\text{CO}_2\text{Et}, R_2=\text{OAc}
\end{align*}
\]

**Figure 12**

16. UTILIZATION OF 2\textH-CYCLOHEPTA[\textb]FURAN-2-ONE AS FUNCTIONAL GROUPS

In the development of organic redox chemistry, 2-oxa-2\textH-cyclohepta[\textb]furan-3-yl group shows electron donating character and contributes to make reversible multistage redox systems as follows.

Tropylium ion, one of the most stable carbonium ion, is known to react with various anionons such as active methylene compounds and aryl compounds such as phenol and azulene. The reaction can also be carried out conveniently using tropyl ethers, in the presence of catalytic amounts of the tropylium ion or acids, in place of tropylium salts. The 3-position of 1a is expected to be capable of electrophilic substitution with tropylium ion to give 3-(cycloheptatrien-7-yl)-2\textH-cyclohepta[\textb]furan-2-one (1p) as mentioned previously. The methine hydrogen of cycloheptatriene ring undergoes 1,5-shift thermally. Then, hydride removes by DDQ and anion-exchange reaction with aq, 42% HBF$_4$ gives (2-oxo-2\textH-cyclohepta[\textb]furan-3-yl)tropyliumBF$_4^-$ (129). From 2\textH-cyclohepta[\textb]thiophen-2-one, (2-oxo-2\textH-cyclohepta[\textb]thiophen-3-yl)tropyliumBF$_4^-$ (132) [dark brown needles mp 170 °C] can also be easily obtained. The p$K_R^+$ values of these cations (129 and 132) are 3.8 and 3.2, respectively.
These values are lower than that (3.9) of tropylium ion.

![Scheme 58](image)

The averaged chemical shifts of seven–membered ring moiety in \(^1\)H NMR and \(^{13}\)C NMR are (8.90 and 152.7 for 129, 9.00 and 155.0 for 132. These chemical shifts appear at higher field compared with tropylium ion (9.26 ppm and 156.2 ppm).\(^{56}\) The ring protons of 2H-cyclohepta[b]furan-2-one moiety of 129 and 132 appear at lower fields compare with that of 1a and 17a.

![Figure 13](image)

The connecting at 3-position of 2H-cyclohepta[b]furan-2-one and 2H-cyclohepta[b]thiophen-2-one connect with tropylium cation works decrease the p\(K_R^+\) value due to increasing the attacking places of hydroxide ion by contribution of 128B and 128C structures.

![Figure 14](image)

Nitta and co-worker\(^{57a}\) have prepared tris(2-oxo-2H-cyclohepta[b]furan-3-yl)methyl cation (134) in excellent yields, starting from 1a by the electrophilic substitution with trimethyl orthoformate in a solution of trifluoromethanesulfonic acid and dichloromethane, and followed by oxidation with DDQ and treatment with HPF\(_6\). Its p\(K_R^+\) value is 9.7. 2-Oxo-2H-cyclohepta[b]furan-3-yl group highly stabilized methyl cation. Its effectiveness is smaller than that of azulen-1-yl group (p\(K_R^+\) is 11.3, \(E_{1\text{red}}\) – 0.78 V, \(E_{2\text{red}}\) – 0.78 V).
The reduction potentials of 134 determined by cyclic voltammetry (CV) in CH$_3$CN are $E^{\text{red}}_1 = -0.31$ V and $E^{\text{red}}_2 = -0.95$ V.

Bis(2-oxo-2$H$-cyclohepta[b]furan-3-yl)methane (137) are prepared by the reaction of 1a with paraformaldehyde quantitatively. It was oxidized with DDQ to give a hydroquinone salt of bis(2-oxo-2$H$-cyclohepta[b]furan-3-yl)methyl cation and exchange the counter anion using HBF$_4$ to give 138. The longest wavelength absorption maxima of 138 appear 603 nm (log $\varepsilon$, 4.73). The $pK_R^+$ value of 138 is 2.6. The stabilization effect is not enough.

The reduction wave in cyclic voltammetry (CV) of 138 is $-0.27$ V and irreversible. This observation expects to dimerize the radical species from 138 during CV measurement. It is treated with Zn to give dimer 139 along with small amount of 137. It is easily reduced with NaBH$_4$ to give 137 in 92% yield.
Bis(2-oxo-2H-cyclohepta[b]furan-3-yl)phenylmethyl cations\textsuperscript{58} (143a-e) were prepared by the electrophilic substitution of 1a with 141c or its derivatives and oxidation with DDQ and treatment with HPF\textsubscript{6}. The pK\textsubscript{R}\textsuperscript{+} values of cations 143a-e depend on the substituents on the phenyl group. The pK\textsubscript{R}\textsuperscript{+} values of 143a-e are determined as shown in Table 1. In order to clarify the stabilizing effect of substituents in benzyl cations 143a-e, related radicals and anion species, they studied the synthesis and properties of bis(2-oxo-2H-cyclohepta[b]furan-3-yl)phenylmethyl cations. The characteristic absorption bands of the counter ion PF\textsubscript{6}\textsuperscript{-} are observed at 838-845 cm\textsuperscript{-1} in the IR spectra of 143a-e. The longest wavelength absorption maxima of 143a-e in CH\textsubscript{3}CN are shown in Table 1. The spectrum of 143a shows remarkable difference. There are two big absorption maxima at 671 nm and 575 nm. Average of the two wavelengths is 623 nm which is similar to the longest wavelength absorption maxima (621 nm) of the other cations (143b-e). This observation could be the contribution of qinodimethane type structure similar to compound 156 which will be described later.

The synthetic method for 1,3- and 1,4-bis[bis(2-oxo-2H-cyclohepta[b]furan-3-yl)methyl]methylenebenzenes are based on a single and stepwise TFA-catalyzed electrophilic aromatic substitution on 1a with isophthalaldehyde and terephthalaldehyde to afford the corresponding 1,3- and 1,4-dimethylbenzene derivatives, followed by oxidative hydrogen abstraction with DDQ, and subsequent exchange of the
counter-anion by using aq. HPF₆ solution. In spite of the dicationic nature of 144 and 145, they exhibited high stability with large pKᵣ⁺ values 9.3 and 9.0 due to the stabilizing effect of the 2-oxo-2H-cyclohepta[b]furan-3-yl units, however, we could not determine pKᵣ⁺ and pKᵣ++ values separately. The electrochemical reduction of the cation 144 exhibits reversible four waves at – 0.04 V, – 0.34 V, – 1.06 V, and – 1.34 V. The electrochemical reduction of the cation 145 exhibits reversible two waves at – 0.33 V and – 1.05 V.

<table>
<thead>
<tr>
<th>143</th>
<th>Compounds (R)</th>
<th>λmax (log ε)</th>
<th>pKᵣ⁺</th>
<th>E₁ red</th>
<th>E₂ red</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>NMe₂</td>
<td>671 (4.17)</td>
<td>12.4</td>
<td>-0.50</td>
<td>-1.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>575 (4.18)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b</td>
<td>OMe</td>
<td>621 (4.55)</td>
<td>10.0</td>
<td>-0.36</td>
<td>-1.08</td>
</tr>
<tr>
<td>c</td>
<td>H</td>
<td>621 (4.18)</td>
<td>9.3</td>
<td>-0.31</td>
<td>-1.03</td>
</tr>
<tr>
<td>d</td>
<td>Cl</td>
<td>621 (4.32)</td>
<td>9.1</td>
<td>-0.29</td>
<td>-0.99</td>
</tr>
<tr>
<td>e</td>
<td>CN</td>
<td>621 (3.62)</td>
<td>7.9</td>
<td>-0.23</td>
<td>-0.88</td>
</tr>
</tbody>
</table>

Table 1. The longest wave length, pKᵣ⁺, and CV data of 138a-e

Bis(2-oxo-2Hcyclohepta[b]furan-3-yl)methylimbenzene(phenyl)methyl cations 144 and 145 are stablized by 2-oxo-2H-cyclohepta[b]furan-3-yl units.

The reaction of 1,3,5-triformylbenzene with six molar equivalent amounts of 1a in CH₂Cl₂- trifluoroacetic acid (5:1) at rt for 48 h afforded 1,3,5-tris[bis(2-oxo-2H-cyclohepta[b]furan-3-ylmethyl)benzene in 68% yield. The oxidative hydrogen abstraction of 1,3,5-tris[bis(2-oxo-2H-cyclohepta[b]furan-3-ylmethyl)benzene with DDQ in CH₂Cl₂ at rt for 1 h, followed by treatment with aqueous 42% HBF₄ in Ac₂O, afforded crystals of stable 1,3,5-tris[bis(2-oxo-2H-cyclohepta[b]furan-3-yl)methylimium]benzene tris(tetrafluoroborate) (146) in 89% yield. The pKᵣ+++ and pKᵣ+ are 9.0 and 6.4. The longest wavelength
absorption maximum of trication **146** is 615 nm.

The reduction potentials of trications are determined by cyclic voltammetry (CV) in CH$_3$CN. The only two reduction waves of $E_3^{\text{red}}$ and $E_6^{\text{red}}$ observed at $-0.30$ V and $-1.13$ V, respectively.

The highly polarized compounds, quinonemethides, $^{60}$ 4-Hydroxyphenyl-bis(2-oxo-2$H$-cyclohepta[b]-furan-3-yl)methane and 3,5-di-tert-butyl-4-hydroxyphenyl-bis(2-oxo-2$H$-cyclohepta[b]furan-3-yl)methane prepared by using described procedure previously. The pKa values of the conjugated acids of **147** and **148** are 4.2 and <0, respectively.

![Figure 16](image)

The reduction and oxidations of quinonemethides **147** and **148** determined by cyclic voltammetry (CV) in CH$_3$CN are $E_1^{\text{red}}$ − 1.07 V, $E_2^{\text{red}}$ − 1.44 V, $E_3^{\text{red}}$ − 1.66 V, $E_1^{\text{ox}}$ (+0.78 V), $E_2^{\text{ox}}$ (+1.47 V) of compound **147**. $E_1^{\text{red}}$ − 1.24 V, $E_2^{\text{red}}$ − 1.56 V, $E_1^{\text{ox}}$ +0.74 V, $E_2^{\text{ox}}$ (+1.09 V) were observed in compound **148**. These reductions exhibit reversible but oxidations do not exhibit reversible except $E_1^{\text{ox}}$ of **148**.

![Scheme 64](image)
The preparation of 7,7-bis(2-oxo-2H-cyclohepta[b]furan-3-yl)-8,8-dicyano-1,4-quinoxidimethane (151) was prepared by the TFA-catalized electrophilic substitution of 1a with 4-(dicyanomethyl)benzaldehyde (149) and subsequent oxidation with DDQ and treatment of triethylamine in good yield. The longest wave length absorption maxima of 151 in CH3CN appears at 663 nm and 531 nm. But the longest wave length absorption maxima of 151 changes to 621 nm by addition of trifluoroacetic acid. The compound 151 become bis(2-oxo-2H-cyclohepta[b]furan-3-yl)phenylmethyl cations by protonization. Reduction waves (reversible) and oxidation waves (irreversible) of 151 by CV spectrum appear E1\textsubscript{red} – 0.70 V, E2\textsubscript{red} – 1.28, E1\textsubscript{ox} (+0.51 V), and E2\textsubscript{ox} (+1.55 V).

![Scheme 65](image)

17. CONCLUSIONS
We have described the variety of synthetic methods for 2H-cyclohepta[b]furan-2-one and its derivatives. Moreover, a variety of methodologies for functionalization of these molecules using electrophilic substitution or nucleophilic reactions and chcloaddition and so on are described here. Now investigation towards the biology and materials science of the impressive number of functionally and structurally modified 2H-cyclohepta[b]furan-2-ons are going to begin. We expect that interesting reports about 2H-cyclohepta[b]furan-2-on chemistry will be increasing from now.

REFERENCES
17. N. Morita, unpublished results.


**Noboru Morita** was born in Kochi, Japan, in 1946. He was appointed at College of General Education in Tohoku University as an assistant in 1972 and received his Ph.D. from Tohoku University in 1973 under the supervision of Prof. Yoshio Kitahara. He moved to Tokyo Institute of Technology in 1974. In 1976–1977 he worked as a postdoctoral fellow with Prof. Sidney I. Miller at Illinois Institute of Technology, Chicago, Illinois (U. S. A). He moved to College of General Education in Tohoku University in 1977 and promoted to assistant professor in 1989 and a professor in 1992. In 1993 he moved to Faculty of Science in Tohoku University as a professor. The research in his group focuses on the synthetic study on the novel aromatic compounds.
Kozo Toyota was born in Tokushima in 1960. He was appointed at Tohoku University as a research associate in 1989, received his Ph.D. from Tohoku University in 1990 under the supervision of Prof. Masaaki Yoshifuji, and was promoted to associate professor in 2004. The research in his group focuses on the study on the peptide-inspired molecular architecture by employing bis(2-ethynyl-3-thienyl)arene \( \pi \)-spacer and the related systems.

Shunji Ito was born in Tokyo in 1962. He was appointed at Tohoku University as an assistant professor in 1989, received his Ph.D. from Tohoku University in 1991 under the supervision of Prof. Toyonobu Asao, and was promoted to associate professor in 2003. In 1996–1998 he worked as a postdoctoral fellow with Prof. Klaus Müllen at Max-Planck-Institüt für Polymerforshung (Germany). In 2003 he moved to Hirosaki University as a professor. The research in his group focuses on the synthetic study on the functional materials by employing the novel \( \pi \)-electron systems.