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

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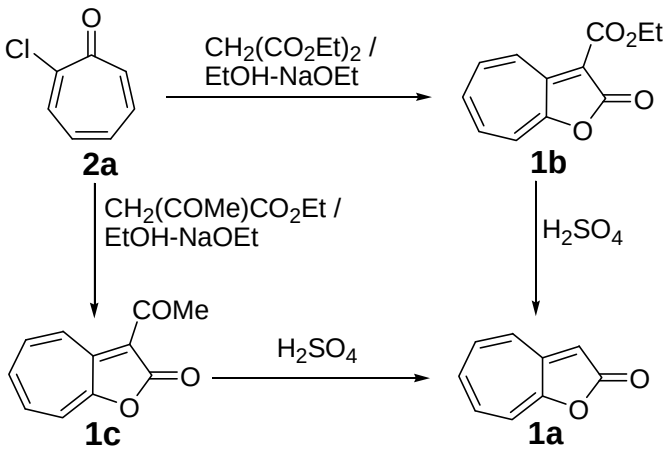
Abstract – Overview of data, obtained in the last 60 years, concerning the synthetic methodology for 2*H*-cyclohepta[*b*]furan-2-one, their reactivity and mechanistic aspects, the synthetic potential for the extended π-electronic systems, and their spectral properties, are described.

1. INTRODUCTION

The chemistry of *2H*-cyclohepta[*b*lfuran-2-one (**1a**) is important in connection with troponoid chemistry, fulvenoid chemistry and azulenoid chemistry. Since the first synthesis of *2H*-cyclohepta[*b*lfuran-2-ones by Nozoe and Seto was reported at 1953[1] during the investigation of reactivities in troponoid compounds, a lot of interesting discoveries about 2*H*-cyclohepta[*b*]furan-2-one have been reported. Therefore, we will described here about the synthetic methodology for 2*H*-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 2*H*-CYCLOHEPTA [*b*]FURAN-2-ONES

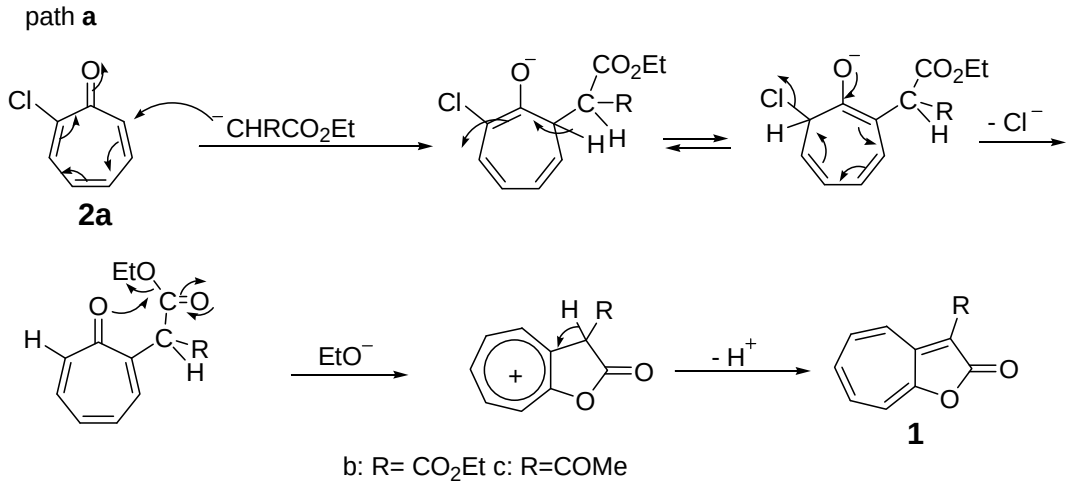


Scheme 1

Nozoe and Seto and their co-workers found the first synthetic way of 2*H*-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-2*H*-cyclohepta[*b*]furan-2-one (**1b**) and 3-aceyl-2*H*-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*lfuran-2-one (**1a**) itself by hydrolysis and decarboxylation or deacetylation with concentrated sulfuric acid.

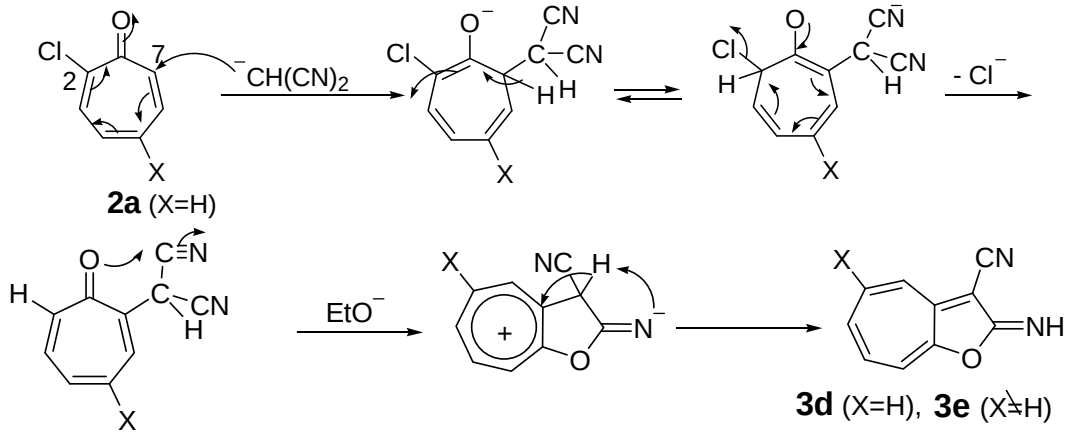
3. MECHANISTIC DETAILS IN REACTION OF TROPONOID WITH ACTIVE METHYLENE COMPOUNDS

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 2*H*-cyclohepta[*b*]furan-2-one (**1**).



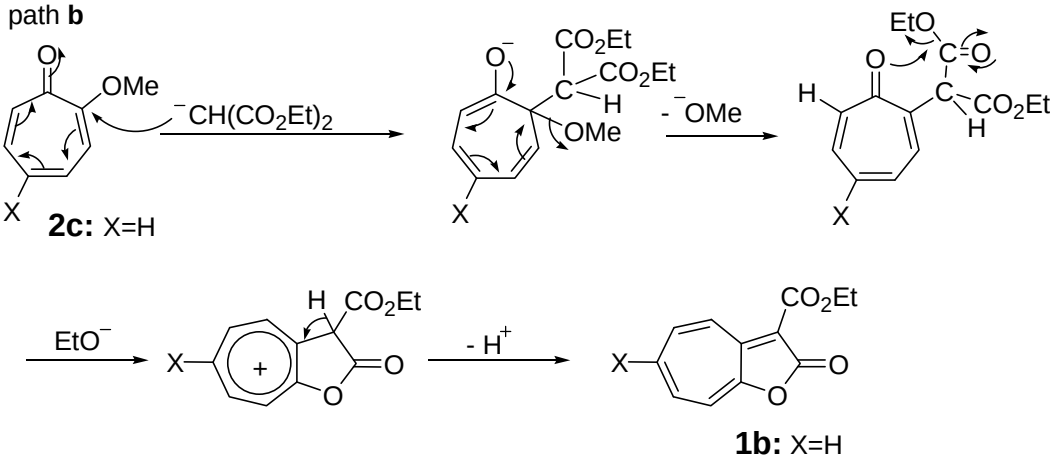
Scheme 2

However, when malononitrile was used as an active methylene reagent, 3-cyano-2*H*-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-2*H*-cyclohepta[*b*]furan-2-imine (**3e**) or the corresponding 2*H*-cyclohepta[*b*]furan-2-one is obtained.



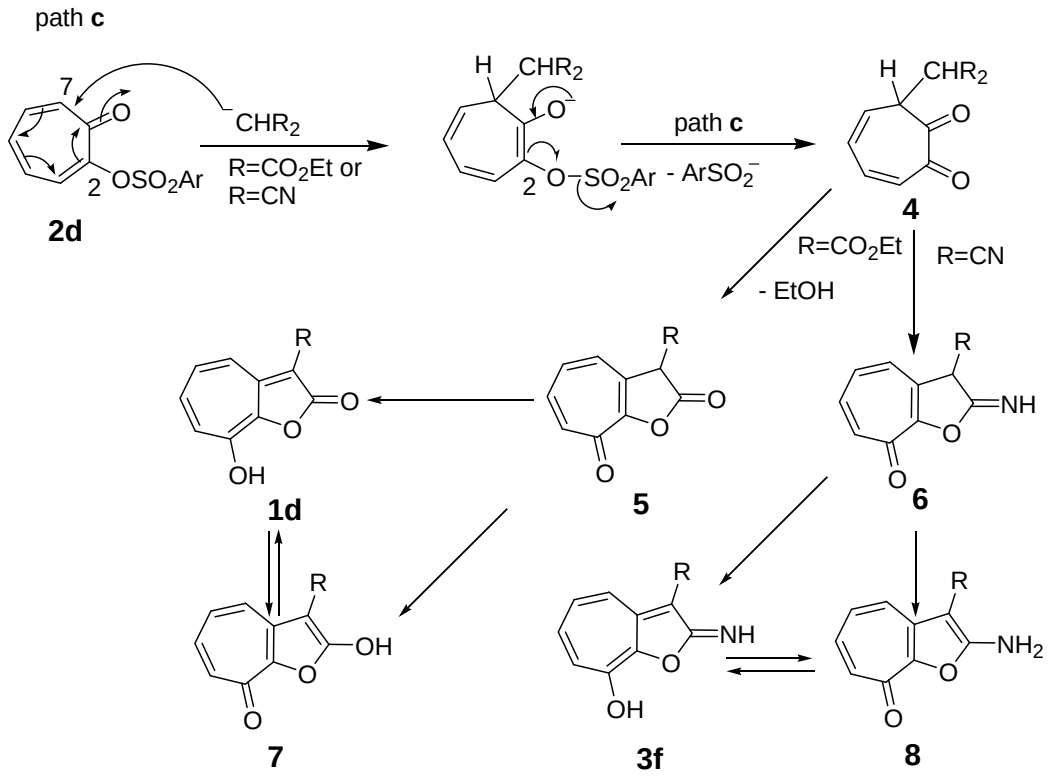
Scheme 3

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-2*H*-cyclohepta[*b*]furan-2-one as shown in Scheme 4 (path **b**).



Scheme 4

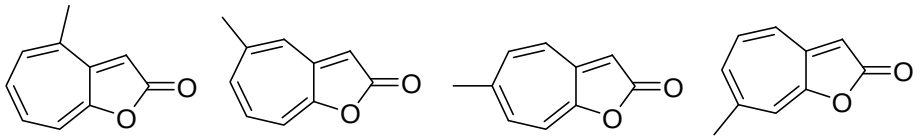
In case of 2-tosyloxytropone (**2d**),[2] the distribution of products are little complicated depend on the reaction conditions. Usually the reactions proceed as similar to those of 2-chloroptopone (path a). When sodium ethoxide is used as a base, the reaction of **2d** with diethyl malonate gives 8-hydroxy-2*H*-cyclohepta[*b*]furane-2-one (**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.



Scheme 5

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]

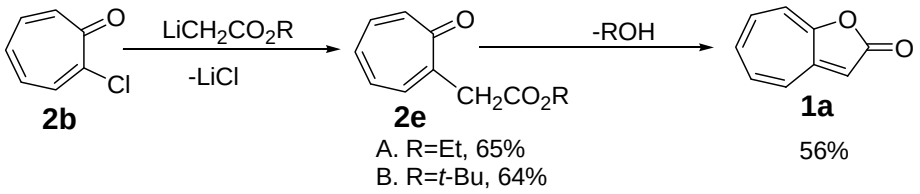


9 mp 117.5°C **10** mp 83.5°C **11** mp 115°C **12** mp 112°C

Figure 1

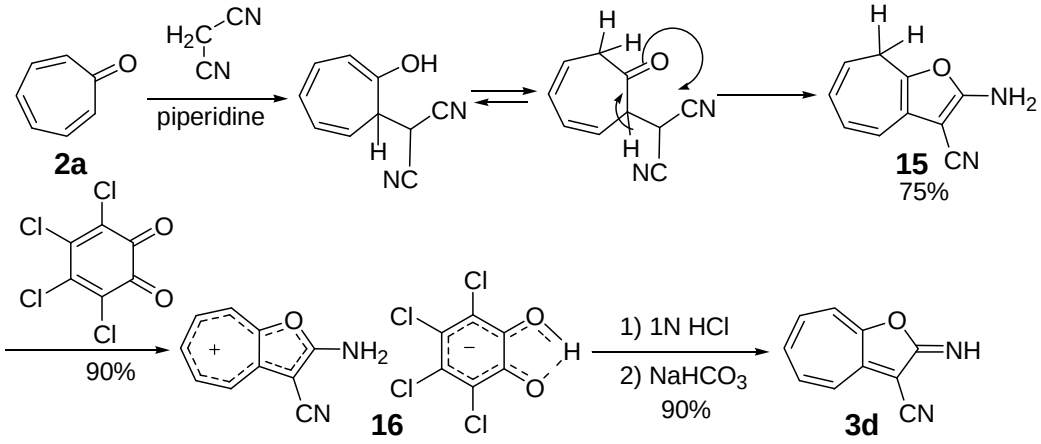
4. SYNTHETIC WAY FOR 2*H*-CYCLOHEPTA [*b*]FURAN-2-ONES BY NUCLEOPHILIC ATTACK

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]



Scheme 6

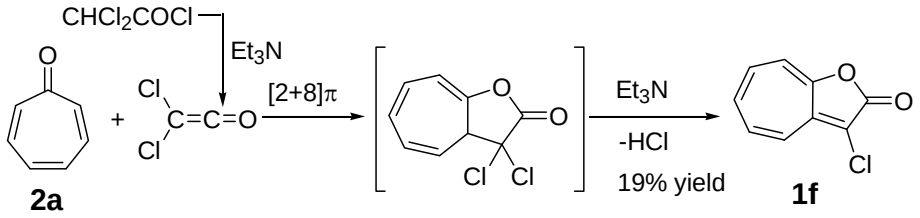
Tropone itself is also shown to be useful in the preparation of 3-cyano-2*H*-cyclohepta[*b*]furan-2-imine (**3d**). Tropone undergoes nucleophilic attack at 2-position by anion of malononitrile. The oxygen of tropone attack to carbon of nitrile and subsequent hydrogen shits to give 2-amino-3-cyano-8*H*-cyclohepta[*b*]furan (**15**). It undergoes dehydrogenation with tetrachloro-1,2-benzoquinone to give ionic complex (**16**). The complex **16** is hydrolyzed to give 3-cyano-2*H*-cyclohepta[*b*]furan-2-imine (**3d**) [orange crystals, mp 143 ºC (decomp.)].[5]



Scheme 7

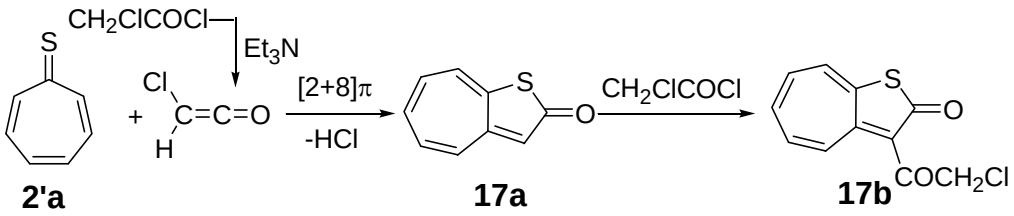
5. SYNTHETIC WAY FOR 2*H*-CYCLOHEPTA [*b*]FURAN-2-ONE AND 2*H*-CYCLOHEPTA-[*b*]THIOPHEN-2-ONE BY USING CYCLOADDITIONS OF SEVEN-MEMBERED RINGS

In 1967, Ciabattoni and Anderson reported the reaction of tropone with dichloroketene as follows.[6] Tropone reacts with dichloroketene which comes from the reaction of dichloroacetyl chloride with triethylamine to give a [2+8]π cycloadduct. But it cannot be isolated. It undergoes further elimination of hydrogen chloride with triethylamine to give 3-chloro-2*H*-cyclohepta[*b*]furan-2-one (**1f**) as yellow-orange needles of mp 179 – 180 °C. However, the yield was not so good (Scheme 8).



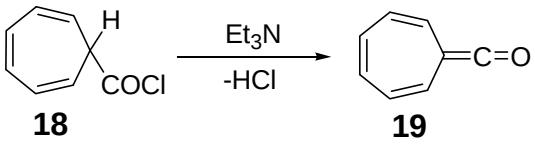
Scheme 8

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]π 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.



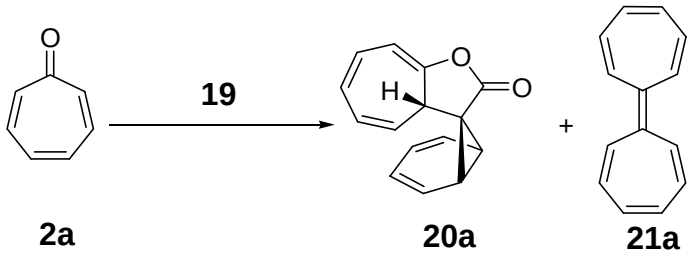
Scheme 9

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



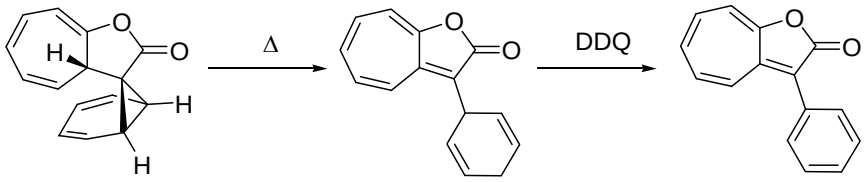
Scheme 10

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



Scheme 11

The [2+8]π 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]



20a **1g** **1h**

Scheme 12

Initially, we thought that the structure of thermal product was 1,3-cyclohexadiene derivative on the basis of 100 M Hz 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.[11] Both planes of 2*H*-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 2*H*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).

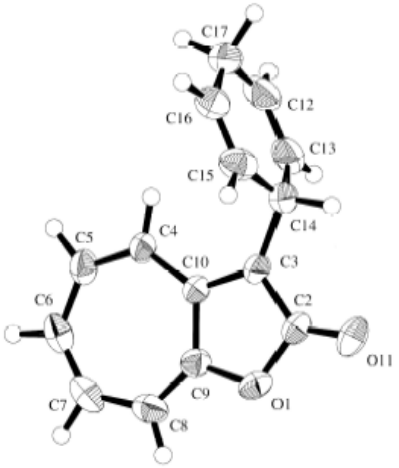
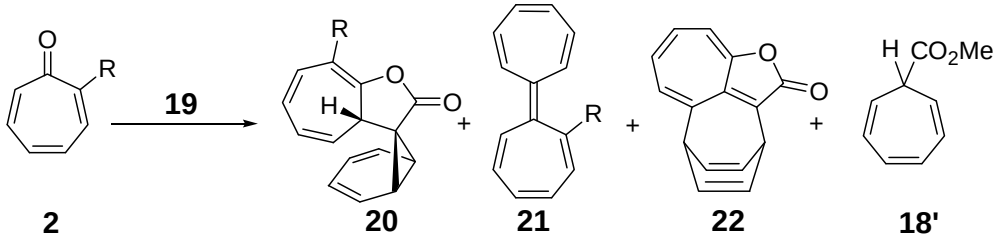


Figure 2

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.[12] 2-Methoxytropone reacts with 8-oxoheptafulvene to give 4 products (**18'**, **20** – **22**). The products **20c** and **21**c are similar to those of previous experiments. The other products are very different.

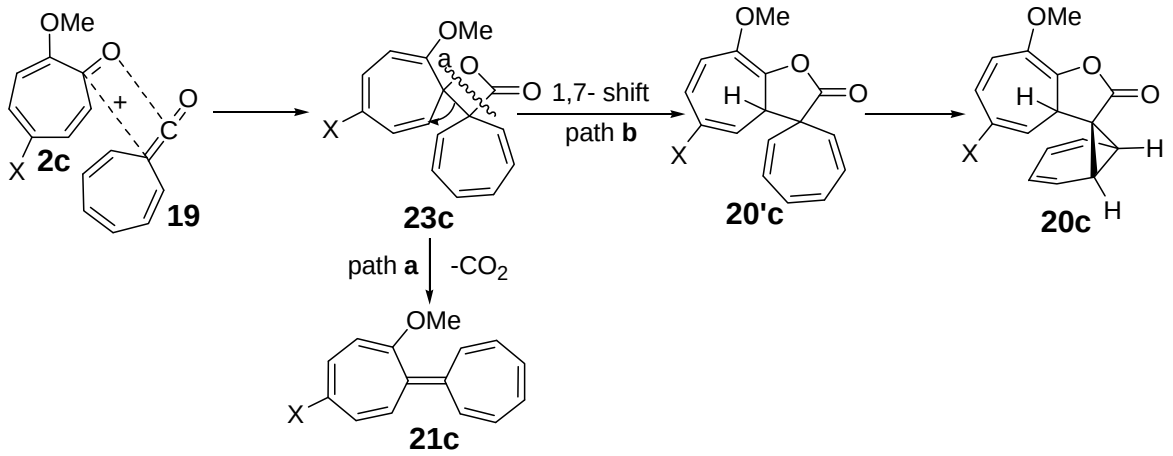


2 **20** **21** **22** **18'**

a: R=H	80 %	0.8%		
b: R=Cl	62.6%	2%		
c: R=OMe	12.3%	11.4%	28%	7%
f: R=Me	84.5%			

Scheme 13

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).



Scheme 14

Especially the structure and occurring mechanism of bridged 2*H*-cylohepta[*b*]furan-2-one **22** are very interesting. The structure of bridged 6-bromo-2*H*-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 2*H*-cylohepta[*b*]furan-2-one moiety which is flat.

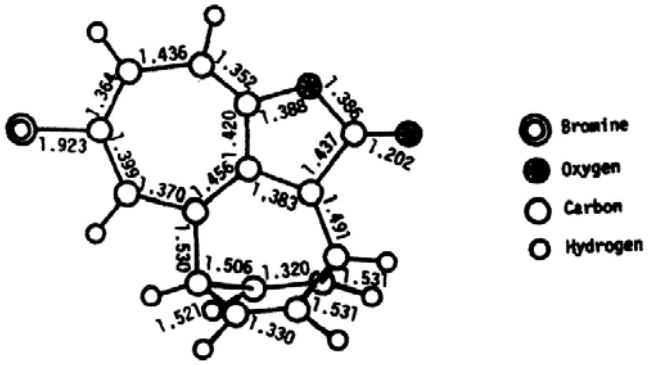
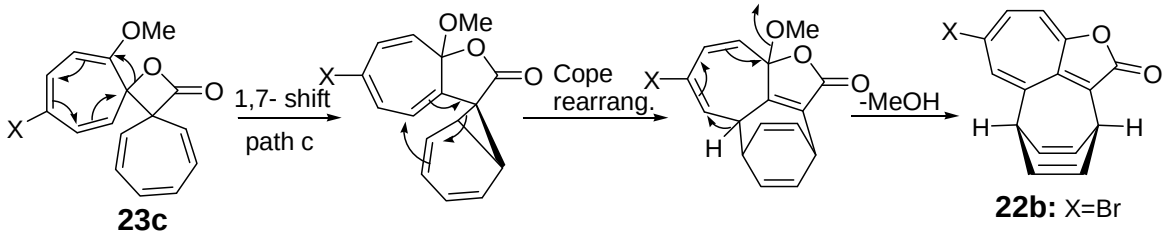


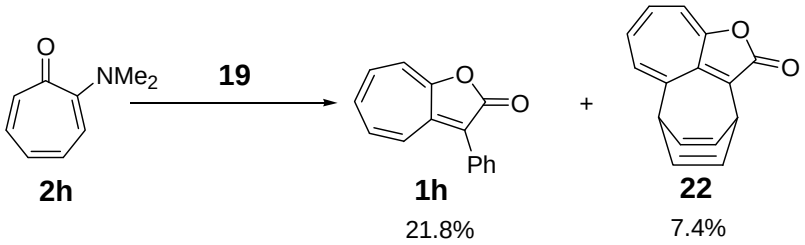
Figure 3 X-Ray structure of **22b**

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]



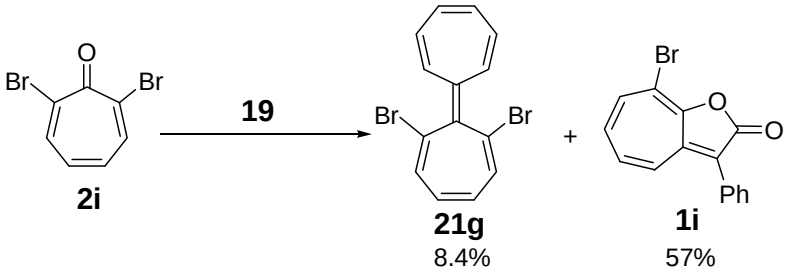
Scheme 15

Furthermore, the reaction of 2-*N*,*N*-dimethyaminotropone (**2h**) with 8-oxoheptafulven also gives bridged 2*H*-cyclohepta[*b*]furan-2-one as a minor product. The main product is 3-phenyl-2*H*-cyclohepta[*b*]furan-2-one (**1h**) although the yield is low.[14]

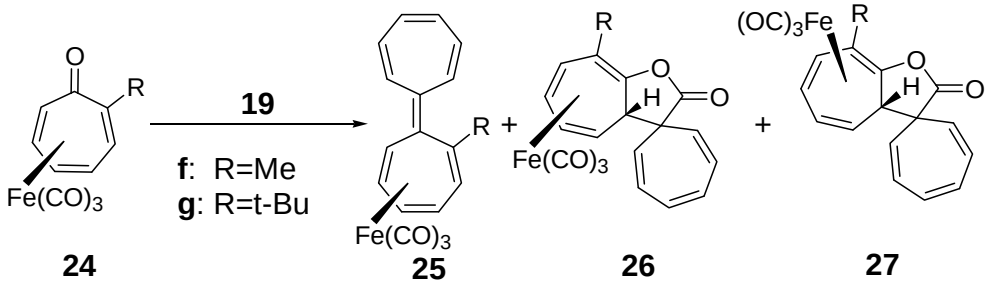


Scheme 16

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



Scheme 17

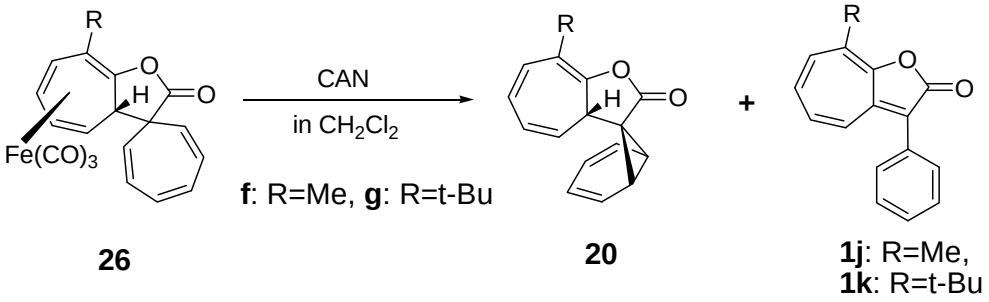


Scheme 18

TroponeFe(CO)$_3$ **24a** (R=H) can be easily prepared by the reaction of tropone with ironcarbonyl reagents such as $Fe_2(CO)_9$, $Fe_3(CO)_{12}$, $Fe(CO)_5$, benzalacetoneFe(CO)$_3$, etc.[15] TroponeFe(CO)$_3$ itself reacts with

8-oxoheptafulvene to give heptafulvaleneFe(CO)$_3$ as a single product.[15g] 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-2*H*-cyclohepta[*b*]furan-2-one (**1j)** in 11% yield. In the case of **26g**, norcaradiene

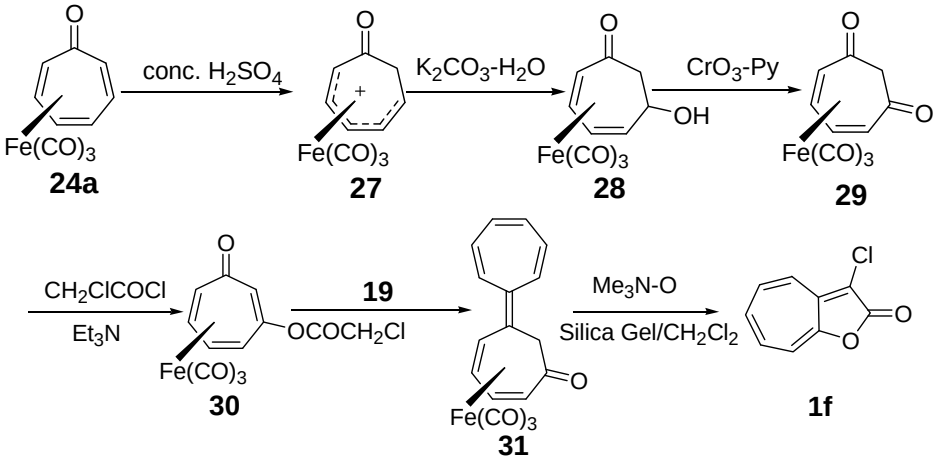


26 **20**

Scheme 19

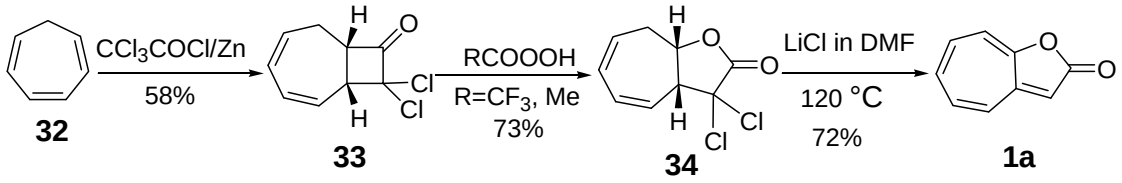
derivative **20g** and 8-*t*-butyl-3-phenyl-2*H*-cyclohepta[*b*]furan-2-one (**1k)** in 63% and, 36% yields, respectively.[17]

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 $Fe_2(CO)_9$. 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-cyloheptadiene-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-2*H*-cyclohepta[*b*]furan-2-one (**1f**) (about 30% yield).[20]



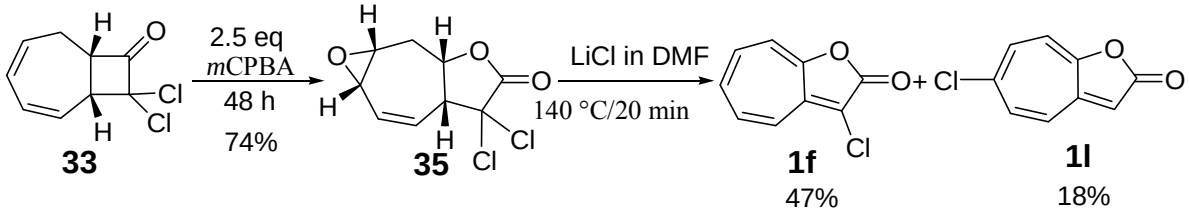
Scheme 20

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



Scheme 21

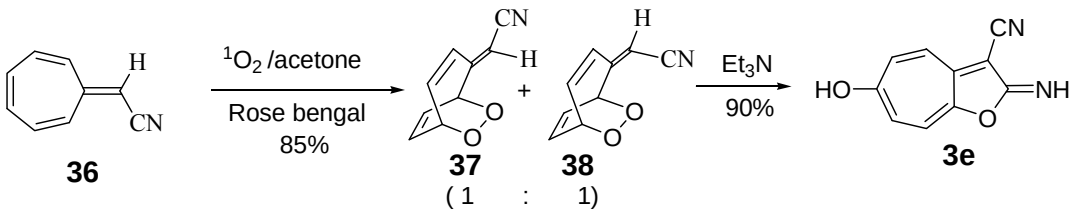
The γ-lactone **34** undergoes epoxidation with *m*-CPBA to give **35** which was directly obtained from [2+2]π cycloadduct **33** by oxidation with *m*-CPBA. The epoxide **35** is treated with LiCl at 140 °C to give a mixture of 3-chloro-2*H*-cyclohepta[*b*]furan-2one (**1f**) and 6-chloro-2*H*-cyclohepta[*b*]furan-2one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



Scheme 22

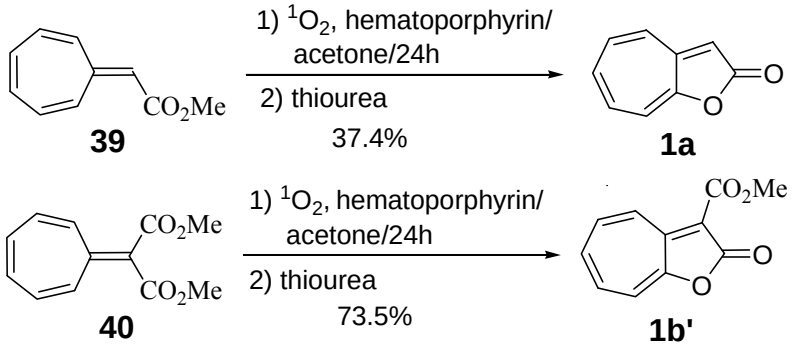
6. SYNTHETIC WAY FOR 2*H*-CYCLOHEPTA [*b*]FURAN-2-ONE FROM HEPTAFULVENE AND CYCLOHEPTATRIENES BY PHOTO-OXYGENATION

Next method for preparation of 2*H*-cyclohepta[*b*]furan-2-ones is photo-sensitized oxygenation of heptafulvenes or cycloheptatrienes.[21] 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 epidioxiede **37** and **38** in 85% yield as colorless crystals which detonates at 106 ºC in a capillary tube. These epidioxides are treated with triethylamine to give 6-hydroxy-3-cyano-2*H*-cyclohepta[*b*]furan-2-imine (**3e**) in 90% yield.



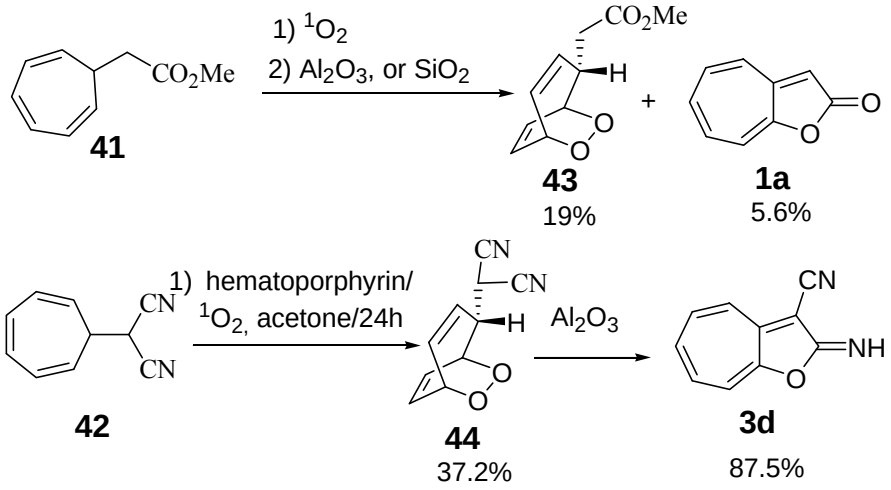
Scheme 23

This reaction is applicable to 8-methoxycarbonylheptafulvene (**39**) and 8,8-dimethoxycarbonylheptafulvene (**40**) to give corresponding 2*H*-cyclohepta[*b*]furan-2-one **1a** and **1b'**. Epidioxide is converted to 2*H*-cyclohepta[*b*]furan-2-one derivatives without hydroxyl group at C-6 using thiourea instead of trietylamine.



Scheme 24

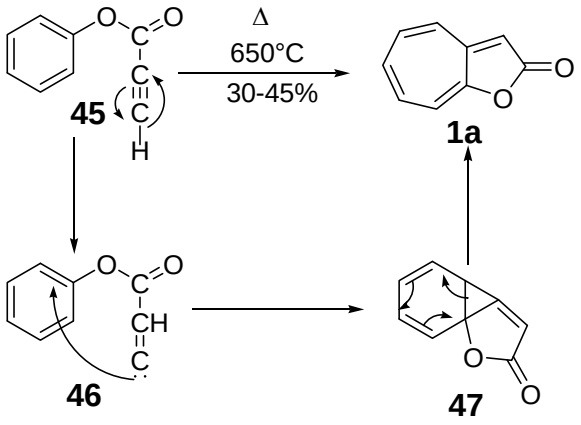
These photo-sensitized reactions are utilized to the synthesis of **1a** and **3d** from cycloheptatriene derivatives **41** and **42** as shown in Scheme 25.



Scheme 25

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

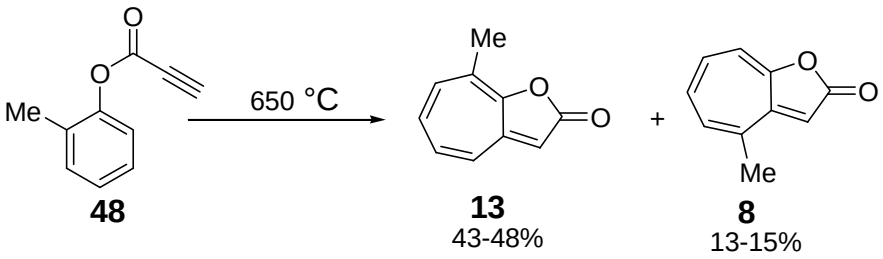
Trahanovsky has found general synthetic way for 2*H*-cyclohepta[*b*]furan-2-ones by the flash vacuum pyrolysis (FVP) of phenyl propargyl ethers at 650 °C and ~10^{-4} Torr.[22a] This method is applicable for methyl substituted phenyl propargyl ethers. On the basis of methyl groups position of starting phenylpropiolate and product 2*H*-cyclohepta[*b*]furan-2-ones the FVP mechanism is shown in Scheme 26.



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 2*H*-cyclohepta[*b*]furan-2-one.[22d]

By this FVP method, 8-methyl-2*H*-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-2*H*-cyclohepta[*b*]furan-2-one (13 – 15%). The isomeric lactones are separated by column chromatography.



Scheme 27

4,8-Dimethyl-2*H*-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-2*H*-cyclohepta[*b*]furan-2-one (**50**) by the FVP.

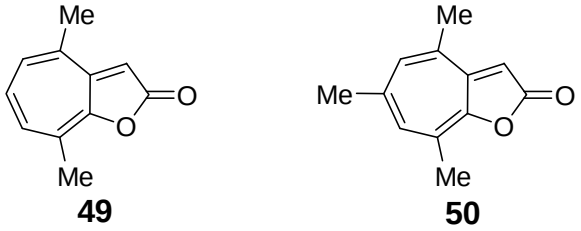
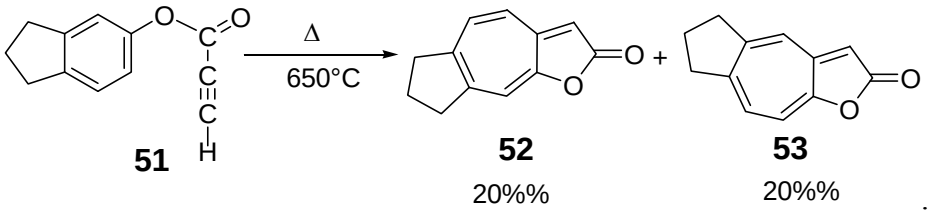


Figure 4

Indane derivative also underwent pylolysis to give a mixture of 2*H*-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.



Scheme 28

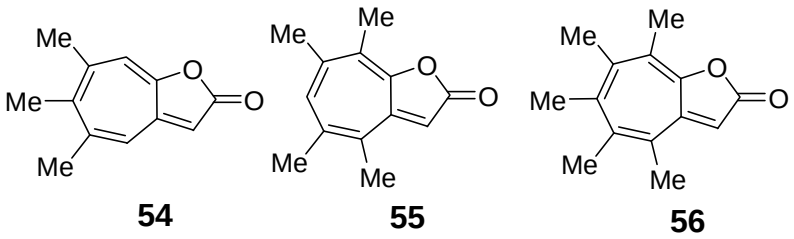
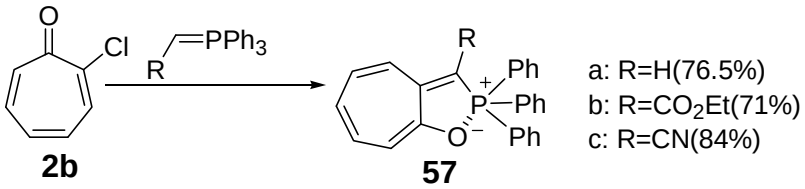


Figure 5

More polymethylated 2*H*-cyclohepta[*b*]furan-2ones (**54** – **56**) have also been prepared from corresponding polymethyl phenylpropiolate by dynamic gas phase thermo-isomerization. 4,5,6,7,8-Pentamethyl-2*H*-cyclohepta[*b*]furan-2-one reveals a slight deviation from planarity on the basis of X-ray analysis and calculation.[22b-d]

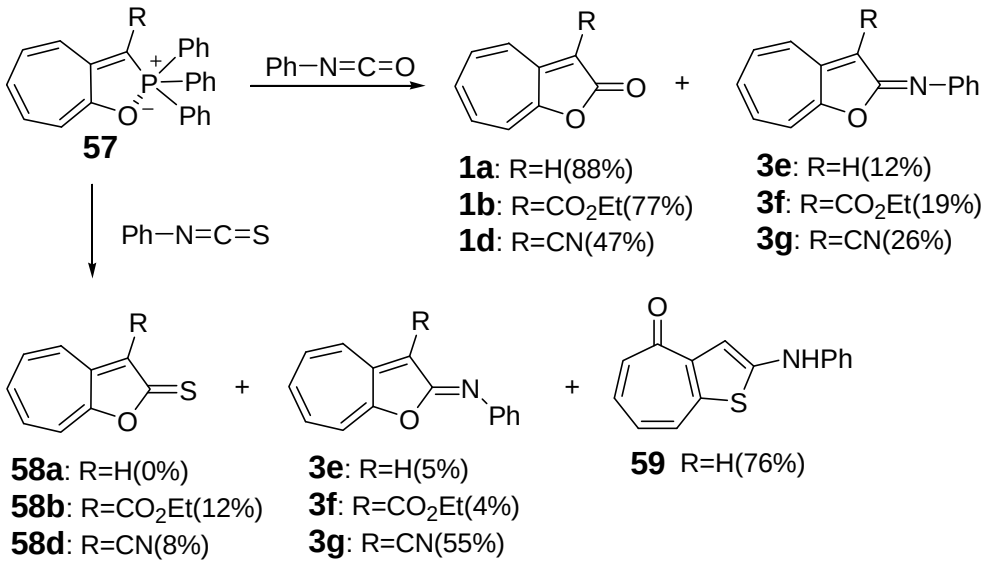
8. SYNTHETIC WAY FOR 2*H*-CYCLOHEPTA[*b*]FURAN-2-ONE BY WAY OF CYCLOHEPTAOXAPHOSPHOLE

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]



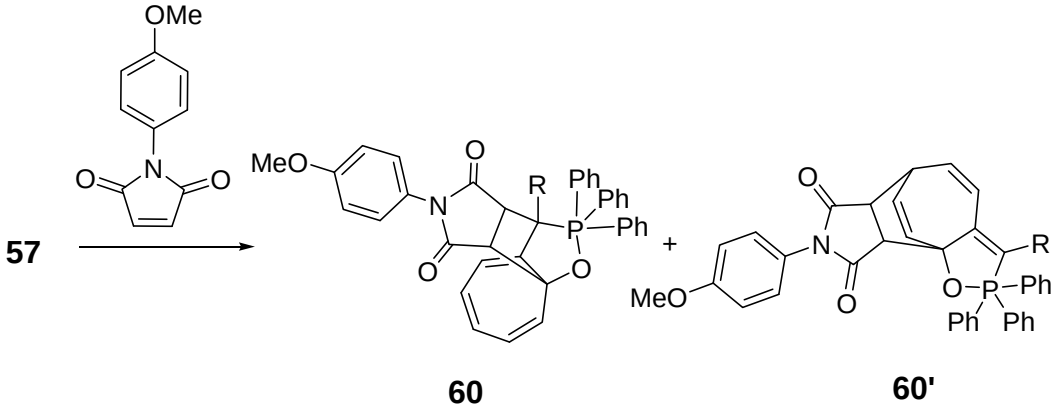
Scheme 29

In the reaction with phenyl isocyanate the cycloheptaoxaphospholes act as an ylide to give corresponding 2*H*-cyclohepta[*b*]furan-2-ones (**1a, 1b,** and **1d**) and 2*H*-cyclohepta[*b*]furan-2-imines (**3e, 3f,** and **3g**) accompanied by the liberation of triphenylphosphine *N*-phenylimine and triphenylphosphinre 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**.



Scheme 30

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 cycloadduct (**60'**) similar to 2*H*-cyclohepta[*b*]furan-2-one.

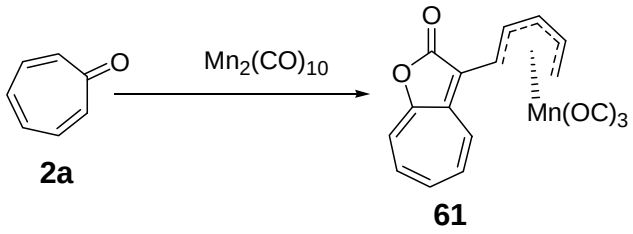


Scheme 31

9. ORGANOMETALLIC COMPOUNDS RELATE TO 2*H*-CYCLOHEPTA [*b*]FURAN-2-ONE

There is not an organometallic compound in which 2*H*-cyclohepta[*b*]furan-2-one moiety coordinates to metal until now. But two unique organometalic 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)η^5-pentadienylmanganese as a main product.[24]



Scheme 32

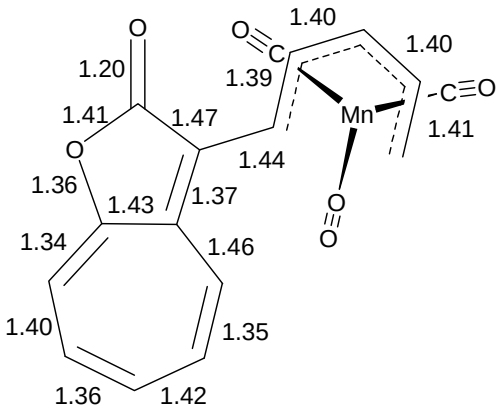
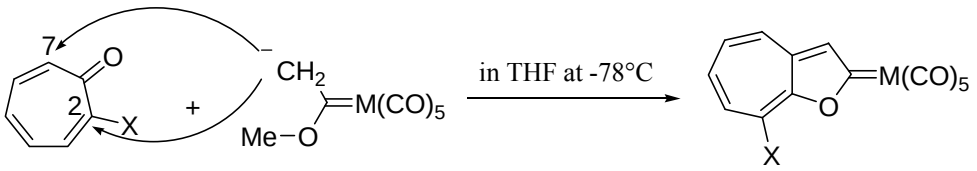


Figure 6

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 2*H*-cyclohepta[*b*]furan-2-one portion exhibits characteristic bond alternation although bond lengths of dienyl porttion is almost same.[24]

The other example is a compound which is replaced carbonyl group of 2*H*-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,[25] although their yields are very low as shown in Scheme 32.



2a: X=H
2b: X=Cl
2c: X=OMe

62: M=Cr
63 M=W

64a: M=Cr, X=H (8%) mp 152°C (d)
65a: M=W, X=H (3%) mp 184°C (d)
64b: M=Cr, X=Cl (1%) 181°C (d)
65b: M=W, X=Cl (2%)mp 201°C(d)
64c: M=Cr, X=OMe (5%) mp 178°C (d)
65c: M=W. X=OMe (1%) mp 197°C (d)

Scheme 33

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 2*H*-cyclohepta[*b*]furan-2-one.

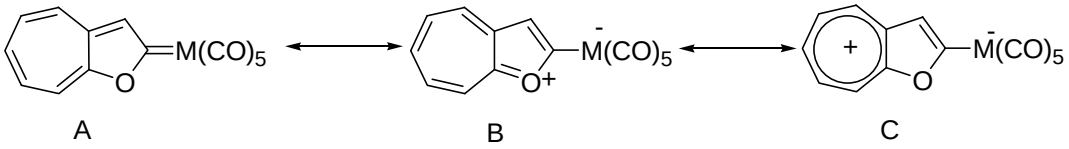
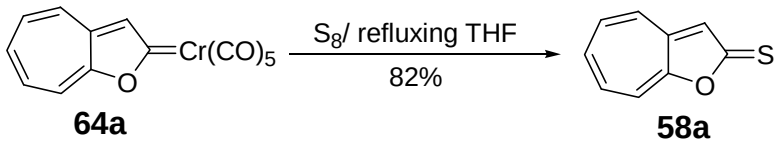


Figure 7



Scheme 34

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 ºC) 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.

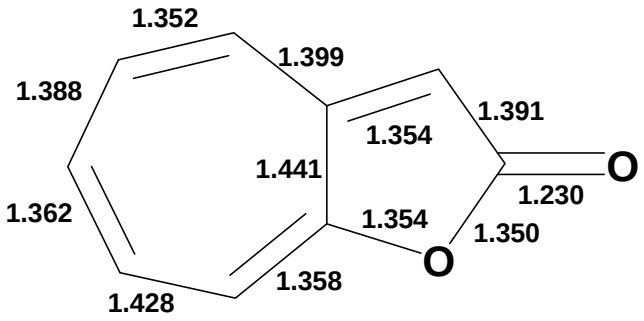


Figure 8

It is recognized clearly that a larger and a shorter C-C bonds are disposed alternately. The mean values for the lager 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.

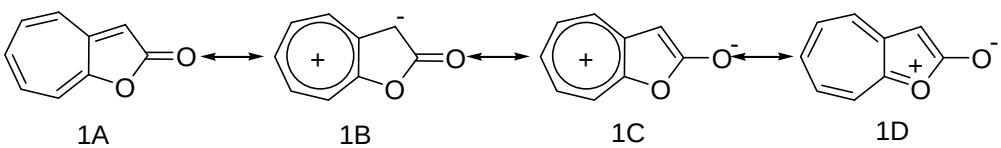


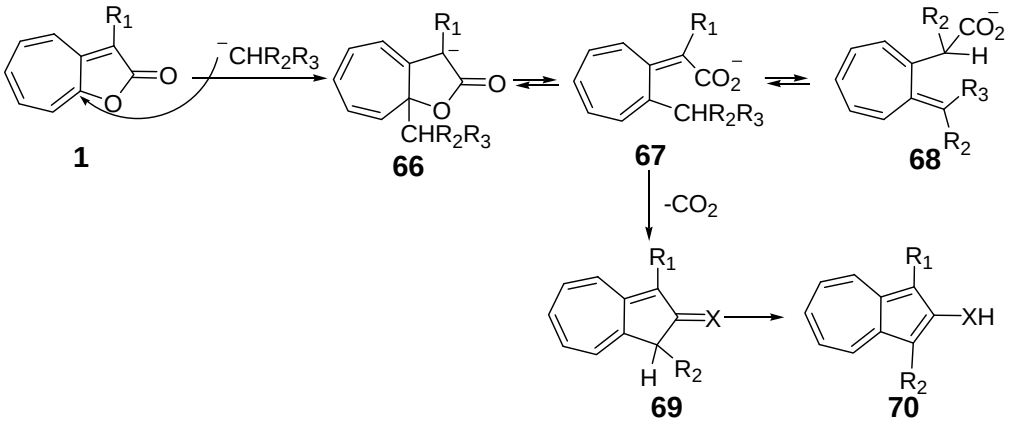
Figure 9

Considering the resonance structures given above, it seems that the seven-membered ring itself is somewhat positively charged. 2*H*-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.[27]

The most intense bands for carbonyl region in the IR spectrum (KBr) appears at1748 cm^{-1}. Absorptions of the longest wave length (MeOH) appear at 427 nm (sh, ε = 1980), 453 nm (sh, 780), and 488 nm (sh, 190), assigned as n→π* transition. The peaks at 373 nm (14660) and 387 nm (14700) are assigned as π→π* (2). The peaks at 223 nm (14350) and 251 nm (23150) are assigned as π→π* (1).[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 ($CDCl_3$) can be assigned completely as follows. 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 (ddt, J=10.8, 8.6, 1.1 Hz, H-6), 5.75 (d, *J*=1.3 Hz, H-3),[13]C NMR ($CDCl_3$), 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).[22b] Thease data are very useful when we will investigate the substitution effects for new 2*H*-cyclohepta[*b*]furan-2-one derivatives.

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

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

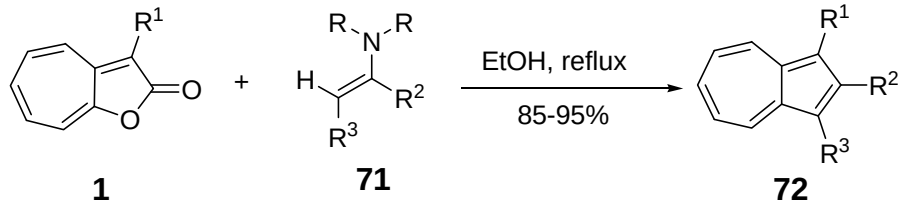


Scheme 35

The carbanions, R_2-$^{-}$CH-R_3, being produced from malononitrile, cyanoacetamide, ethyl cyanoacetate or diethylmalonate, attack 2*H*-cyclohepta[*b*]furan-2-ones 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 2*H*-cyclohepta[*b*]furan-2-ones bearing the substituent at the seven-membered ring.

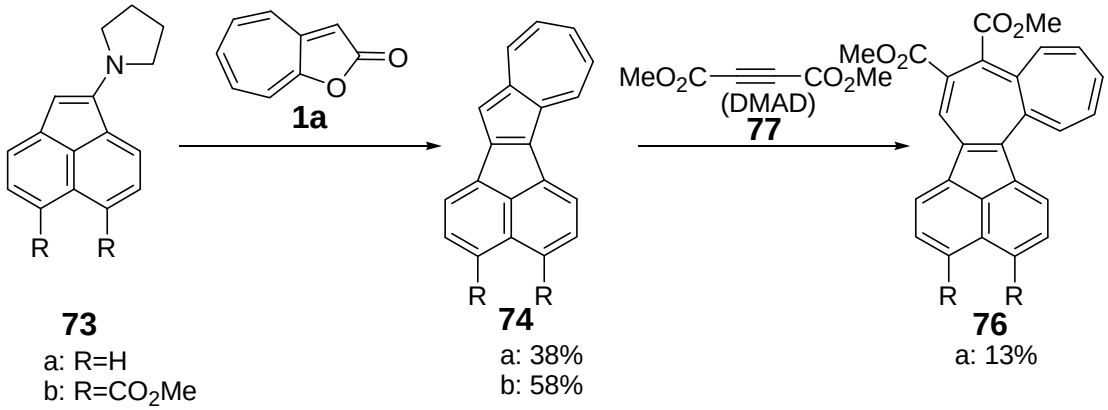
12. REACTION OF 2*H*-CYCLOHEPTA[*b*]FULAN-2-ONE WITH ENAMINES, ETHERS, OTHER ALKENE, AND ALKYNE

Yasunami and Takase found 2*H*-cycylohepta[*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]



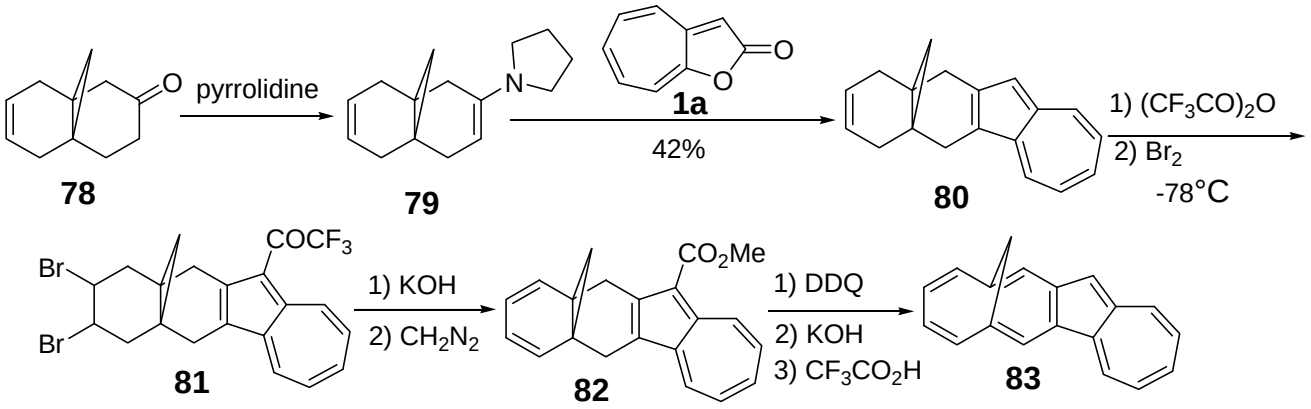
Scheme 36

As there is the review of this reaction in1981 by Yasunami,[30] the preparation of new azulenes condenced 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-*a*]acenaphthylene **74a** or **74b**. Compound **74a** reacts further with dimethyl acetylenedicarboxylate (**77b**) to give dimethyl acenaphthyleno[1,2-*d*]heptalene-8,9-dicarboxylate (**76**).[31]



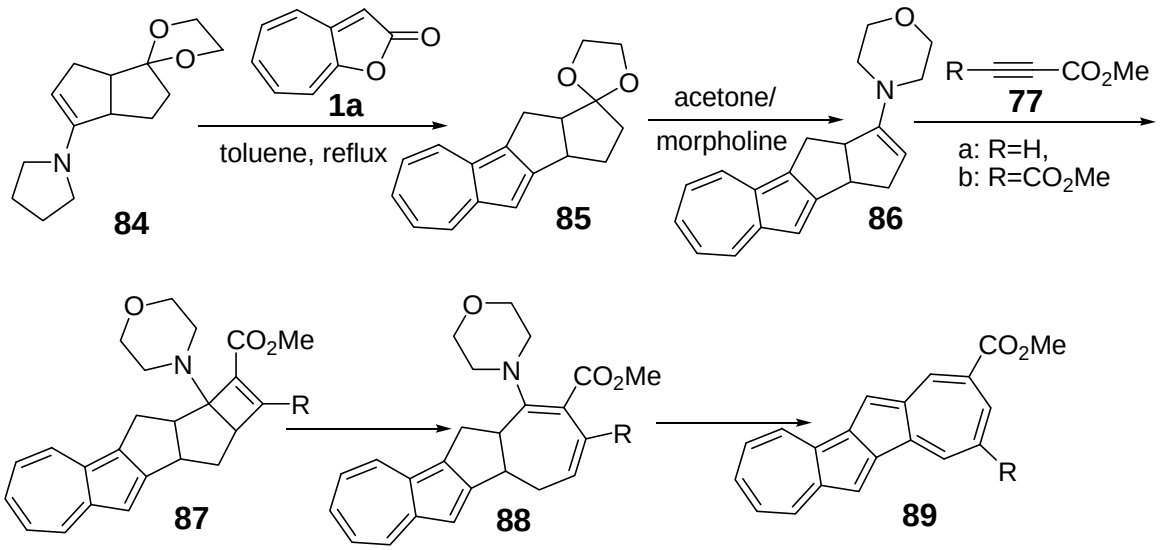
Scheme 37

The compound **80** is prepared by the reaction of 2*H*-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 CF_3CO_2H gave 2,7-methanocyclodeca[*a*]azulene (**83**). The NMR spectrum of 2,7-methanocyclodeca[*a*]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.



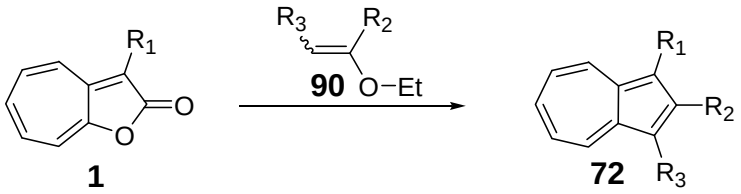
Scheme 38

The cata condenced nonalternant hydrocarbon of new azulenazulenes **89a** and **89b** have been synthesized by combination of the reaction of 2*H*-cycylohepta[*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]



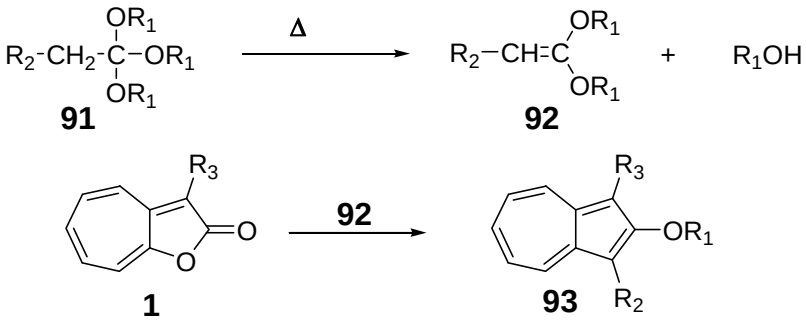
Scheme 39

Nozoe, Wakabayashi and co-workers found that 2*H*-cyclohepta[*b*]furan-2-one reacts with enol ethers instead of enamines to give corresponding azulens by [2+8]π cycloaddition and followed by decarboxylation and elimination of alcohol. Sometimes, during this reaction, [2+4]π cycloaddition as a side reaction is observed. This experiments carried out as follows, a mixture of 2*H*-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]



Scheme 40

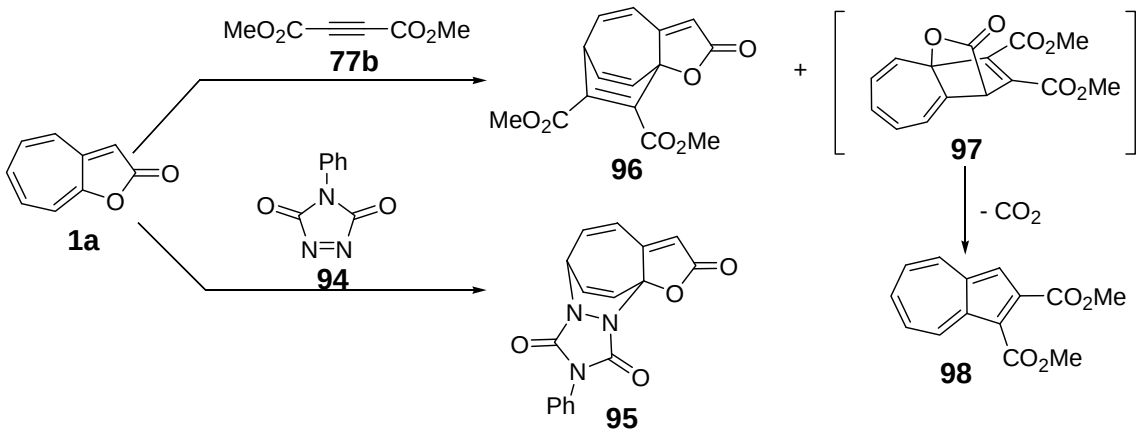
Instead of enolethers, trialkyl orthoformates can be applicable for preparation of 2-alkyloxyazulenes **93**, because it can be converted to ketene acetal **92** by heating. The ketene acetal **92** react with 1 to give 2-alchoxyazulene **93** (Scheme 41).



Scheme 41

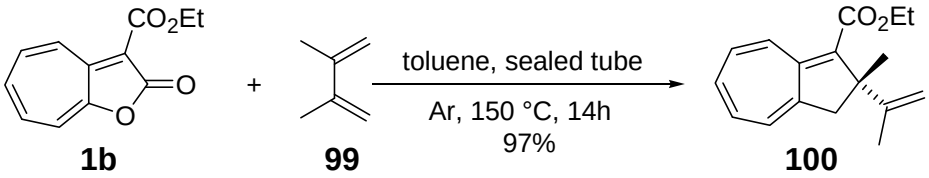
2*H*-Cycylohepta[*b*]furan-2-one reacts with electron deficient olefins such as 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) and dimethyl acetylenedicarboxylate (DMAD) to give a [4+2]π cycloadduct and /or a [8+2]π cycloadduct.

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



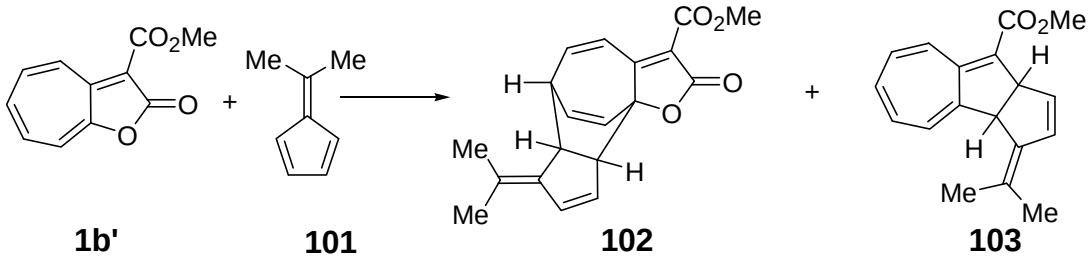
Scheme 42

1,3-Butadiene derivatives which are nonpolar olefins react with 2*H*-cycylohepta[*b*]furan-2-one under similar reaction condition to enamines to give heptafulvene (or dihydroazulene) derivatives in good yields.[36]



Schem 43

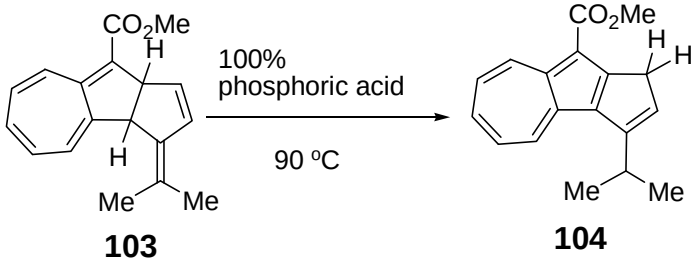
Methyl 2*H*-cylohepta[*b*]furan-2-one-3-carboxylate reacts with 6,6-dimethylfulvene by [4+2]π cycloaddition in ethanol refluxed preferably. In refluxing xylene, product **103** is obtained as a sole product. It is produced by [8+2]π cycloaddition and decarboxylation. The adduct **102** is heating to give a mixture of retro Diels-Alder reaction product **1b'** and **101** along with **103**.[37]



Scheme 44

Solvent (reflux)	Reaction time (h)	Product **102**	Yield (%) **103**	**1b'**
xylene	25.5	-	35.0	-
benzene	24.0	28.0	21.0	38.0
ethanol	27.0	44.1	16.5	35.8

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



Scheme 45

Coefficients and energy levels of molecular orbitals (NHOMO, HOMO, LUMO, and NLUMO) of 2*H*-cyclohepta[*b*]furan-2-one are as follows (Figure 10). The periselectivity of [2+8]π and [2+4]π cycloadditions is discussed on the basis of these data.[22c, 37a, 38, 39]

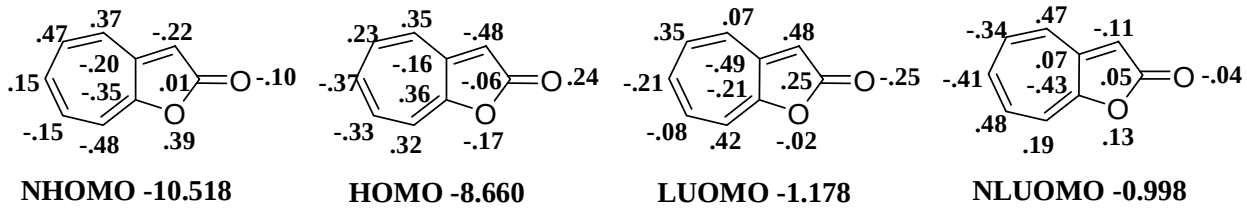
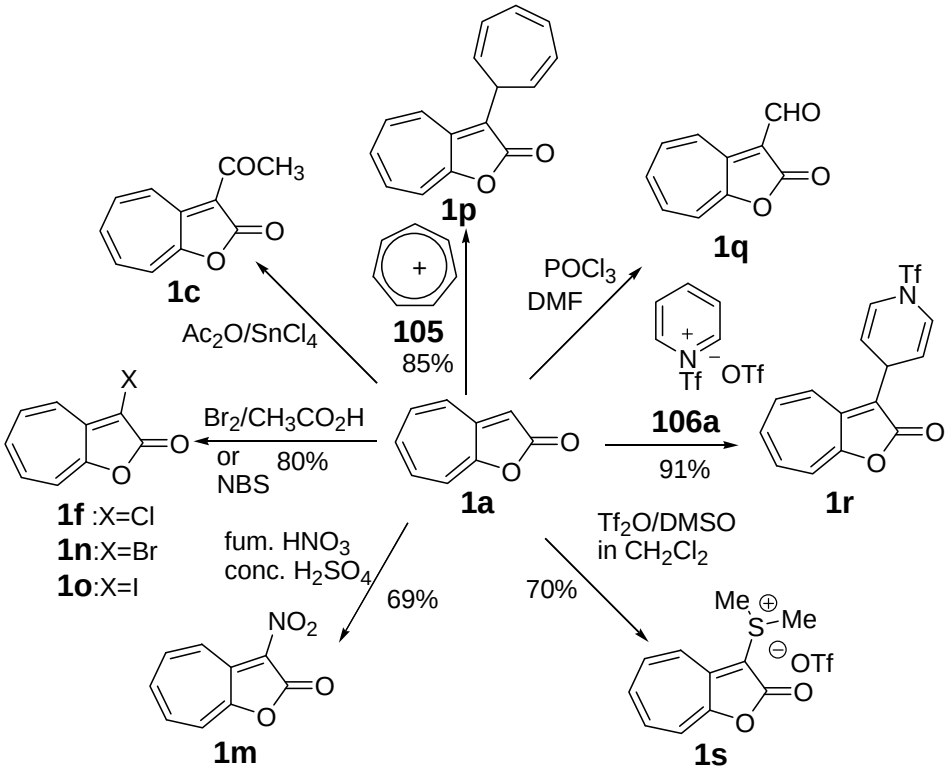


Figure 10

13. ELECTROPHILIC SUBSTITUTION OF 2*H*-CYCLOHEPTA[*b*]FURAN-2-ONE

Because 2*H*-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.

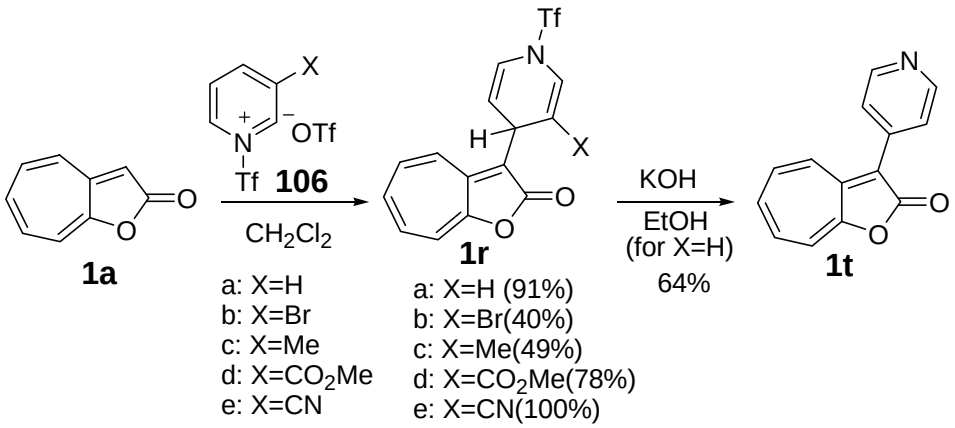


Scheme 46

Thease reactions occur at 3-position of **1a** regiospecifically, in good yields.[1d, 40] After them, Nozoe and co-worker have investigated the reaction of tropyl ethers with various 1-oxaazulan-2-one to give corresponding 3-tropyl-2*H*-cyclohepta[*b*]furan-2-ones.[41a] 3-Formyl-2*H*-cyclohepta[*b*]furan-2-one is obtained in 63% yield by Vilsmeier reaction of **1a**.[41b]

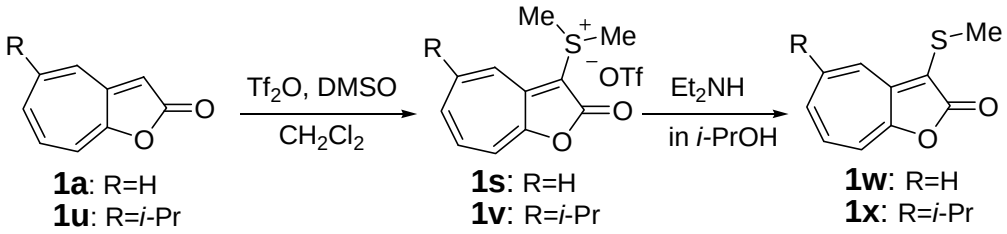
It is well known[42] that pyridine react with tifluoromethanesulfonic anhydride to give 1-trifluoromethanesulfonylpyridinium trifluoromethanesulfonate (TPT) which is used as a reagent for trifuloromethanesulfonation of hydroxyl group such as phenol. Recently we found this reagent acts as an electrophile in the reaction of azulene to give 1-(*N*-trifuluoromethanesulfonyl-dihydropyridyl)azulene. It

is easily remove trifluoromethanesulfinic acid by potassium hydroxide to give 1-pyridyl-azulene. This reaction is applicable for 2*H*-cyclohepta[*b*]furan-2-one to give 3-(4-pyridyl)-2*H*-cyclohepta[*b*]furan-2-one.[43]



Scheme 47

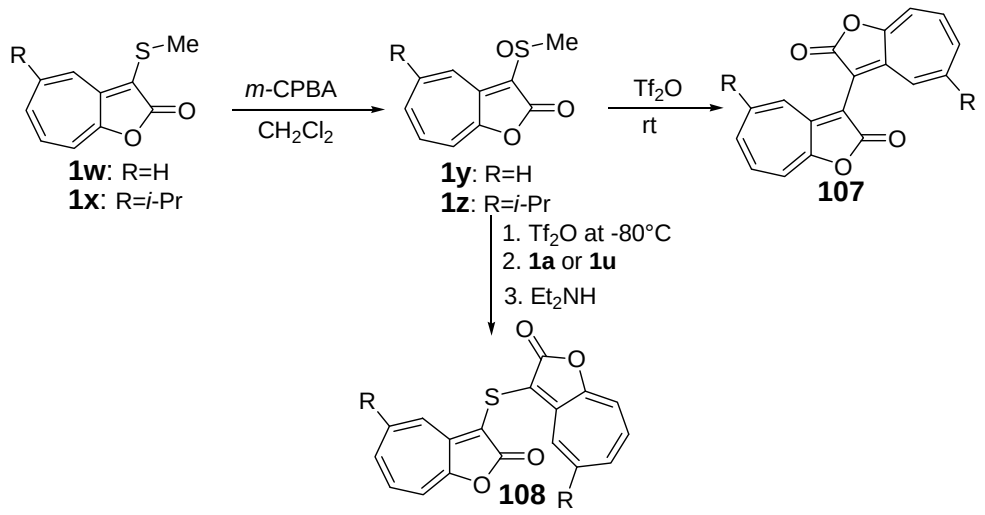
The reaction of triflic anhydride with dimethylsulfoxide leads to formation of dimethyl (trifluoromethanesulfonyloxy)sulfonium trifluoromethanesulfonate, "dimethyl sulfide ditriflate" (DMSD). It is also a good electrophile for benzenoid compound to give aryldimethylsulfonium trifluoeomethanesulfonate.[44]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



Scheme 48

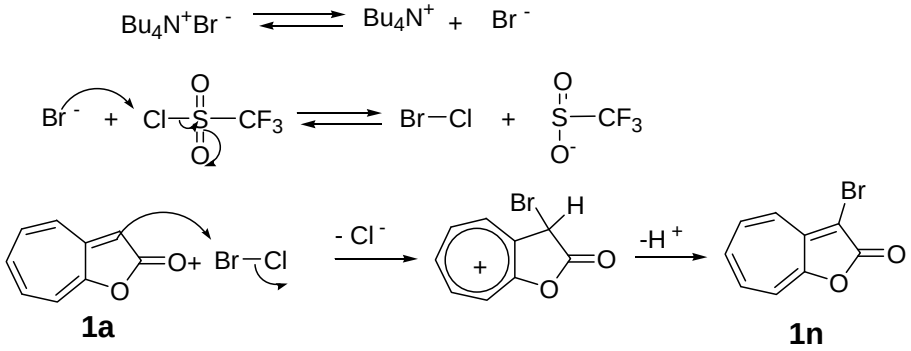
These methylthio derivatives **1w** and **1x** are oxidized with *m*-CPBA to give 3-methylsulfinyl-2*H*-cyclohepta[*b*]furan-2-one (**1y**) and isopropyl derivative **1z**.

3-Methylsulfinyl-2*H*-cyclohepta[*b*]furane-2-one (**1y**) is heated at ca. 40 ºC to give 3,3'-bi(2-oxo-2*H*-cyclohepta[*b*]furanyl) (**107**). Its reaction is carried out -80 C to give bis(2-oxo-2*H*-cyclohepta[*b*]furan-3-yl)sulfide (**108**).



Scheme 49

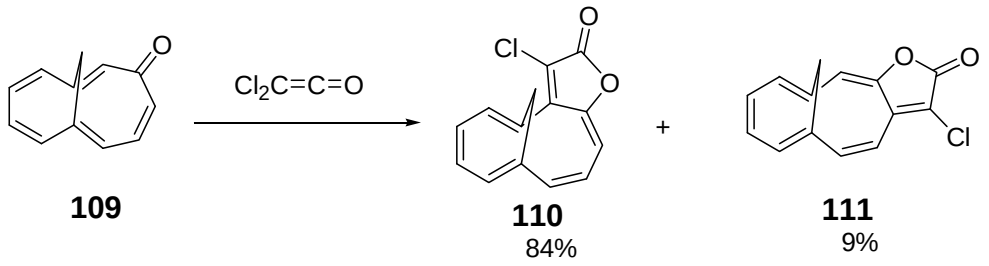
Recently, we reported 2-hydroxyazulene reacts with trifluoromethanesulphonyl chloride in the presence of pyridine to give 1,3-dichloro-2-hydroxyazulene.[46a] On the basis of this observation, we found new haloganation with trifluoromethanesulphonyl chloride and halogenide ion. For example, azulene reacts with tetrabuthylammmonium bromide and trifluoromethanesulphonyl chloride to give 1-bromoazulene and/or 1,3-dibromoazulene. Under similar conditions, 2*H*-cyclohepta[*b*]furan-2-one gives 3-bromo-2*H*-cyclohepta[*b*]furan-2-one (**1n**) (Scheme 50). By the combination of trifluoromethanesulphonyl chloride and potassium iodide, 3-iodo-2*H*-cyclohepta[*b*]furan-2-ones (**1o**) is obtained in 88% yield. 2*H*-Cyclohepta[*b*]furan-2-one also undergoes halogenations with halosuccinimide.[46b]



Scheme 50

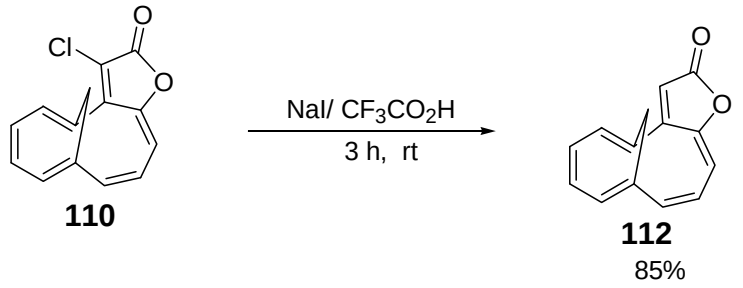
14. CYCLOADDITIONS OF METHANO[11]ANNULENONES WITH DICHLORO- AND CHLOROKETENES. PREPARATION OF 2*H*-METHANOCYCLOUNDECA[*b*]FURAN-2-ONE RING SYSTEMS

There are a few 2*H*-cyclohepta[*b*]furan-2-one analogues. One of them is 2*H*-methanocycloundeca[*b*]furan-2-one. It is prepared from methano[11]annulenones by Nitta and co-workers.[47] Methano[11]annulenones reacted with dichloroketene by [2+2]π cycloaddition and subsequent elimination of hydrogen chloride to give two products **110** and **111**.

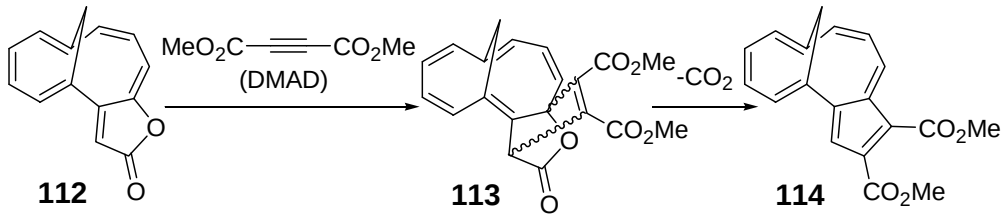


Scheme 51

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



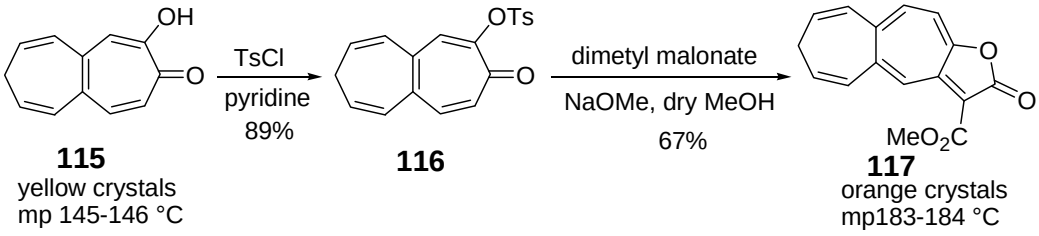
Scheme 52



Scheme 53

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

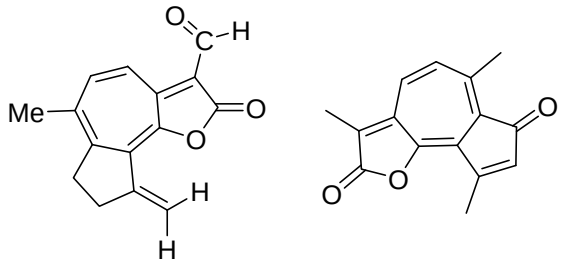
8*H*-Cyclohepta[*c*]tropolone (**115**) which is prepared from azulene[48] reacts with tosyl chloride and dimethyl malonate in the presence of sodium methoxide by Nozoe's method (70%), to give 8*H*-heptaleno[*b*]furan-2-one (**117**) as orange crystals.[49] This derivative will have potentiality as a synthetic key intermediate for a lot of compounds containing 2*H*-cyclohepta[*b*]furan-2-one skeleton.



Scheme 54

15. THE ROLE OF 2*H*-CYCLOHEPTA[*b*]FURAN-2-ONE IN THE CHEMISTRY OF NATURAL PRODUCTS

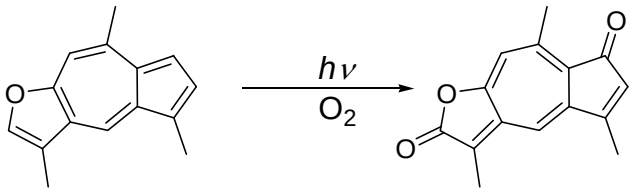
Two derivatives (Lettucenine A. and Malophylidin) of 2*H*-cyclohepta[*b*]furan-2-one are found in plant.[50] Named lettucenin A has been isolated from leaves of the lettus (Lactuca sativa var. capitata, compositae). Isolated yield from the dried leaves is 0.00084% yields. Lettucenine A is the first guaianolide phytoalexin containing a unique 2*H*-cyclohepta[*b*]furan-2-one ring system. Lettucenine A completely inhibits spore germination of Ceratocystis fimbriataat concentrations of 2 μg/ml.



118 **119**

lettucenine A malophylidin

Figure 11



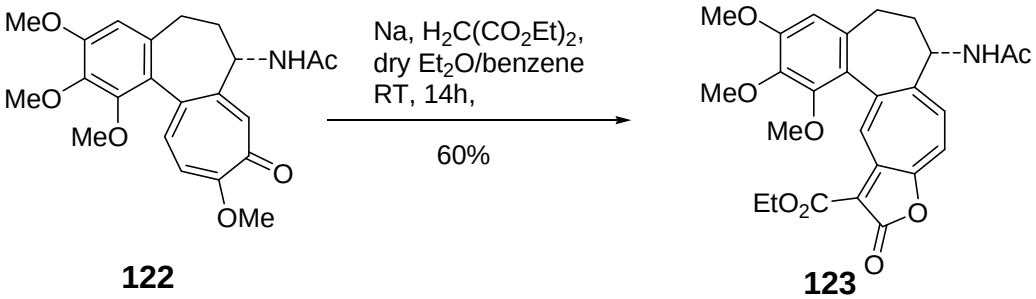
120 **121**

linderaazulene

Scheme 55

An isomeric extended azulenequinone malophylidin (**119**) is isolated from the root of Ferula Malacophylla by Baginov *et al*.[51] During the isolation of violet pigment linderaazulene from gorgonian Paramuricea Chamaeleon. Alpertunga *et al*. [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.[51]

The 2*H*-cyclohepta[*b*]furane 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.[53]

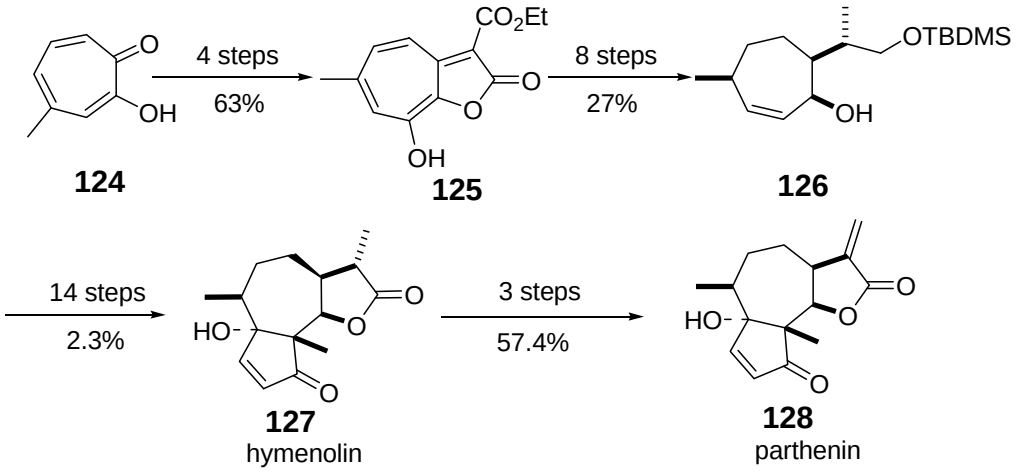


122 **123**

Scheme 56

As an example of availability of 2*H*-cyclohepta[*b*]furan-2-ones for total syntheses of natural products,

Ando and co-workers reported synthesis of bioactive molecules Hymenolin and Parthenin used for 8-hydroxy-6-methyl-2-oxo-2*H*-cyclohepta[*b*]furan-3-carboxylate (**124**) as a key intermediate (Scheme 57).[54]



Scheme 57

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*H*-cyclohepta[*b*]furan-2-ones such as **1b**, **1d**, and **1d**'. However, they cannot get a good result until now.[55]

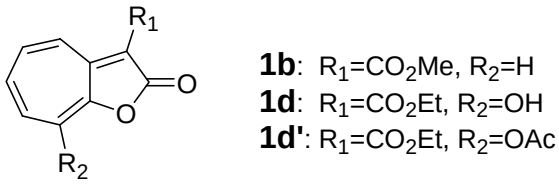


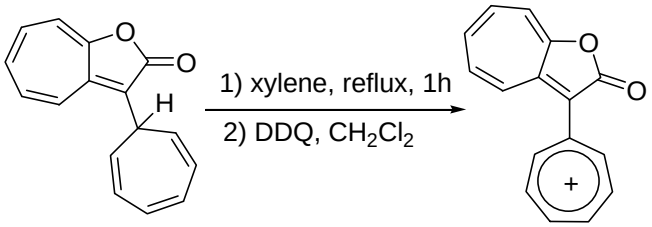
Figure 12

16. UTILIZATION OF 2*H*-CYCLOHEPTA[*b*]FURAN-2-ONE AS FUNCTIONAL GROUPS

In the development of organic redox chemistry, 2-oxa-2*H*-cyclohepta[*b*]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 tropyliun 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*H*-cyclohepta[*b*]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*H*-cyclohepta[*b*]furan-3-yl)tropyliumBF_4^- (**129**). From 2*H*-cyclohepta[*b*]thiophen-2-one, (2-oxo-2*H*-cyclohepta[*b*]thiophen-3-yl)tropyliumBF_4^- (**132**) [dark brown needles mp 170 –171 ºC] can also be easily obtained. The pK_R^+ values of these cations (**129** and **132**) are 3.8 and 3.2, respectively.

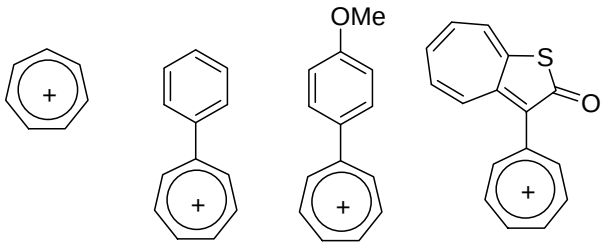
These values are lower than that (3.9) of tropylium ion.



1m **129**

Scheme 58

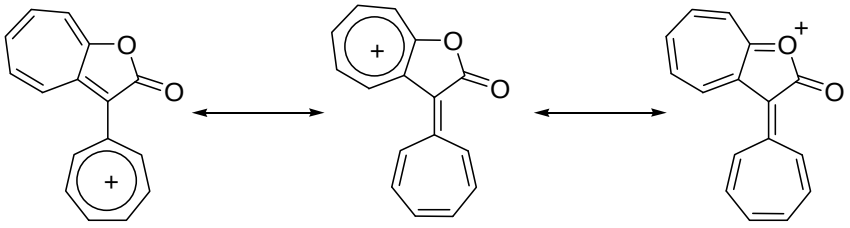
The averaged chemical shifts of seven–membered ring moiety in ^{1}H NMR and ^{13}C NMR are (8.90 and 152.7 for **129**, 9.00 and 155.0 for **132**. These chemical shifts appear at higher field compared with tropylium ion (9.26 ppm and 156.2 ppm).[56] The ring protons of 2*H*-cyclohepta[*b*]furan-2-one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



106 **130** **131** **132**

Figure 13

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

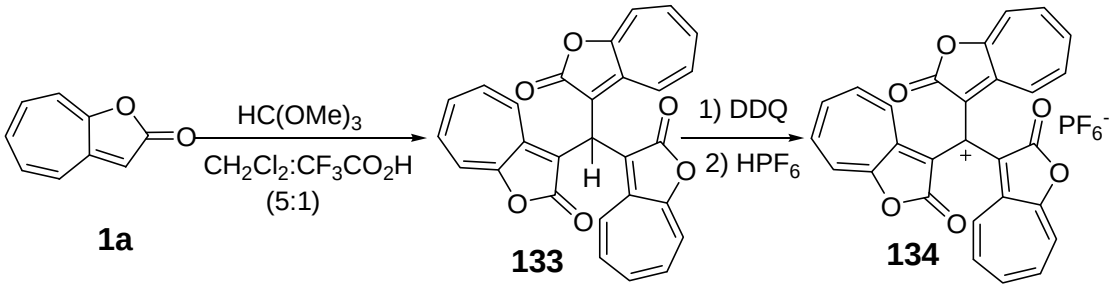


129A **129B** **129C**

Figure 14

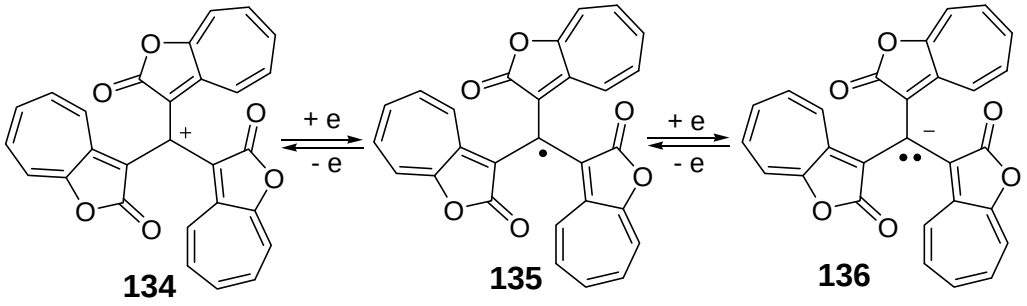
Nitta and co-worker[57a] have prepared tris(2-oxo-2*H*-cyclohepta[*b*]furan-3-yl)methyl cation (**134**) in excellent yields, starting from **1a** by the electrophilic substitution with trimethyl orthoformate in a solution of trifluoromethanesulfonic acid and dichloromethane, and followed by oxidation with DDQ and treatment with HPF_6. Its pK_R^+ value is 9.7. 2-Oxo-2*H*-cyclohepta[*b*]furan-3-yl group highly stabilized methyl cation. Its effectiveness is smaller than that of azulen-1-yl group (pK_R^+ is 11.3, E_1^{red} – 0.78 V, E_2^{red}

–1.56 V, CH_3CN).



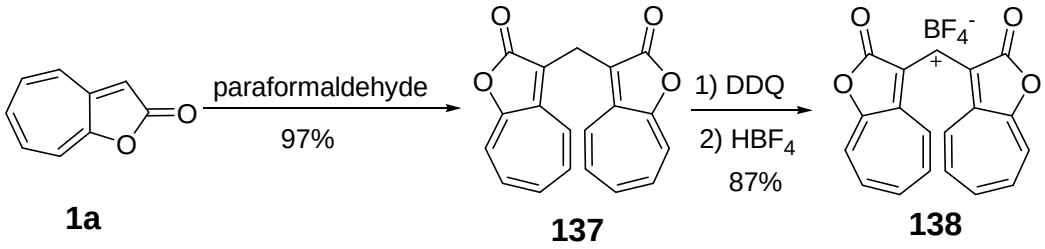
Scheme 59

The reduction potentials of **134** determined by cyclic voluammetry (CV) in CH_3CN are E_1^{red} – 0.31 V and E_2^{red} – 0.95 V.



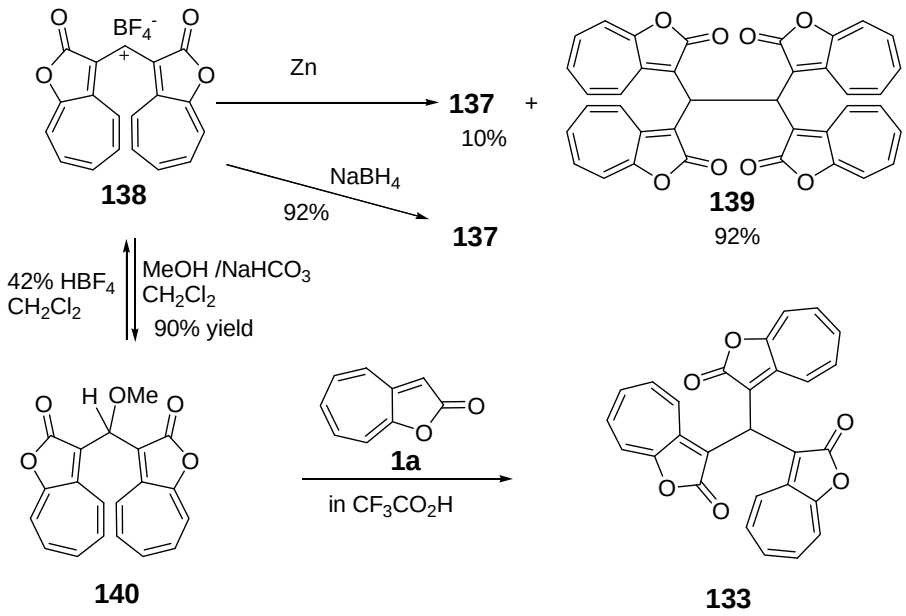
Scheme 60

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**.[57b] The longest wavelength absorption maxima of **138** appear 603 nm (log ε, 4.73). The pK_R^+ value of **138** is 2.6. The stabilization effect is not enough.



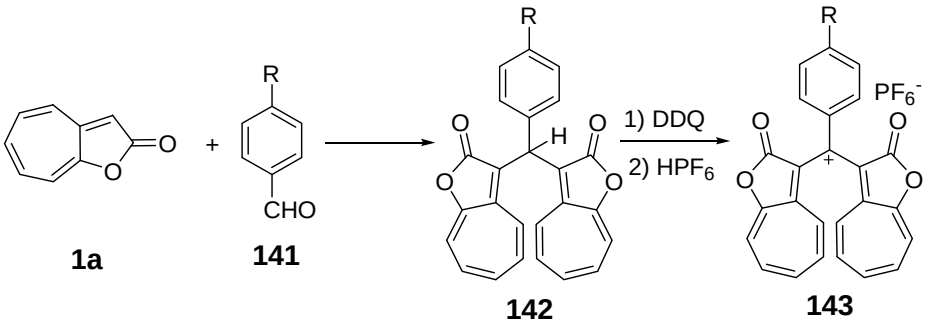
Scheme 61

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.



Scheme 62

Bis(2-oxo-2*H*-cyclohepta[*b*]furan-3-yl)phenylmethyl cations[58] (**143a-e**) were prepared by the electrophilic substitution of **1a** with **141c** or its derivatives and oxidation with DDQ and treatment with HPF_6. The pK_R^+ values of cations **143a-e** depend on the substituents on the phenyl group. The pK_R^+ 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-2*H*-cyclohepta[*b*]furan-3-yl)phenylmethyl cations. The characteristic absorption bands of the counter ion PF_6^- are observed at 838-845 cm^{-1} in the IR spectra of **143a-e**. The longest wavelength absorption maxima of **143a-e** in CH_3CN 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 wave lengths 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.



Scheme 63

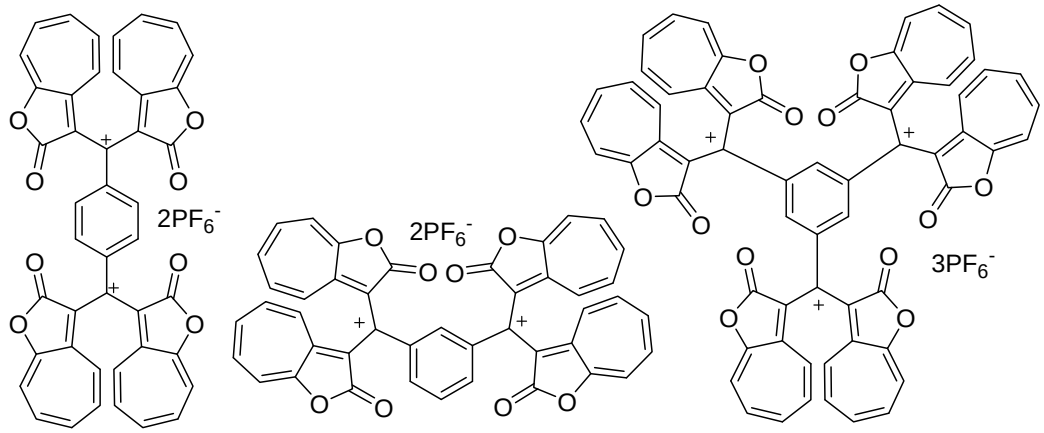
The synthetic method for 1,3- and 1,4-bis[bis(2-oxo-2*H*-cyclohepta[*b*]furan-3-yl)methyliumyl]benzenes are based on a single and stepwise TFA-catalyzed electrophilic aromatic substitution on **1a** with isophthalaldehyde and terephthalaldehyde to afford the corresponding 1,3- and1,4-dimethylbenzene derivatives, followed by oxidative hydrogen abstraction with DDQ, and subsequent exchange of the

counter-anion by using aq. HPF_6 solution. In spite of the dicationic nature of **144** and **145**, they exhibited high stability with large pK_R^+ values 9.3 and 9.0 due to the stabilizing effect of the 2-oxo-2*H*-cyclohepta[*b*]furan-3-yl units, however, we could not determine pK_R^+ and pK_R^{++} 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 1. The longest wave length, pK_R^+, and CV data of **138a-e**

143	Compounds (R)	λmax (log ε)	pK_R^+	E_1^{red},	E_2^{red}
a	NMe_2	671 (4.17) 575 (4.18)	12.4	-0.50	-1.15
b	OMe	621 (4.55)	10.0	-0.36	-1.08
c	H	621 (4.18)	9.3	-0.31	-1.03
d	Cl	621 (4.32)	9.1	-0.29	-0.99
e	CN	621 (3.62)	7.9	-0.23	-0.88

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



144 **145** **146**

Figure 15

The reaction of 1,3,5-triformylbenzene with six molar equivalent amounts of **1a** in CH_2Cl_2- trifluoroacetic acid (5:1) at rt for 48 h afforded 1,3,5-tris[bis(2-oxo-2*H*-cyclo- hepta[*b*]furan-3-ylmethyl)benzene in 68% yield.[59b] The oxidative hydrogen abstraction of 1,3,5-tris[bis(2-oxo-2*H*-cyclohepta[*b*]furan-3-yl)methyl]benzene with DDQ in CH_2Cl_2 at rt for 1 h, followed by treatment with aqueous 42% HBF_4 in Ac_2O, afforded crystals of stable 1,3,5-tris[bis(2-oxo-2*H*-cyclohepta[*b*]furan-3-yl)methyliumyl]benzene tris(tetrafluoroborate) (**146**) in 89% yield. The pK_R^{+++} and pK_R^+ are 9.0 and 6.4. The longest wavelength

absorption maximun of trication **146** is 615 nm.

The reduction potentials of trications are determined by cyclic volutammetry (CV) in CH_3CN. The only two reduction waves of E_3^{red} and E_6^{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 p*K*a values of the conjugated acids of **147**and **148** are 4,2 and <0, respectively.

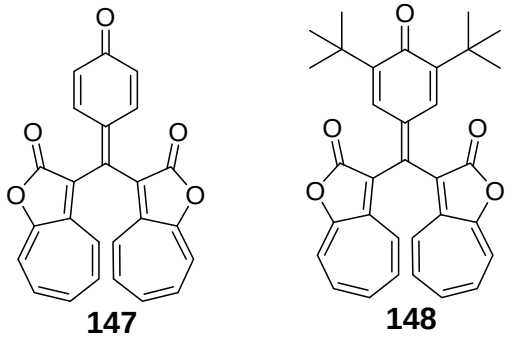
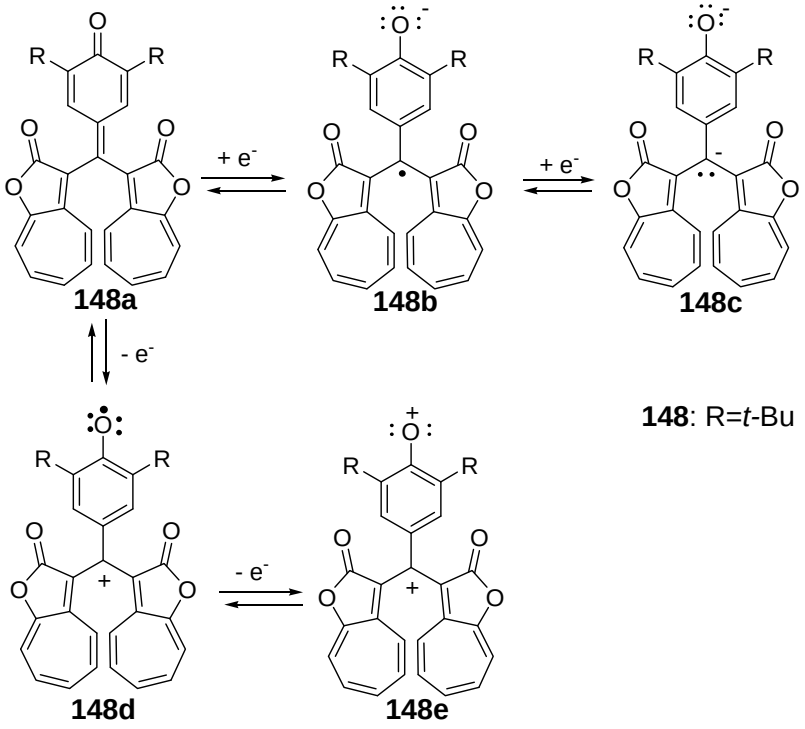


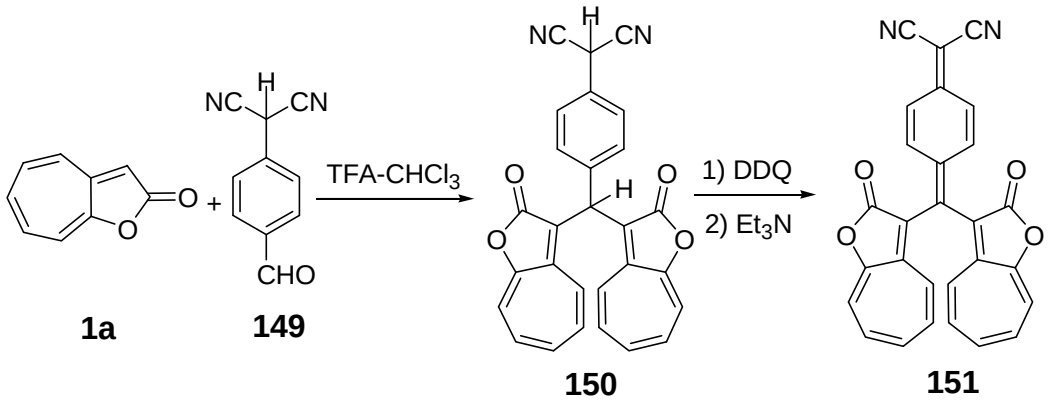
Figure 16

The reduction and oxidations of quinonemethides **147** and **148** determined by cyclic volutammetry (CV) in CH_3CN are E_1^{red} – 1.07 V, E_2^{red} – 1.44 V, E_3^{red} – 1.66 V, E_1^{ox} (+0.78 V), E_2^{ox} (+1.47 V) of compound **147**. E_1^{red} – 1.24 V, E_2^{red} – 1.56 V, E_1^{ox} +0.74 V, E_2^{ox} (+1.09 V) were observed in compound **148**. These reductions exhibit reversible but oxidations do not exhibit reversible except E_1^{ox} of **148**.



Scheme 64

The preparation of 7,7-bis(2-oxo-2*H*-cyclohepta[*b*]furan-3-yl)-8,8-dicyano-1,4-qunoinodimethane (**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.[61] The longest wave length absorption maxima of **151** in CH_3CN 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-2*H*-cyclohepta[*b*]furan-3-yl)phenylmethyl cations by protonization. Reduction waves (reversible) and oxidation waves (irreversible) of **151** by CV spectrum appear E_1^{red} – 0.70 V, E_2^{red} – 1.28, E_1^{ox} (+0.51 V), and E_2^{ox} (+1.55 V).



Scheme 65

17. CONCLUSIONS

We have described the variety of synthetic methods for 2*H*-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 2*H*-cyclohepta[*b*]furan-2-ons are going to begin. We expect that interesting reports about 2*H*-cyclohepta[*b*]furan-2-on chemistry will be increasing from now.

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