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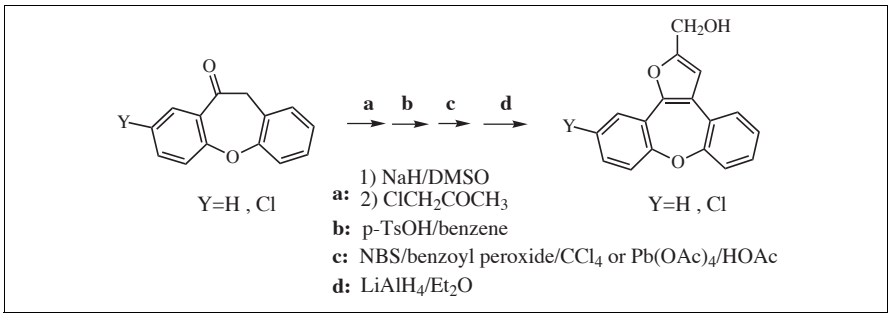

A novel synthetic route to 2-methyl-1,8-dioxa-dibenzo[*e,h*]azulenes [1] *via* cyclisation of the corresponding 1,4-dicarbonyl compound is described. 1,4-Dicarbonyl compounds were synthesized by the alkylation reaction of the 11*H*-dibenzo[*b,f*]oxepine-10-one while analogous alkylation of 11*H*-dibenzo[*b,f*]thiepine-10-one resulted in formation of *O*-alkylated products. Selective oxidation of 2-methyl group afforded 1,8-dioxa-dibenzo[*e,h*]azulenes with formyl and hydroxymethyl functionality at C(2) position.

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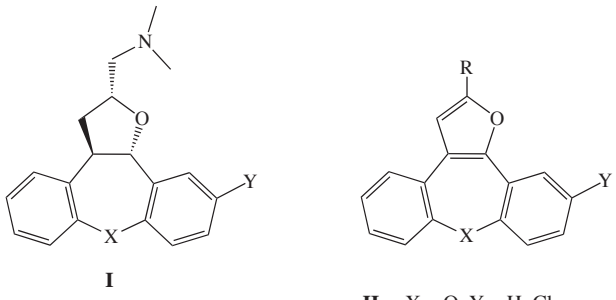
Introduction.

Dibenzo[*b,f*]oxepines and dibenzo[*b,f*]thiepines are heterocycles identified as pharmacologically important because their biological activity is well reported in various pharmacological areas. Numerous compounds that belong to these classes are known as antidepressants, analgesics, antipyretic and anti-inflammatory drugs [2-6].

Tetracyclic compounds derived from dibenzo[*b,f*]-oxepines, dibenzo[*b,f*]thiepines and dibenzo[*b,f*]azepines, which contain a fused tetrahydrofuran ring at the central seven membered ring (**I**, Figure 1), are also recognized as molecules that posses antipsychotic, cardiovascular and gastrokinetic activity [7].

Searching for novel anti-inflammatory agents, particularly inhibitors of tumor necrosis factor alpha (TNF-α) production, we have identified fused furan derivatives of dibenzooxepine and dibenzothiepine as promising pharmacologically active units. Syntheses of 2-oxa-dibenzo[*e,h*]azulenes, where the furan ring is fused to seven membered ring of dibenzo[*b,f*]thiepines, dibenzo-[*b,f*]oxepines and dibenzo[*b,f*]azepines, were accomplished by cycloaddition reactions [8,9]. However, 1-oxa-dibenzo[*e,h*]azulenes, like 1,8-dioxa-dibenzo[*e,h*]azulenes (**II**) and 1-oxa-8-thia-dibenzo[*e,h*]azulenes (**III**) (Figure 1), were not described.

Herein we report novel synthetic approach to compounds **II** starting from 11*H*-dibenzo[*b,f*]oxepine-10-one. Using the same strategy, we attempted synthesis of **III** from 11*H*-dibenzo[*b,f*]thiepine-10-one, but surprisingly different reactivity of thia- vs. oxa-analogues



I

X = O, S, CH_2, N, NR'
Y = H, F, Cl, Br

II X = O, Y = H, Cl
R = CH_3, CHO, CH_2OH

III X = S, Y = H, Cl
R = CH_3, CHO, CH_2OH

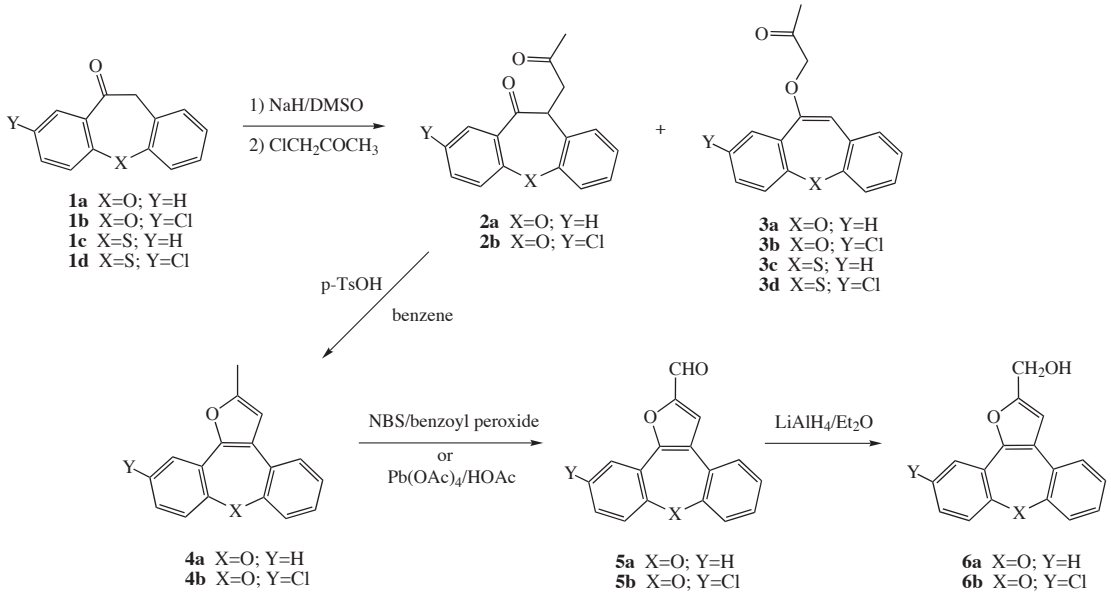
Figure I

in the step of carbanion alkylation drove reaction to *O*-alkylated compounds **3**. To further functionalize compounds in order to provide intermediates for final pharmaceutically acceptable molecules, we converted methyl group of **II** at position C(2) to carbaldehyde and hydroxymethyl group.

Results and Discussion.

One of the most important methods for the preparation of furans is the acid-catalyzed Paal-Knorr cyclisation of 1,4-dicarbonyl compounds. The limitation of this reaction has been the availability of suitably substituted starting diones [10]. Using a modified synthesis of 1,4-dicarbonyl benzoine derivatives, 1,4-dicarbonyl compounds **2** were synthesized (Scheme 1) [11].

Scheme 1



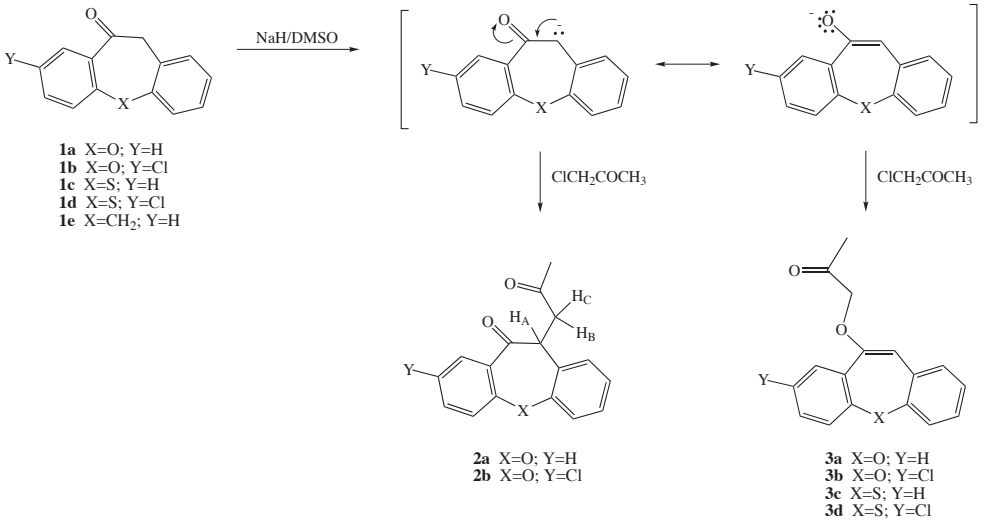
Reaction of ketones **1** [12] with chloroacetone in the presence of base in dimethyl sulfoxide (DMSO) resulted in formation of *C*- and *O*-alkylation products. Depending on the heteroatom in the seven membered ring, unexpected selectivity of *C*- vs. *O*-alkylation was observed for two pairs of compounds **1**. Oxa analogues **1a,b** reacted prevalently to form *C*-alkylated product (up to 10% of *O*-alkylated product was isolated) in contrast to nearly complete *O*-alkylation of thia analogues **1c,d**. This result was repeatedly observed for sodium hydride/ dimethyl sulfoxide, which was the most effective base for both pairs of analogues. However, when (**1e**) was used in the same reaction conditions only starting compound was isolated without even traces of *C*- or *O*-alkylated products (Scheme 2).

The molecular orbital calculations concur that the majority of the negative charge resides on the oxygen center in enolate ions [13-15]. Nevertheless, reactions of enolates result in predominant *C*-alkylation. In hard-soft acid base (HSAB) terms, the *O*-center of an enolate anion is hard compared with the *C* site. Therefore, the enolate *O*-center would be expected to interact preferentially with the hard (metal) cation. The soft *C*-center, on the other hand, would be expected to react primarily with the *C*-center of the alkylating agent. Significantly, the degree of *C*- versus *O*-alkylation is modified by the reaction conditions, as well as by the choice of enolate ion. Thus, the enolate formed by the sterically hindered diphenylacetophenone has been found to react with methyl iodide to yield 50% of the *O*-methylated product in DMSO [16,17]. DMSO with a soft sulfur center would not coordinate to the same degree with the oxygen as hard as metal cations do, and *O*-alkylation would be favored. Evidently, the *C*/*O* alkylation ratio decreases as the sterically more hindered anion is involved and if DMSO is used as solvent. In our case, compounds **1a-d** are similarly hindered and reactions were carried in DMSO which could direct some *O*-alkylated product.

The difference in the *C*/*O* alkylation for oxa analogues **1a,b** versus thia analogues **1c,d** may be explained by invoking HOMO–LUMO interactions (HOMO, highest occupied molecular orbital; LUMO, lowest unoccupied molecular orbital) [18] and the HSAB description of nucleophilicity. The small HOMO–LUMO gaps of the soft acids and bases would enhance HOMO–LUMO electron density transfer and concomitant covalent bonding which would drive reaction toward *C*-alkylation. However, in the case of the thia analogues **1c,d**, we believe that sulfur as heteroatom may contribute by its *d*-orbitals through conjugated system, and additionally lower the HOMO-LUMO gap between the oxygen as nucleophil and electrophil [19]. That additional “softness” would make oxygen atom nucleophilic enough and since it is not sterically hindered, the *O*-alkylation product would be dominant (Scheme 2).

The structure of **2a,b** is supported by NMR spectra where diastereotopic protons H_B and H_C are characterized by doublet of doublets, which is a consequence of their mutual coupling and subsequent coupling with vicinal H_A atom. The signal of H_A proton is represented with multiplet (doublet of doublet), which is the result of coupling with non-equivalent H_B and H_C protons.

Scheme 2

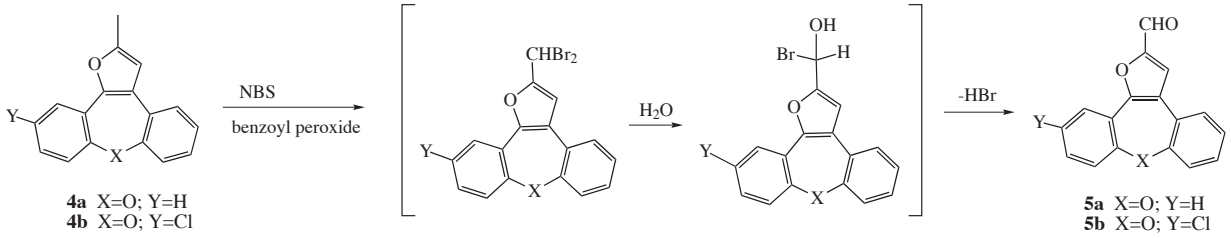


However, more simple NMR spectra of **3a-d** are characterized with well-resolved singlets corresponding to methyl, methylene and olefine protons.

Dehydration of compounds **2** with *p*-toluenesulfonic acid in benzene led to formation of 1,8-dioxa-dibenzo-[*e,h*]azulene scaffold substituted with a methyl group in the C(2) position. Reaction was carried out at reflux temperature and resulted in 90-95% yields.

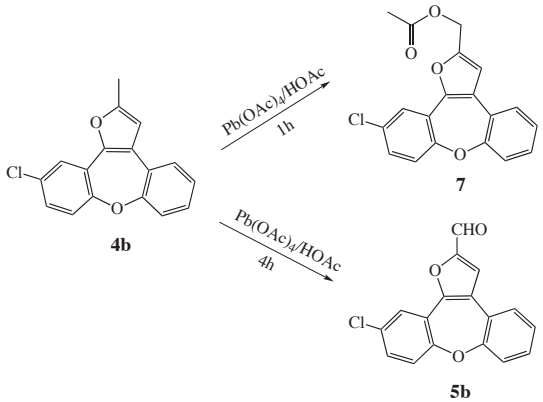
dibromide in reaction with *N*-bromosuccinimide and its fast hydrolysis into corresponding carbonyl compound **5** (Scheme 3) [20,24]. Alternatively, carbonyl derivative **5b** was also isolated as the final product when lead(IV) acetate was used as a reagent for acyloxylation of the compound **4b** (Scheme 4) [25,26]. This reaction proceeded through formation of an intermediary acetate ester **7**, which was on prolonged reaction time further

Scheme 3



In order to prepare functionalized derivatives with drug-like properties modification of **4** was performed. Reaction of **4a,b** and *N*-bromosuccinimide in the presence of catalytic quantity of benzoyl peroxide [20] resulted in oxidation of the methyl group and formation of carbonyl compounds **5a,b** in a single reaction step. This was unexpected since previously reported transformation of methyl substituted furans to corresponding aldehydes comprised formation of a bromomethyl derivate, subsequent formation of a quaternary ammonium salt, hydrolysis of this salt to an amine and, finally, formation of an aldehyde, a reaction known as Sommelet oxidation [21-23]. Direct transformation of a methyl to a formyl group can be explained by preferred formation of geminal

Scheme 4



oxidized to corresponding aldehyde. Reduction of carbonyl group in **5** was completed with lithium aluminum hydride in diethyl ether and resulted in hydroxymethyl derivatives **6** (Scheme 1), useful intermediates for further functional group interconversion reactions.

EXPERIMENTAL

Commercial reagents were used as received without additional purification. All chemicals and solvents were p.a. purity. Melting points were determined with a Büchi Melting Point B-545 apparatus and are uncorrected. IR spectra were recorded as potassium bromide pastilles or as a film on a sodium chloride plate, on Nicolet Magna IR 760 FT IR-spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on Varian Unity 600, Bruker Avance DPX 300 spectrometer at 300 MHz. Deuterated chloroform ($CDCl_3$) was used as solvent and tetramethylsilane (TMS) as internal standard. Purity of the compounds was obtained on HPLC-MS system Waters 2690 + Micromass Quattro Micro and on HPLC-UV system Waters 2690 + Waters 996 Photodiode Array Detector. HRMS data were acquired using Q-TOF 2 Waters system. Microanalyses were performed using Perkin-Elmer 2400 C H N S analyzer. Thin layer chromatography (TLC) was performed on aluminum plates Merck Silica gel 60 F_{254} with UV light detection at 254 nm and/or 365 nm. Proportions of solvents used for TLC are by volume. Column chromatography was performed on silica gel 60 (Merck, 0,063-0,200 nm). Compounds **1a-d** were synthesized as described before [12].

General Procedure for Reaction of Ketones **1** with Chloroacetone (Preparation of Compounds **2** and **3**).

To a solution of ketone **1** (0.017 mol) in dimethyl sulfoxide (30 ml), sodium hydride was added (1.31 g, 60% suspension in mineral oil) and reaction mixture was stirred at room temperature. When the evolution of hydrogen was finished (about 30 minutes), chloroacetone (0.075 mol, 6 ml) was added and reaction mixture stirred at room temperature until TLC (ethyl acetate/hexane 1:2) confirmed constant ratio between product and reactant (*ca*. 2:1) (30-60 minutes). Then a little quantity of water was added and product extracted with ethyl acetate. The combined organic extracts were dried (sodium sulfate), concentrated and then purified by column chromatography (silica gel-toluene) to give **2** and/or **3**.

11-(2-Oxo-propyl)-11*H*-dibenzo[*b*,*f*]oxepin-10-one (**2a**).

This compound was obtained from **1a** as white solid: Yield 25%; mp 110-113 °C; ir (potassium bromide): 3071, 1938, 1714, 1684, 1598, 1470, 1419 cm^{-1}; ^{1}H nmr: δ 2.34 (s, 3H, CH_3), 2.88 (dd, 1H, J = 3.8, 17.3 Hz), 3.72 (m, 1H), 4.94 (dd, 1H, J = 3.8, 10.4 Hz); 7.14-7.58 (m, 7H, arom. protons); 7.98 ppm (dd, 1H, J = 1.7, 7.9 Hz, arom. proton); ^{13}C nmr: δ 30.08 (*C*H_3), 39.55 (*C*H_2), 47.82 (*C*H), 120.35, 120.87, 123.36, 125.83, 126.04, 128.10, 130.23, 134.48 (arom. *C*H), 125.76, 156.54, 159.62, 190.23 (arom. *C*), 205.44 ppm (*C*=O); hrms: m/z calcd. for $C_{17}H_{14}NaO_3$: 289.0841 (M+Na$^+$), found 289.0886.

Anal. Calcd. for $C_{17}H_{14}O_3$: C, 76.68; H, 5.30. Found C, 76.75; H, 5.30.

8-Chloro-11-(2-oxo-propyl)-11*H*-dibenzo[*b*,*f*]oxepin-10-one (**2b**).

This compound was obtained from **1b** as white solid: Yield 13%; mp 155-158 °C; ir (potassium bromide): 3068, 2909, 1716, 1691, 1597, 1463, 1449 cm^{-1}; ^{1}H nmr: δ 2.34 (s, 3H, CH_3), 2.89 (dd, 1H, J = 3.7, 17.4 Hz), 3.7 (dd, 1H, J = 10.5, 17.4 Hz), 4.9 (dd, 1H, J = 3.7, 10.4 Hz), 7.16-7.36 (m, 5H, arom. protons), 7.48 (dd, 1H, J = 2.7, 8.7 Hz, arom. proton), 7.92 ppm (d, 1H, J = 2.7 Hz, arom. proton); ^{13}C nmr: δ 29.79 (*C*H_3), 47.43 (*C*H_2), 39.24 (*C*H), 120.07, 122.34, 125.71, 126.11, 128.09, 129.38, 133.95 (arom. *C*H), 126.63, 127.29, 128.75, 156.06, 157.84, 188.87 (arom. *C*), 204.92 ppm (*C*=O); hrms: m/z calcd. for $C_{17}H_{14}ClO_3$: 301.0632 (M+H$^+$), found 301.0637.

Anal. Calcd. for $C_{17}H_{14}O_3$: C, 76.68; H, 5.30. Found C, 76.75; H, 5.30.

1-(Dibenzo[*b*,*f*]oxepin-10-yloxy)-propan-2-one (**3a**).

This compound was obtained from **1a** as yellow oil: Yield 10%; ir (film): 3072, 2922, 1724, 1631, 1604, 1487 cm^{-1}; ^{1}H nmr: δ 2.37 (s, 3H, CH_3), 4.58 (s, 2H, CH_2), 5.89 (s, 1H, CH), 7.05-7.51 (m, 7H, arom. protons), 7.65 ppm (dd, 1H, J = 1.7, 7.7 Hz, arom. proton); ^{13}C nmr: δ 26.53 (*C*H_3), 72.68 (*C*H_2), 102.95 (*C*H), 120.59, 120.99, 124.57, 124.72, 126.45, 127.89, 128.68, 130.93 (arom. *C*H), 127.95, 128.28, 152.97, 157.28 (arom. *C*); 205.04 ppm (*C*=O); hrms: m/z calcd. for $C_{17}H_{15}O_3$: 267.1021 (M+H$^+$), found 267.1000.

Anal. Calcd. for $C_{17}H_{14}O_3$: C. 76.68; H. 5.30. Found C, 76.55; H, 5.46.

1-(8-Chloro-dibenzo[*b*,*f*]oxepin-10-yloxy)-propan-2-one (**3b**).

This compound was obtained from **1b** as yellow solid: Yield 2%; mp 93-97 °C; ir (potassium bromide): 3050, 2896, 1715, 1630, 1481 cm^{-1}; ^{1}H nmr: δ 2.37 (s, 3H, CH_3), 4.58 (s, 2H, CH_2), 5.90 (s, 1H, CH), 7.09-7.35 (m, 6H, arom. protons), 7.61 ppm (d, 1H, J = 2.6 Hz, arom. proton); ^{13}C nmr: δ 26.28 (*C*H_3), 72.44 (*C*H_2), 103.54 (*C*H), 120.28, 122.07, 124.75, 126.08, 127.99, 128.62, 130.42 (arom. *C*H), 127.59, 128.79, 129.82, 151.52, 155.28, 155.35 (arom. *C*), 204.26 ppm (*C*=O); hrms: m/z calcd. for $C_{17}H_{14}ClO_3$: 301.0631 (M+H$^+$), found 301.0617.

Anal. Calcd. for $C_{17}H_{13}ClO_3$: C, 67.89; H, 4.36. Found C, 67.63; H, 4.11.

1-(Dibenzo[*b*,*f*]thiepin-10-yloxy)-propan-2-one (**3c**).

This compound was obtained from **1c** as yellow solid: Yield 23%; mp 115-118 °C; ir (potassium bromide): 3450, 3024, 2897, 1738, 1620 cm^{-1}**;** ^{1}H nmr: δ 2.38 (s, 3H, CH_3), 4.61 (s, 2H, CH_2), 6.31 (s, 1H, CH), 7.18-7.71 (m, 7H, arom. protons), 8.21 ppm (dd, 1H, J = 1.6, 7.9 Hz, arom. proton); ^{13}C nmr: δ 26.36 (*C*H_3), 72.68 (*C*H_2), 107.61 (*C*H), 127.16, 127.27, 127.62, 127.74, 128.61, 129.82, 131.75, 132.03 (arom. *C*H), 133.40, 135.63, 137.186, 137.67, 155.89 (arom. *C*), 204.81 ppm (*C*=O); ms: m/z 282 (MH$^+$).

Anal. Calcd. for $C_{17}H_{13}ClO_3$: C, 72.31; H, 5.00. Found C, 72.03; H, 5.19.

1-(8-Chloro-dibenzo[*b*,*f*]thiepin-10-yloxy)-propan-2-one (**3d**).

This compound was obtained from **1d** as yellow solid: Yield 8%; mp 137-139 °C; ir (potassium bromide): 3053, 3004, 1712, 1620, 1548, 1473, 1432 cm^{-1}; ^{1}H nmr: δ 2.37 (s, 3H, CH_3), 4.61 (s, 2H, CH_2), 6.29 (s, 1H, CH), 7.18-7.33 (m, 3H, arom. protons), 7.32 (dd, 1H, J = 2.4, 8.3 Hz, arom. proton), 7.45-7.50 (m, 2H, arom. protons), 7.65 ppm (d, 1H, J = 2.3 Hz, arom.

proton); ^{13}C nmr: δ 26.56 (*C*H$_3$), 72.83 (*C*H$_2$), 108.39 (*C*H), 127.49, 127.66, 128.08, 128.97, 129.98, 131.98, 133.32 (arom. *C*H), 133.20, 134.08, 134.18, 137.56, 138.86, 154.88 (arom. *C*), 204.56 ppm (*C*=O); ms: m/z 316 (M$^+$).

Anal. Calcd. for $C_{17}H_{13}ClO_2S$: C, 64.45; H, 4.14. Found C, 64.24; H, 4.28.

General Procedure for Reaction of Diketones **2** with *p*-Toluenesulfonic Acid (Preparation of Compounds **4**).

To the solution of **2** (8.73 mmol) in 50 ml of benzene a catalytic quantity of *p*-toluenesulfonic acid was added. The reaction mixture was stirred at reflux temperature until TLC (ethyl acetate/hexane 1:2) confirmed that all starting diketone was reacted (60 minutes). The reaction mixture was cooled to room temperature, diluted with water and extracted with ethyl acetate. Organic extracts were washed with saturated sodium hydrogencarbonate and brine, dried, concentrated and then purified by column chromatography (silica gel) to give compound **4**.

2-Methyl-1,8-dioxa-dibenzo[*e,h*]azulene (**4a**).

This compound was obtained from **2a** as yellow oil: Yield 95%; ir (potassium bromide): 3066, 2920, 1603, 1580, 1502, 1485, 1447 cm^{-1}; ^{1}H nmr: δ 2.45 (s, 3H, CH$_3$), 6.39 (s, 1H, furan proton), 7.13-7.37 (m, 7H, arom. protons), 7.57 ppm (m, 1H, arom. proton); ^{13}C nmr: δ 13.76 (*C*H$_3$), 105.88, 121.59, 121.89, 124.59, 125.10, 125.27, 126.64, 128.75, 129.23 (arom. *C*H), 121.97, 124.79, 126.46, 146.50, 153.07, 154.61, 155.09 ppm (arom. *C*); hrms: m/z calcd. for $C_{17}H_{13}O_2$: 249.0916 (M+H$^+$), found 249.0907.

Anal. Calcd. for $C_{17}H_{12}O_2$: C, 82.24; H, 4.87. Found C, 81.95; H, 4.98

11-Chloro-2-methyl-1,8-dioxa-dibenzo[*e,h*]azulene (**4b**).

This compound was obtained from **2b** as white solid: Yield 90%; mp 145-148 °C; ir (potassium bromide): 3448, 3053, 2919, 1502, 1485, 1443 cm^{-1}; ^{1}H nmr: δ 2.40 (s, 3H, CH$_3$), 6.37 (d, 1H, J = 1.0 Hz, furan proton), 7.13-7.35 (m, 6H, arom. protons), 7.55 ppm (d, J = 2.5 Hz); ^{13}C nmr: δ 13.17 (*C*H$_3$), 105.47, 121.26, 122.26, 123.64, 124.94,1 26.20, 128.17, 128.49 (arom. *C*H), 125.46, 125.56, 129.91, 144.82, 152.22, 153.16, 154.25 ppm (arom. *C*).

Anal. Calcd. for $C_{17}H_{11}ClO_2$: C, 72.22; H, 3.92. Found C, 72.02; H, 3.77.

General Procedure for Preparation of Compounds **5**.

Method A.

To the solution of **4** (3.47 mmol) in tetrachloromethane (50 ml), *N*-bromosuccinimide (0.64 g, 3.6 mmol) and catalytic quantity of benzoyl peroxide were added. The reaction mixture was heated at reflux temperature until TLC (ethyl acetate/hexane 1:2) confirmed that all starting compound was reacted (2 hours). The reaction mixture was then cooled to room temperature, the precipitate filtered off, and the filtrate evaporated. Crude material was dissolved in ethyl acetate and washed with water and brine. After drying of organic layers over sodium sulfate, solvent was evaporated and crude material purified by silica gel column chromatography providing compound **5**.

Method B.

To the solution of **4** (1.63 mmol) in acetic acid (20 ml) lead(IV) acetate was added. The reaction mixture was heated at reflux temperature until TLC (ethyl acetate/hexane 1:2) confirmed that all starting compound was reacted and transformed into more polar product (4 h). The reaction was cooled to room temperature, solvent evaporated, and the crude residue diluted with water and extracted with ethyl acetate. Organic layers were washed with saturated sodium hydrogencarbonate and brine, dried (sodium sulfate), concentrated, and then purified by silica gel column chromatography to give compound **5**.

Before formation of an aldehyde was observed, an aliquot of the reaction mixture was taken off (for the purpose of identifying the intermediate), solvent evaporated, and crude residue diluted with water and extracted with ethyl acetate. Organic layers were washed with saturated sodium hydrogencarbonate and brine, dried, concentrated, and then purified by silica gel column chromatography to give compound **7**.

1,8-Dioxa-dibenzo[*e,h*]azulene-2-carbaldehyde (**5a**).

This compound was obtained from **4a** as light yellow oil with 47% yield by method A and 22% by method B; ir (potassium bromide): 2963, 2925, 2854, 1670, 1530, 1502 cm^{-1}; ^{1}H nmr: δ 7.22-7.79 (m, 9H, arom. protons), 9.76 ppm (s, 1H, CHO); ms: m/z 263 (MH$^+$); hrms: m/z calcd. for $C_{17}H_{11}O_3$: 263.0708 (M+H$^+$), found 263.0683.

Anal. Calcd. for $C_{17}H_{10}O_3$: C, 77.85; H, 3.84. Found C, 77.72; H, 3.75.

11-Chloro-1,8-dioxa-dibenzo[*e,h*]azulene-2-carbaldehyde (**5b**).

This compound was obtained from **4b** as light white solid with 64% yield by method A: mp 165-168 °C; ir (potassium bromide): 3061, 2843, 1680, 1529, 1501, 1483 cm^{-1}; ^{1}H nmr: δ 7.16-7.45 (m, 6 H, arom. protons), 7.56 (s, 1H, furan proton), 7.74 (d, 1H, J = 2.6 Hz, arom. proton), 9.77 ppm (s, 1H, CHO); ^{13}C nmr: δ 118.79, 121.59, 122.77, 125.33, 125.46, 126.53, 129.785, 131.01 (arom. *C*H), 123.55, 123.89, 130.49, 151.83, 154.36, 154.88, 185.33 (arom. *C*), 177.15 (*C*HO); hrms: m/z calcd. for $C_{17}H_{10}ClO_3$: 297.0318 (M+H$^+$), found 297.0283.

Anal. Calcd. for $C_{17}H_9ClO_3$: C, 68.82; H, 3.06. Found C, 68.59; H, 2.95.

Acetic acid 11-chloro-1,8-dioxa-dibenzo[*e,h*]azulen-2-ylmethyl ester (**7**).

This compound was obtained from **4b** as yellow oil; ir (potassium bromide): 3060, 2963, 1745, 1502, 1484 cm^{-1}; ^{1}H nmr: δ 2.14 (s, 3H, CH$_3$), 5.16 (s, 2H, CH$_2$), 6.80 (s, 1H, furan proton), 7.17-7.39 (m, 6H, arom. protons), 7.57 ppm (d, 1H, J = 2.5 Hz, arom. proton); ^{13}C nmr: δ 19.91 (*C*H$_3$), 56.97 (*C*H$_2$), 120.91, 121.99, 123.79, 124.68, 125.91, 128.48, 128.69 (arom. *C*H), 124.40, 129.63, 149.56, 152.55, 154.07, 169.58 ppm (arom. *C*); ms: m/z 296,.88 (M-CH$_3$CO), 280.90 (M-CH$_3$COO).

Anal. Calcd. for $C_{19}H_{13}ClO_4$: C, 66.97; H, 3.85. Found C, 67.02; H, 3.87.

General Procedure for Reduction of Aldehydes **5** (Preparation of Compounds **6**).

To the solution of **5** (1.3 mmol) in tetrahydrofuran (50 ml), lithium aluminum hydride (0.20 g, 5.26 mmol) was added. Reaction mixture was stirred at room temperature until TLC confirmed that all starting aldehyde reacted. The white precipitate was filtered off, and the filtrate dried over sodium

sulfate, concentrated, and purified by column chromatography (silica gel) yielding compound **6**.

1,8-Dioxa-dibenzo[*e,h*]azulene-2-yl)-methanol (**6a**).

This compound was obtained from **5a** as white solid: Yield 35%; ^{1}H nmr: δ 1.98 (bs, 1H, OH), 4.74 (s, 2H, CH_2), 6.70 (s, 1H, furan proton), 7.12-7.39 (m, 7H, arom. protons), 7.61 ppm (dd, 1H, J = 7.7, 1.6 Hz, arom. proton); ms: m/z 265 (MH^+), 248 (M-OH); hrms: m/z calcd. for $C_{17}H_{11}O_2$: 247.0759 [M-OH], found 247.0698.

Anal. Calcd. for $C_{17}H_{12}O_3$: C, 77.26; H, 4.58. Found C, 77.12; H, 4.60.

(11-Chloro-1,8-dioxa-dibenzo[*e,h*]azulene-2-yl)-methanol (**6b**).

This compound was obtained from **5b** as white solid: Yield 83%; mp 135-139 °C; ir (potassium bromide): 3268, 2928, 2866, 1502, 1484, 1446, 1408 cm^{-1}; ^{1}H nmr: δ 1.59 (s, 1H, OH), 4.08 (d, 2H, J = 0.25 Hz, CH_2); 7.19-7.35 (m, 6H, arom. protons), 7,47 (dd, 1H, J = 2.6, 8.7 Hz, arom. proton), 8.0 (d, 1H, J = 2.8 Hz, furan proton); ^{13}C nmr: δ 47.42 (CH_2), 119.76, 122.72, 126.03, 128.15, 129.35, 134.09 (arom. *C*H), 125.12, 126.95, 128.91, 158.16, 188.57 (arom. *C*); hrms: m/z calcd. for $C_{17}H_{10}ClO_2$: 281.0369 (M-OH), found 281.0340.

Anal. Calcd. for $C_{17}H_{11}ClO_3$: C, 68.35; H, 3.71. Found C, 68.12; H, 3.60.

Conclusion.

A novel synthetic route for synthesis of 2-methyl-1,8-dioxa-dibenzo[*e,h*]azulenes *via* cyclisation of the appropriate 1,4-dicarbonyl compound is developed. 1,4-Dicarbonyl compounds were synthesized by the alkylation of 11*H*-dibenzo[*b,f*]oxepine-10-one and its 8-chloro derivative respectively with chloro-acetone, while alkylation of thia analogues under the same reaction conditions resulted in formation of *O*-alkylated products exclusively.

Reaction of 2-methyl-1,8-dioxa-dibenzo[*e,h*]azulenes with *N*-bromosuccinimide in the presence of catalytic quantity of benzoyl peroxide provides 1,8-dioxa-dibenzo[*e,h*]azulenes substituted with formyl group in the C(2) position. The same compound was isolated when lead(IV) acetate was used as the oxidation reagent. 1,8-Dioxa-dibenzo[*e,h*]azulenes substituted with hydroxymethyl group at C(2) position were synthesized by reduction of formyl derivative.

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REFERENCES AND NOTES

[1a] The substitutive nomenclature is used here for this class of compounds, but the correct IUPAC defined nomenclature is as follows: **4a**, 2-methyl-furo[2,3-*d*]dibenzo[*b,f*]oxepine; **4b**, 11-chloro-2-methyl-furo[2,3-*d*]dibenzo[*b,f*]oxepine; **5a**, furo[2,3-*d*]dibenzo[*b*,f]oxepine-2-carbaldehyde; **5b**, 11-chloro-furo[2,3-*d*]dibenzo[*b,f*]oxepine-2-carbalde-hyde; **6a**, furo[2,3-*d*]dibenzo[*b,f*]oxepine-2-methanol; **6b**, 11-chloro-furo[2,3-*d*]dibenzo[*b,f*]oxepine-2-methanol; **7**, 11-chloro-furo[2,3-*d*]-dibenzo[*b,f*]oxepine-2-ylmethyl acetate; [b] R. Olivera, R. SanMartin, F. Churruca and E. Domínguez, *J. Org. Chem.*, **67**, 7215 (2002).

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