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Regio- and Chemoselective Bromination of 2,3-Diarylcyclopent-2-en-1-ones

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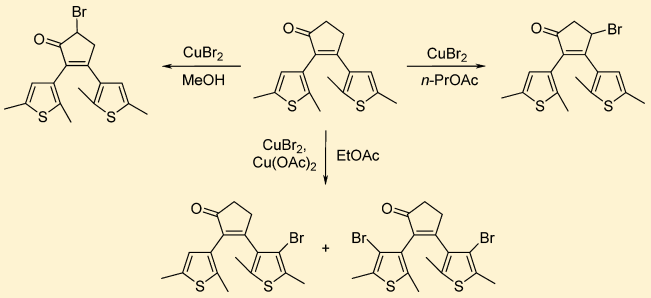
Supporting Information

ABSTRACT: The bromination of 2,3-diarylcyclopent-2-en-1-ones under various conditions has been studied. It was found that depending on the brominating reagent and nature of solvent the bromine atom can be introduced at the 4- or 5-position of the ethene "bridge", as well as into the aryl moieties. Aryl group bromination is accomplished with such reagents as molecular bromine, *N*-bromosuccinimide, or tetrabutylammonium tribromide. 5-Bromocyclopentenones with very high efficiency can be obtained by the reaction with copper(II) bromide in methanol, while 4-bromoketones are prepared in *n*-propyl acetate. The developed methods can be highly useful for the synthesis of bromo-substituted 2-cyclopenten-1-ones and their close analogues, which are important synthons in organic synthesis and for the preparation of a variety of useful substances.



INTRODUCTION

α-Bromination of carbonyl compounds is an important transformation of organic chemistry, as the α-brominated products are useful intermediates in organic synthesis[1−3] and they can be transformed into a number of other functionalities under moderate reaction conditions.[2,4] Traditionally, this reaction is difficult to control due to its fast reaction rate and exothermic character. In addition, owing to easy enolization of the monobrominated ketones they readily react further to the double-brominated product.

The carefully performed analysis of the scientific literature testifies that there is no general method of ketone bromination, although some patterns of this process are available.[2,5] It should be noted that the process of the ketone bromination depends not only on their functionalities, but also on the nature of the solvent and brominating agent. Even a minor change of substituent pattern (electronic or/and steric factors) can significantly affect both the process of bromination and the yields of final products. So, the systematic study of the bromination reaction even by the example of a narrow class of ketones allows not only development of a convenient preparative methods for their functionalization and to obtain practically useful products, but also insights into the patterns of the course of this process.

In this paper, we have investigated the bromination of the cyclopentenone ring of 2,3-diarylcyclopent-2-ene-1-ones and studied the dependence of reaction regioselectivity and final product yields on the nature of the substituents and the reaction conditions.

2-Cyclopenten-1-ones derivatives are key and valuable intermediates in organic synthesis, and are widely applied as precursors for preparation of a various practically useful products.[6−10] 2,3-Diaryl-substituted-2-cyclopenten-1-ones are widely investigated for the development of drugs[11−15] and pesticides;[16−19] in particular, they were studied as nonsteroidal anti-inflammatory,[13,20] antitumor[15,21,22] drugs and pyrethroid insecticides.[19] Besides, the cyclopentenone fragment is the basic framework of many important biologically active natural compounds, including jasmone, methylenomicine B, tetrahydrodicranenone B, acetylene dicranenone A, the aflatoxins, and several prostaglandins. Some 2,3-substituted-2-cyclopenten-1-ones have been used in perfumes and cosmetics as fragrances[8,23] and in medicine as antibiotics.[6,24,25] In the past decade, much interest has grown in natural and synthetic cyclopentenone prostaglandins which represent a promising model for the development of novel antiviral drugs that can affect different targets during the virus life cycle.[9,26]

Recently, we showed that 2,3-diaryl-substituted-2-cyclopenten-1-ones are also a promising class of photochromic diarylethenes for the development of the smart materials.[27−29] Photochromic diarylethenes have been extensively investigated for the development of new high technology materials, including elements for 3D optical storage and molecular switches.[30−32] One of the key issues for the practical application of photochromic compounds is to establish correlations between the structure and their spectral and kinetic properties to obtain new materials with improved characteristics.[27,31,32] In turn, this problem is solved by the development of convenient methods for modification of photochromic compounds and the

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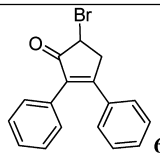
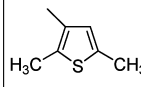
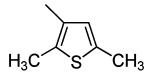
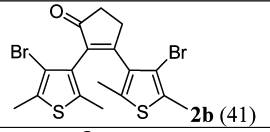
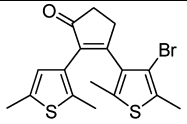
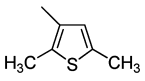
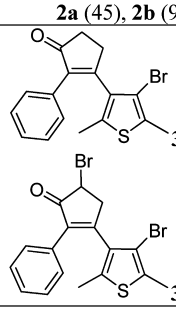
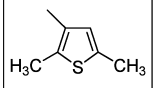
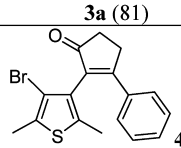
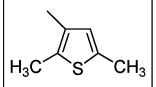
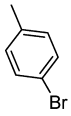
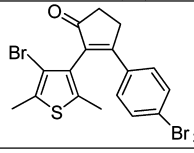
Table 1. Diarylcyclopentenones 1a−e Bromination: Reaction Conditions, Reagents, and Products

Entry	2,3-Diarylcyclopent-2-en-1-one structure			Method*	Products (yields, %)
	Compound Number	Ar^1	Ar^2		
1	**1a**			**A**	 **6a** (74)
2	**1b**			**B**	 **2b** (41)
3				**C**	 **2a** (63), **2b** (26)
4				**D**	**2a** (45), **2b** (9)
5	**1c**			**B**	 **3a**(62), **3b** (19)
6				**C**	**3a** (81)
7	**1d**			**B**	 **4** (62)
8				**C**	**4** (64)
9	**1e**			**B**	 **5** (90)
10				**C**	**5** (92)

*Method A: NBS, MeOH, r.t.. Method B: Br_2, AcOH, r.t.. Method C: NBS, CH_3CN, r.t. Method D: n-$BuNBr_3$, CH_3CN, r.t.

introduction of various functional groups. The 2,3-diarylcyclopent-2-ene-1-ones bromination and its further functionalization seems to be a promising way to solve this issue.

RESULTS AND DISCUSSION

The various protocols of α-bromination of cyclopentenone derivatives and its closest analogues—indanones—have been developed including the basic method using Br_2 in acetic acid,[33−35] in ether,[36−38] and in some other solvents.[39−42] The unfriendly and dangerous nature of bromine, however, urged on the invention of milder conditions making use of manageable reagents such as *N*-bromosuccinimide (NBS). NBS is known to be a superior brominating agent in terms of the ease of handling and to be used increasingly for α-bromination of carbonyl compounds, including indanone and cyclopentenone derivatives in different solvents and in the presence of a radical initiator such as azabisisobutyronitrile (AIBN) or dibenzoyl peroxide (BPO)[43,44] or some acid catalysts such as toluene-4-sulfonic acid, trimethylsilyltrifluoromethanesulfonate.[45−48] *Tetra-n*-butylammonium tribromide, copper(II) bromide, pyridinium tribromide, and some other brominating reagents are less commonly used in the bromination of alkyl carbonyl compounds.[49−52] However, despite many methods for the α-bromination of carbonyl compounds the choice of an effective technique of bromination of diarylcyclopentenones bearing thiophene ring is complicated by the presence of several active centers (double bond, π-donor aromatic systems, active methylene groups).

Recently, it has been reported that 2,3-diphenylcyclopent-1-ene-2-ones can easily be brominated into the α-position to the carbonyl group under the action of NBS in acetonitrile in the presence of trimethylsilyltrifluoromethanesulfonate as a catalyst with 60−65% yields.[47] However, our studies show that in the bromination of diarylcyclopentenones bearing thiophene cycles as the aryl moieties NBS is not suitable. So, the bromination by NBS occurs in the thiophene ring even when the reaction

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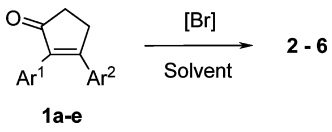
proceeds at room temperature without a catalyst, whereas the bromination in the cyclopentenone ring is not observed. Also, the addition of catalytic amounts of trimethylsilyltrifluoromethanesulfonate does not change the reaction direction. Both with catalyst and without it monobrominated and dibrominated in thiophene rings products **2**−**5** are formed.

To test the technique described,[47] bis-phenylcyclopentenone **1a** in the presence of freshly prepared trimethylsilyltrifluoromethanesulfonate as a catalyst was brominated, but the conversion of the starting compound **1a** after 24 h under room temperature was low. However, it was surprising that the replacement of acetonitrile by methanol and the absence of the catalyst led to the desired product **6a** in good yields (74%), and the bromination of the benzene ring is not observed. Analogous results have been obtained for bis-naphthyl-derivative **1h** (entry 1 in Table 1 and entries 1and 16 in Table 3). However, under similar conditions (NBS in methanol) the thiophene-containing cyclopentenones nevertheless were brominated in thiophene cycles.

These results prompted us to examine in more detail the bromination reaction of the diarylcyclopentenones of thiophene series to develop a convenient method for the preparation of 5-bromo-2,3-diarylcyclopent-2-en-1-ones. The different conditions, including molecular bromine in acetic acid, *n*-BuNBr$_3$ in acetonitrile, as well as copper(II) bromide in various solvents, have been investigated. In the bromination of bis-thiophene derivative **1b** by molecular bromine in acetic acid, only the dibrominated thiophene ring product **2b** is formed (entry 2 in Table 1). The replacement of one thiophene ring in compound **1b** by the phenyl moiety (compounds **1c**−**e**) also leads to the bromination in the thiophene cycle (entries 5, 7, 9 in Table 1), and only for compound **1c** along with the product **3a** (62%) was double-brominated **3b** with low yield (19%) also isolated (entry 5 in Table 1). The application of *N*-BuNBr$_3$ in acetonitrile as bromination agent also results in a complex mixture from which only products of bromination in one and two thiophene rings were isolated (compounds **2a** and **2b**, entry 4 in Table 1).

Scheme 1. Diarylcyclopentenones 1a−e Bromination with Different Reagents under Various Conditions



Some very interesting results were obtained when copper(II) bromide was used as brominating agent. First, the use of $CuBr_2$ excludes bromination of the thiophene ring, which significantly reduces the number of byproduct. It was also found that in the bromination of diatylcyclopentenones with copper(II) bromide the reaction direction and the yields of target products strongly depend on the nature of the solvent, reaction temperature and also on the substituents in the aromatic cycle. Bis(2,5-dimethylthiophen-3-yl)cyclopent-2-ene-1-one **1b** was used as a model compound in this study (Scheme 2).

The reaction was carried out in various solvents such as methanol, ethyl acetate, acetonitrile, tetrahydrofuran, propyl acetate, *iso*-propyl acetate, butyl acetate, and so forth (Table 2). The best results for the bromination at the α-position to the carbonyl group were obtained when the reaction was carried out in methanol and the reaction temperature increased gradiently (for 4 h at room temperature than for 3 h at 40 °C and refluxing of the reaction mixtures until the complete disappearance of the starting diarylcyclopentenone, entry 6 in Table 2). At room temperature, the reaction rate is much slower, but the side processes are not observed (entry 1 in Table 2). Due to the formation of 5,5-dibromo derivative **7b** and 4-methoxy-substituted **9b**, a significant reduction in the yield of the target product is observed when the original reaction mixture is refluxed (entry 2 in Table 2).

The replacement of methanol with ethyl acetate leads to the formation of two products—5- and 4-bromosubstituted compounds **6b** and **8b**, respectively. The reaction at room temperature does not occur, but the heating of the reaction mixture under reflux results in the formation of both these products in moderate yields. The same pattern is observed in a number of ether solvents, "methyl acetate − ethyl acetate − *i*-propyl acetate − *n*-propyl acetate" (entries 9, 10, 12, 13 in Table 2). The increase of the reaction temperature leads to the increase of the 4-isomer **8b** yield, with *n*-butyl acetate being an exception; in this case, there is a strong drop in the yields of both isomers, probably due to resinification of the reaction mixture at high temperatures (>120 °C, entry 14 in Table 2).

Unexpected results were obtained when the reaction between dithienylcyclopentenone **1b** and copper(II) bromide was carried out in ethyl acetate in the presence of copper acetate (entry 11 in Table 2). It was found that the addition of copper acetate completely changes the reaction direction and only the brominated in thiophene ring products (mono- **2a** and disubstituted **2b**) under these conditions were obtained. These results are similar to those obtained by the bromination in acetonitrile using *N*-bromosuccinimide (see entry 3 in Table 1). In the case where a mix of copper bromide and copper acetate is used, the reaction is likely also to proceed by a radical mechanism, a possible cause for which is the formation of copper bromoacetate (CuBrOAc) from copper acetate and hydrogen bromide.

The mechanism of the reaction of carbonyl compounds with copper(II) bromide has been studied previously in details in several works (Scheme 3).[1,2,54−57] A key stage of this process is the coordination of carbonyl group of ketone **1** to copper atom resulting in complexes **I** and **II** followed by the enolization of carbonyl compounds.

In this case, the bromination at 5-position (compound **6**) is likely to proceed via intermediate **III**, and the formation of 4-substituted isomer **8** is probably due to enolization of vinyl ketone **II** to form an intermediate cyclopentadienol **IV**. The formation of 4-brominating product **8** by a radical mechanism seems to be unlikely, because our attempts to brominate at the 4-position of cyclopentenone ring by NBS in the presence of *m*-chloroperbenzoic acid or AIBN were unsuccessful, although it is known that the bromination of some indanone derivatives in the β-position to the carbonyl group by NBS under these conditions in the presence of these radical initiators was very useful.[58−60]

The main side process in the monobromination of carbonyl compounds is the formation of α,α-dibromo-derivatives, since the enolization is facilitated for the resulting product as compared to the parent compound. However, when dihetarylcyclopentenones **6b,i** were brominated by copper(II) bromide in refluxing methanol along with dibromo-derivatives **7b,i** (10−15%), 4-methoxyderivatives **9b,i** (8−18%) as a byproduct were also formed (entry 2 in Table 2). The formation of 4-methoxyderivative in this reaction can be explained by the

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Scheme 2. Bromination of Diarylcyclopentenone 1b by Cupric Bromide under Different Conditions

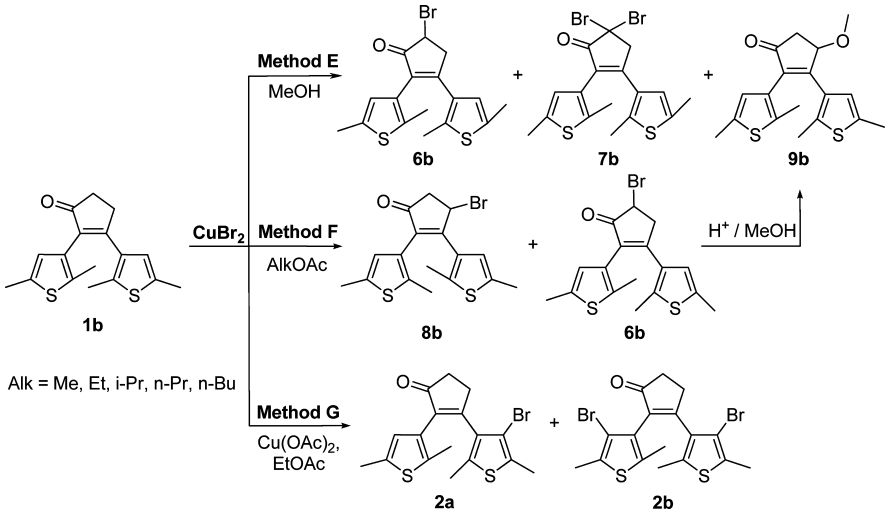
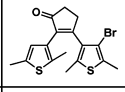
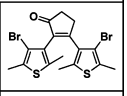


Table 2. Diarylcyclopentenone 1b Bromination by $CuBr_2$ under Different Conditions[53]

Entry	Conditions (solvents, temperature)	The composition of resulting reaction mixture, %						
								
		1b	**6b**	**7b**	**8b**	**9b**	**2a**	**2b**
1	Methanol, r.t.	40	60	-	-	-	-	-
2	Methanol, b.p.	-	45	15	-	18	-	-
3	Methanol, H-sponge[¶], b.p.	30	65	-	-	-	-	-
4	Methanol, calcium carbonate, b.p.	30	50	5	-	-	-	-
5	Methanol, methanesulfonic acid, b.p.	-	42	traces	-	50	-	-
6	Methanol, opt.[#]	-	95	traces	-	traces	-	-
7	Tetrahydrofuran, b.p.	-	35	15	25	-	-	-
8	Acetonitrile, b.p.	30	35	15	8	-	-	-
9	Methyl acetate, b.p.	20	52	traces	10	-	-	-
10	Ethyl acetate, b.p.	30	45	traces	22	-	-	-
11	Ethyl acetate/copper acetate, b.p.	traces	-	-	-	-	40	45
12	Isopropyl acetate, b.p.	20	34	traces	31	-	-	-
13	Propyl acetate, b.p.	traces	10	traces	48	-	-	-
14	Butyl acetate, b.p.	traces	7	10	32	-	-	-

[*]Th = 2.5-dimethylthiophen-3-yl. [¶]1,8-Bis(dimethylamino)naphtaline. [#]Optimal conditions: 4 h under room temperature, then 3 h under 40 °C and eventually under reflux to maximum conversion of initial diarylethene **1b**.

protonation on the first stage of the bromine atom in the 5-bromketones **6** (cation **V**) with subsequent formation of carbocation **VI**, which in turn eliminates a proton by E1-elimination mechanism giving adduct **VII** (Scheme 4). The latter reacts with methanol to form 4-methoxyderivative **9** (Michael reaction). It should be noted that in the literature there are no data on the formation of either 4- or 5-alkoxy-substituted product in the bromination of ketones in the alcohols. Indirect evidence in favor of the protonation of bromine atom and the E1-elimination mechanism can be a transformation of bromoketone **6b** to methoxyderivative **9b** by refluxing in alcohol in the presence of acid catalyst (hydrochloric acid, hydrobromic acid, or copper bromide) (Scheme 2). Besides, it was found that the yields of 4-methoxyderivative **9b** considerably increase (up to 50%) when methanesulfonic acid as catalyst was added to the reaction of dithienylcyclopentenone with copper(II) bromide in methanol (entry 5 in Table 2). And in contrast, when proton sponge (1,8-bis(dimethylamino)naphtaline) or calcium carbonate was added to this reaction mixture the impurity of 4-methoxyderivative **9b** was not detected (entries 3 and 4 in Table 2).

Thus, the development and optimization of the cyclopentenone ring monobromination conditions allowed synthesizing a wide range of 4- and 5-bromo-substituted diarylcyclopentenones with different aryl groups (benzene, naphthalene, thiophene, and benzothiophene) in good yields (Table 3).

The structure of synthesized compounds was proven by elemental analyses, ^{1}H NMR and ^{13}C NMR spectroscopy, and mass spectrometry. The position of the bromine atom in structure **6b** was determined by the analysis of one- and two-dimensional NMR spectra. The correlations in the NOESY spectrum between methylene group protons H-4a, 4b and proton H-4′ of thienyl group (Figure 1) is found that confirm

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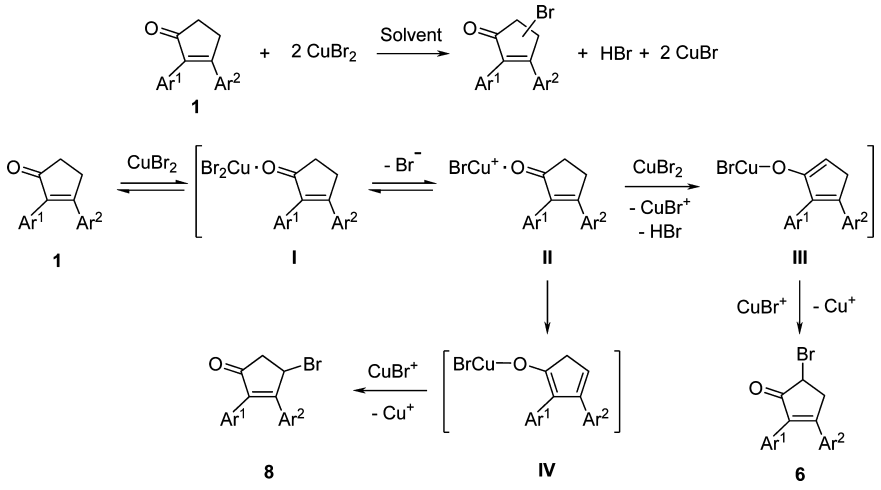
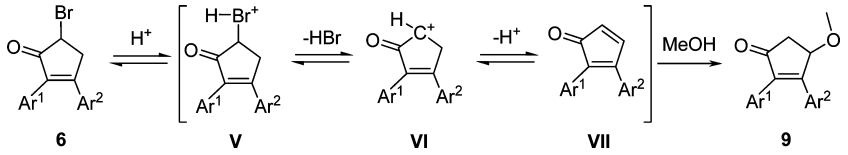
Scheme 3. Reaction Mechanism of the Bromination of Ketones 1 with Copper(II) Bromide



Scheme 4. Reaction Mechanism of 4-Methoxyderivative 9 Formation



the location of bromine atom at 5-position of cyclopentenone ring. The presence of the methoxy-group at the 4-position of the cyclopentenone ring of diarylethene **9b** has been verified by correlation between proton H-4 of cyclopentenone cycle and proton H-4′ of thienyl ring (Figure 1).

In addition, the structures of 5-bromoketones **6b**,**h** were proven by chemical transformations (Scheme 5). Thus, it was shown that 5-bromoketones in contrast to 4-isomers, as would be expected, react with phenylthioamide giving thiazole derivatives **10a**,**b**, which is indirect proof of the structures of these bromoketones.

Also, we have found that both 4- and 5-bromo-substituted cyclopentenones (compound **6b** and **8b**) react with *N*-, *O*-, and *S*-nucleophiles (phenol, thiophenol, succinimide, and morpholine) forming the products of nucleophilic substitution (Scheme 6). The reaction with these nucleophiles apparently proceeds by the SN2-reaction mechanism. The only exception is the interaction of bromketone **6b** with sodium methylate in absolute methanol, which leads to the formation of 2,3-bis(2,5-dimethylthiophen-3-yl)-4-methoxycyclopent-2-en-1-one **9b** instead of the expected 5-methoxysubstituted product **16** (Scheme 7). 4-Substituted product **9b** is also formed upon the treatment of 4-bromo-substituted isomer **8b** with sodium methoxide in absolute methanol. The formation of 4-methoxy-substituted product **9b** from α-bromoketone **6b** can be explained by assuming that the reaction proceeds by the E2-elimination reaction mechanism. The formation of the intermediate **14** which interacts with methanol via a Michael reaction giving the 4-substituted product is likely to take place by the synchronous cleavage of the H−C and Br−C bonds of the two adjacent carbon atoms under the influence of a strong base—sodium methylate. An indirect confirmation of Michael adduct **14** formation is the reaction of morpholine with the 5-bromketone **6b** in the presence of DBU (diaza(1,3)-bicyclo[5.4.0]undecane) that leads to 4-morpholino-substituted product **15**. The latter is also obtained from the 4-bromocyclopentenone **8b** by the treatment with morpholine.

CONCLUSION

The bromination of 2,3-diarylcyclopent-2-en-1-ones under various conditions has been studied, and it was found that the direction of the reaction depends on the nature of the brominating reagent, solvent, as well as of the aryl moieties. The regio- and chemoselective methods of the bromination of 2,3-diarylcyclopent-2-en-1-ones have been developed. The reaction of 2,3-diarylcyclopent-2-en-1-ones with copper(II) bromide in methanol proved to result in 5-bromoketones with very high efficiency, while 4-bromoketones are prepared in *n*-propyl acetate. The use of the mixture of copper(II) bromide and copper(II) acetate as brominating reagent in ethyl acetate leads to bromination only in aromatic (thiophene) cycles. The reactions of 5-bromoketones synthesized with different nucleophiles have also been studied, and it turned out that depending on the basicity of the nucleophile it can be introduced either at the 5-position (by SN2-mechanism) or at the 4-position (E2-elimination followed by Michael addition reaction) of the cyclopentenone ring. The methods developed can be highly useful for the synthesis of different bromo-substituted 2-cyclopenten-1-ones and their close analogues.

EXPERIMENTAL SECTION

Proton nuclear magnetic resonance spectra (^{1}H NMR), carbon nuclear magnetic resonance spectra (^{13}C NMR), and two-dimensional gNOESY, COSY, HSQC, and HMBC experiments (2D-NMR) were recorded in deuterated solvents on a spectrometers working at 300 MHz for ^{1}H, 75 MHz for ^{13}C, and 400 MHz for 2D-NMR. Both ^{1}H and ^{13}C NMR chemical shifts are referenced relative to the solvents residual signals ($CHCl_3$: δ 7.27 for ^{1}H NMR and δ 77.16 for ^{13}C NMR) and reported in parts per million (ppm) at 25 °C, unless otherwise stated. Data are represented as follows: chemical shift, multiplicity (s, singlet; d, doublet; t, triplet; m, multiplet; br, broad), coupling constant in hertz (Hz), integration, and assignment.

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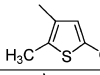
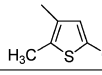
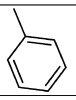
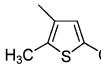
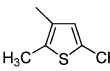
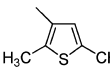
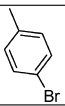
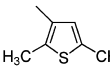
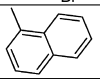
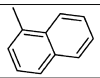
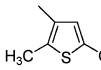
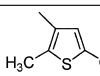
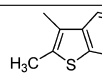
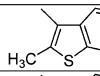
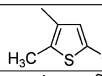
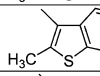
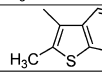
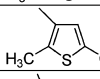
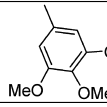
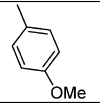
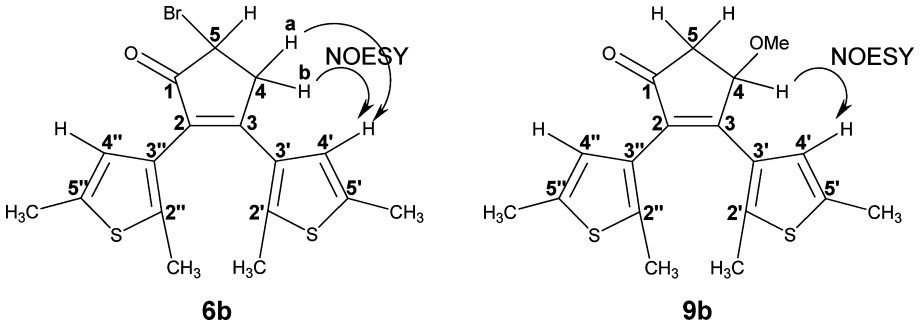
Table 3. Bromination of Diarylcyclopentenones 1a−m under Different Optimal Conditions

Entry	2,3-Diarylcyclopent-2-en-1-one structure			Method*	Products (yields, %)
	Number	Ar^1	Ar^2		
1	**1a**			**E**	**6a** (74)
2	**1b**			**E**	**6b** (95)
3				**F**	**8b** (48), **6b** (10)
4				**G**	**2a** (45), **2b** (50)
5	**1c**			**E**	**6c** (72)
6				**F**	**8c** (29), **6c** (25)
7				**G**	**3a** (65)
8	**1d**			**E**	**6d** (58)
9				**F**	**8d** (25), **6d** (21)
10				**G**	**4** (75)
11	**1e**			**E**	**6e** (75)
12				**F**	**8e** (35), **6e** (31)
13	**1f**			**E**	**6f** (82)
14	**1g**			**E**	**6g** (88)
15	**1h**			**E**	very low conversion of **1h**
16				**A**	**6h** (65)
17	**1i**			**E**	**6i** (80)
18	**1j**			**E**	**6j** (80)
19	**1k**			**E**	**6k** (96)
20	**1l**			**E**	**6l** (75)
21	**1m**			**E**#	**6m** (93)

*Method A: NBS, MeOH, r.t.. Method E: $CuBr_2$, MeOH, 4 h under room temperature, then 3 h under 40 °C and eventually under reflux to maximal conversion of initial diarylethenes **1**. Method F: $CuBr_2$, n-PrOAc, b.p.. Method G: $CuBr_2$, $Cu(OAc)_2$, EtOAc, b.p. #The full conversion of initial cyclopentenone **1m** has already been attained under room temperature.



6b **9b**

Figure 1. 2D-NOESY spectra correlations used for verifying the position of the bromine atom in diarylethene **6b** and the methoxy-group in diarylethene **9b**.

Infrared spectra were measured on a FT-IR spectrometer in KBr pellets and are reported in terms of frequency of absorption (cm^{-1}). Melting points (Mp) were recorded using an apparatus and not corrected. Mass spectra were obtained on a mass spectrometer (70 eV) with direct sample injection into the ion source. High resolution mass spectra were obtained from a TOF mass spectrometer with an ESI source. Microanalyses were obtained using an automatic CHNS/O Elemental Analyzer.

All chemicals and anhydrous solvents were purchased from commercial sources and used without further purification. Silica

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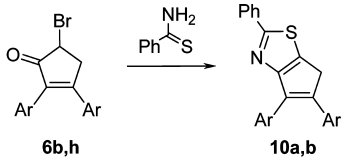
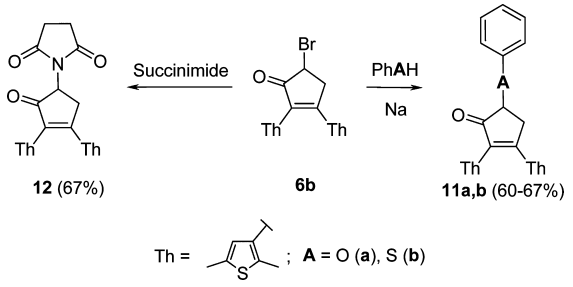
Scheme 5. Reaction of 5-Bromo-2,3-diarylcyclopent-2-en-1-ones 6 with Thioamides

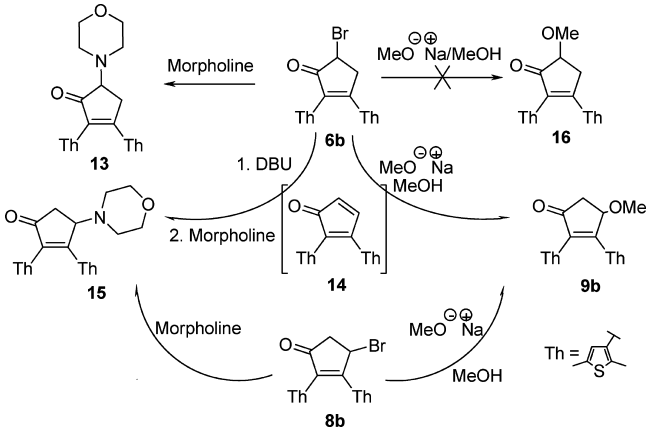


6: Ar = 2,5-dimethylthien-3-yl (**b**), 1-naphthyl (**h**)
10: Ar = 2,5-dimethylthien-3-yl (**a**), 1-naphthyl (**b**)

Scheme 6. Nucleophilic Substitutions of Bromine Atom at the 5-Position of Dithienylcyclopentenone 6b



Scheme 7. Reactions of 4- (8b) and 5-Bromo-substituted (6b) Dithienylcyclopentenones with Morpholine and Sodium Methylate



column chromatography was performed using silica gel 60 (70−230 mesh); TLC analysis was conducted on silica gel 60 F_{254} plates.

Bromination of 2,3-Diarylcyclopent-2-en-1-ones (General Procedures). *Method A (for Bromoketones **6a** and **6h**).* The mixture of cyclopentenones **1** (1.00 mmol) and *N*-bromosuccinimide (2.00 mmol) in absolute methanol (12 mL) was stirred at room temperature for 12 h. The precipitate was filtered off and recrystallized from acetonitrile.

Method B. To the solution of ketone **1** (1.00 mmol) in glacial acetic acid (5 mL), the solution of bromine (1.05 mmol) in glacial acetic acid (2 mL) was added dropwise at 20 °C. The mixture was stirred at room temperature for 15 min, poured into diluted sodium sulfite water solution (40 mL), extracted with ethyl acetate (3 × 20 mL). The combined extracts were washed with water (2 × 15 mL), dried with magnesium sulfate, and evaporated in vacuum, the residue was purified by column chromagraphy eluting with petroleum ester/ethyl acetate 5:1 (for compounds **4**, **5**) or 11:1 (for compounds **2b**, **3a**, **3b**).

Method C. The mixture of ketone **1** (1.00 mmol) and *N*-bromosuccinimide (1.10 mmol) in abs acetonitrile (10 mL) was stirred at room temperature for 1 h, poured into water (130 mL), extracted with methylene chloride (3 × 40 mL). The combined extracts were washed with diluted sodium sulfite water solution (2 × 40 mL), water (40 mL), dried with magnesium sulfate, and evaporated in vacuum; the residue was purified by column chromagraphy eluting with petroleum ester/ethyl acetate 5:1 (for compounds **2a**, **4**, **5**) or 11:1 (for compounds **2b**, **3a**).

*Method D (for Ketone **1b**).* The mixture of ketone **1b** (1.00 mmol) and tetrabutylammonium tribromide (1.10 mmol) in acetonitrile (10 mL) was stirred at room temperature for 2 h, poured into water (130 mL), extracted with methylene chloride (3 × 40 mL). The combined extracts were washed with diluted sodium sulphite water solution (2 × 40 mL), water (40 mL), dried with magnesium sulfate, and evaporated in vacuum; the residue was purified by column chromagraphy eluting with petroleum ester/ethyl acetate 11:1.

Method E. The mixture of cyclopentenones **1** (3.00 mmol) and cupric bromide (7.50 mmol) in methanol (15 mL) was stirred at room temperature for 4 h, then for 3 h at 40 °C, and eventually under reflux to maximal conversion of initial diarylethenes **1** (TLC-analysis), poured into ice−water (200 mL), and extracted with methylene chloride (3 × 60 mL). The combined organic phases were washed with water (3 × 40 mL), filtered through 1 cm layer of silica gel, evaporated, and the residue was recrystallized from appropriate solvent. In case of need, the residue was purified by column chromatography eluting by petroleum ester/ethyl acetate 10:1.

Method F. The mixture of cyclopentenones **1** (3.00 mmol) and cupric bromide (7.50 mmol) in abs *n*-propyl acetate (15 mL) was stirred under reflux for 1−2 h, poured into ice−water (200 mL), and extracted with methylene chloride (3 × 60 mL). The combined organic phases were washed with water (3 × 40 mL), filtered through 1 cm layer of silica gel, and evaporated. The residue was purified by column chromatography eluting by petroleum ester/ethyl acetate 10:1, and 5-bromoketones **6** and 4-bromoketones **8** were isolated.

Method G. The mixture of ketone **1** (1.00 mmol), cupric bromide (2.50 mmol), and cupric acetate (2.50 mmol) in ethyl acetate was refluxed for 3 h, poured into water (130 mL), extracted with methylene chloride (3 × 40 mL). The combined extracts were washed with diluted sodium sulfite water solution (2 × 40 mL), water (40 mL), dried with magnesium sulfate, and evaporated in vacuum; the residue was purified by column chromagraphy eluting with petroleum ester/ethyl acetate 5:1 (for compounds **2a**, **4**) or 11:1 (for compounds **2b**, **3a**).

*Method H (for Ketones **1b,i**).* The mixture of cyclopentenones **1** (3.00 mmol) and cupric bromide (7.50 mmol) in methanol (15 mL) was stirred under reflux for 3−4 h to maximal conversion of initial diarylethenes **1** (TLC-analysis), poured into ice−water (200 mL), and extracted with methylene chloride (3 × 60 mL). The combined organic phases were washed with water (3 × 40 mL), filtered through 1 cm layer of silica gel, and evaporated. The residue was purified by column chromatography eluting by petroleum ester/ethyl acetate 10:1→6:1, and corresponding 5-bromoketones **6**, dibromoketones **7**, and methoxy-derivatives **9** were isolated.

*Method I (for Ketone **1b**).* The mixture of cyclopentenone **1b** (3.00 mmol), cupric bromide (7.50 mmol), and methanesulfonic acid (1.50 mmol) in methanol (15 mL) was stirred under reflux for 3 h, poured into ice−water (200 mL), and extracted with methylene chloride (3 × 60 mL). The combined organic phases were washed with water solution of $NaHCO_3$ (40 mL), water (2 × 30 mL), filtered through 1 cm layer of silica gel, and evaporated. The residue was purified by column chromatography eluting by petroleum ester/ethyl acetate 10:1→6:1, and corresponding 5-bromoketone **6b** and methoxy-derivative **9b** were isolated.

*Methods J, K (for ketone **1b**).* The mixture of cyclopentenone **1b** (3.00 mmol), cupric bromide (7.50 mmol), and calcium carbonate (method J) or 1,8-bis(dimethylamino)naphtaline (method K) (3.00 mmol) in methanol (15 mL) was stirred under reflux for 5 h, poured into ice−water (200 mL), and extracted with methylene chloride (3 × 60 mL). The combined organic phases were washed with water (2 × 30 mL), filtered through 1 cm layer of silica gel, and evaporated. The residue was purified by column chromatography eluting by petroleum ester/ethyl acetate 10:1→6:1, and corresponding 5-bromoketone **6b** and dibromoketones **7b** were isolated.

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2a. *3-(4-Bromo-2,5-dimethylthiophen-3-yl)-2-(2,5-dimethylthiophen-3-yl)cyclopent-2-en-1-one*. Yield: method C 0.24 g (63%), method D 0.17 g (45%), method G 0.17 g (45%), light brown powder. Mp 137−139 °C (ethanol). IR (KBr), cm^{-1}: 2950 (CH_3, C−H^{thioph}), 2917 (CH_3, C−H^{thioph}), 2853 (CH_3, C−H^{thioph}), 1697 (C═O), 1620, 1433, 1494, 1378, 1271, 1142, 1984, 824, 815, 553, 491. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.97 (s, 3H, Me^{thioph}), 2.04 (s, 3H, Me^{thioph}), 2.34 (s, 3H, Me^{thioph}), 2.36 (s, 3H, Me^{thioph}), 2.64−2.73 (m, 2H, CH_2), 2.99−3.10 (m, 2H, CH_2), 6.49 (s, 1H, H^{thioph}). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.5, 14.79, 15.0, 15.8, 31.2, 34.9, 110.4 (CBr), 125.1, 130.1, 131.0, 133.4, 134.2, 135.3, 136.5, 137.7, 168.0, 206.6 (C═O). MS, *m*/*z* (%): 380, 382 (3, $[M]^+$), 301 (100, $[M - Br]^+$), 286 (18, $[M - Br - CH_3]^+$). HRMS−FAB: *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_{17}BrOS_2$: 404.9776; found: 404.9762.

2b. *2,3-Bis(4-bromo-2,5-dimethylthiophen-3-yl)cyclopent-2-en-1-one*. Yield: method B 0.19 g (41%), method C 0.12 g (26%), method D 0.04 g (9%), method G 0.23 g (50%), yellow powder. Mp 123−125 °C (ethanol). IR (KBr), cm^{-1}: 2917 (CH_3), 2851 (CH_3), 1713 (C═O), 1631, 1437, 1262, 1148, 1081, 788. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.92−1.99 (m, 6H, 2Me), 2.32 (br. s, 3H, Me), 2.36 (s, 3H, Me), 2.64−2.79 (m, 3H, 1.5CH_2), 3.36−3.75 (m, 1H, 1/2CH_2). ^{1}H NMR (300 MHz, C_6D_6, 298 K): δ 1.93−2.15 (m, 12H, 4Me), 2.31−2.48 (m, 3H, 1.5CH_2), 3.03−3.61 (m, 1H, 1/2CH_2). ^{1}H NMR (300 MHz, C_6D_6, 333 K): δ 1.98 (br. s, 3H, Me), 2.09 (s, 3H, Me), 2.10 (s, 3H, Me), 2.12 (br. s, 3H, Me), 2.35−2.44 (m, 2H, 2CH_2), 2.59−3.20 (m, 2H, 2CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.8 (2 signals), 14.9, 15.0, 30.8, 35.2, 111.0 (CBr), 112.8 (CBr), 128.7, 128.9, 131.0, 131.1, 132.2, 134.5, 135.0, 168.4, 206.7 (C═O). MS, *m*/*z* (%): 458, 460, 462 (4, $[M]^+$), 379, 381 (100, $[M - Br]^+$), 364, 366 (78, $[M - Br - CH_3]^+$), 300 (52, $[M - 2Br]^+$), 285 (30, $[M - 2Br - CH_3]^+$). HRMS−FAB: *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{16}Br_2OS_2$: 460.9061; found: 460.9060.

3a. *3-(4-Bromo-2,5-dimethylthiophen-3-yl)-2-phenylcyclopent-2-en-1-one*. Yield: method B 0.22 g (62%), method C 0.28 g (81%), method G 0.23 g (65%), brown oil. IR (KBr), cm^{-1}: 3055 (CH_3, C−H^{arom}), 2951 (CH_3, C−H^{arom}), 2918 (CH_3, C−H^{arom}), 2852 (CH_3, C−H^{arom}), 1706 (C═O), 1629, 1496, 1443, 1435, 1365, 1293, 1166, 1149, 1116, 918, 793 (C−H^{phenyl}), 762 (C−H^{phenyl}), 744 (C−H^{phenyl}), 697 (C−H^{phenyl}), 564. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.89 (s, 3H, Me), 2.39 (s, 3H, Me), 2.52−2.81 (m, 3H, 1.5CH_2), 3.26−3.48 m, 1H, 1/2CH_2), 7.17−7.38 (m, 5H, CH^{phenyl}). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.3, 14.9, 30.5, 35.4, 108.3 (CBr), 127.9, 128.2, 128.6, 131.5, 132.3, 132.4, 133.9, 142.8, 166.1, 207.4 (C═O). MS, *m*/*z* (%): 346, 348 (42, $[M]^+$), 331, 333 (35, $[M - CH_3]^+$), 289, 291 (21, $[M - C(O)CH_2CH_2]^+$), 267 (100, $[M - Br]^+$). HRMS−FAB: *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_{15}BrOS$: 368.9919, 370.9899; found: 368.9918, 370.9898.

3b. *5-Bromo-3-(4-bromo-2,5-dimethylthiophen-3-yl)-2-phenylcyclopent-2-en-1-one*. Yield: method B 0.08 g (19%), brown oil. IR (KBr), cm^{-1}: 3056 (C−H^{arom}), 2953 (CH_3, C−H^{arom}), 2919 (CH_3, C−H^{arom}), 2852 (CH_3, C−H^{arom}), 1715 (C═O), 1626, 1444, 1427, 1367, 1297, 1149, 1112, 797, 748, 701 (C−H^{phenyl}). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.80−1.94 (m, 3H, Me), 2.40 (s, 3H, Me), 3.89−3.01 (m, 1/2H, 1/4CH_2), 3.18−3.37 (m, 1/2H, 1/4CH_2), 3.62−3.80 (m, 1/2H, 1/4CH_2), 3.91−4.06 (m, 1/2H, 1/4CH_2), 4.57−4.72 (m, 1H, CH), 7.21−7.40 (m, 5H, CH^{phenyl}). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.3, 14.9, 42.1, 42.3, 128.4, 128.5, 128.6, 132.7, 133.6, 136.4, 139.1, 141.2, 144.9, 162.8, 200.4 (C═O). MS, *m*/*z* (%): 424, 426, 428 (32, $[M]^+$), 345, 347 (26, $[M - Br]^+$), 330, 332 (16, $[M - Br - CH_3]^+$), 266 (100, $[M - 2Br]^+$). HRMS−FAB: *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{14}Br_2OS$: 424.9205; found: 424.9209.

4. *2-(4-Bromo-2,5-dimethylthiophen-3-yl)-3-phenylcyclopent-2-en-1-one*. Yield: method B 0.22 g (62%), method C 0.23 g (64%), method G 0.26 g (75%), brown oil. IR (KBr), cm^{-1}: 3057 (C−H^{arom}), 2918 (CH_3, C−H^{arom}), 2853 (CH_3, C−H^{arom}), 1702 (C═O), 1625, 1445, 1367, 1271, 1185, 1042, 808, 763 (C−H^{phenyl}), 691 (C−H^{phenyl}). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.04 (s, 3H, Me), 2.37 (s, 3H, Me), 2.65−2.79 (m, 2H, CH_2), 3.11−3.28 (m, 2H, CH_2), 7.29−7.49 (m, 5H, CH^{phenyl}). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.4, 15.1, 29.3, 34.6, 110.2 (CBr), 127.4, 128.7, 130.1, 130.5, 131.6, 133.9, 135.46, 135.49, 170.0, 206.9 (C═O). MS, *m*/*z* (%): 346, 348 (48, $[M]^+$), 267 (100, $[M - Br]^+$). HRMS−FAB: *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_{15}BrOS$: 368.9919, 370.9899; found: 368.9915, 370.9894.

5. *2-(4-Bromo-2,5-dimethylthiophen-3-yl)-3-(4-bromophenyl)-cyclopent-2-en-1-one*. Yield: method B 0.38 g (90%), method C 0.39 g (92%), light yellow powder. Mp 123−125 °C (ethanol). IR (KBr), cm^{-1}: 3070 (C−H^{arom}), 2956 (C−H^{arom}), 2918 (CH_3, C−H^{arom}), 2851 (CH_3, C−H^{arom}), 1699 (C═O), 1617, 1582, 1481, 1358, 1287, 1186, 1171, 1007, 818 (C−H^{phenyl}). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.05 (s, 3H, Me), 2.37 (s, 3H, Me), 2.66−2.80 (m, 2H, CH_2), 3.07−3.18 (m, 2H, CH_2), 7.23 (d, *J* = 8.7 Hz, 2H, CH^{phenyl}), 7.47 (d, *J* = 8.3 Hz, 2H, CH^{phenyl}). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.4, 15.1, 29.1, 34.5, 109.9 (CBr), 125.0, 128.9, 129.7, 131.9, 132.0, 134.1, 134.3, 135.9, 168.3, 206.5 (C═O). MS, *m*/*z* (%): 424, 426, 428 (43, $[M]^+$), 345, 347 (77, $[M - Br]^+$), 266 (39, $[M - 2Br]^+$). Anal. Calcd for $C_{17}H_{14}Br_2OS$: C, 47.91; H, 3.31; Br, 37.50; S, 7.52. Found: C, 47.83; H, 3.26; Br, 37.45; S, 7.50.

6a. *5-Bromo-2,3-diphenylcyclopent-2-en-1-one*. Yield: method A 0.23 g (74%), yellow powder. Mp 121−123 °C (lit.[28] 122−123 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.38 (dd, *J* = 2.2, 18.7 Hz, 1H, 1/2CH_2), 3.74 (dd, *J* = 6.7, 18.7 Hz, 1H, 1/2CH_2), 4.66 (dd, *J* = 2.3, 6.7 Hz, 1H, CH), 7.21−7.42 (m, 10H, H^{phenyl}).

6b. *5-Bromo-2,3-bis(2,5-dimethylthiophen-3-yl)cyclopent-2-en-1-one*. Yield: method E 1.09 g (95%), method F 0.11 g (10%), method H 0.51 g (45%), method I 0.48 g (42%), method J 0.57 g (50%), method K 0.74 g (65%), green powder. Mp 125−127 °C (ethanol). IR (KBr), cm^{-1}: 2952 (C−H^{thioph}), 2916 (CH_3, C−H^{thioph}), 2852 (CH_3, C−H^{thioph}), 1696 (C═O), 1604, 1496, 1440, 1284, 716, 504. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.95 (s, 6H, 2Me), 2.38 (s, 6H, 2Me), 3.25 (dd, *J* = 2.2, 18.8 Hz, 1H, 1/2CH_2), 3.61 (dd, *J* = 6.9, 18.8 Hz, 1H, 1/2CH_2), 4.57 (dd, *J* = 2.2, 6.9 Hz, 1H, CH), 6.47 (s, 1H, H^{thioph}), 6.53 (s, 1H, H^{thioph}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2, 14.8, 15.1, 15.2, 42.1, 42.4, 124.8 (CH^{thioph}), 126.4 (CH^{thioph}), 128.2, 132.9, 133.0, 136.0, 136.2, 137.2, 138.8, 162.1, 200.5 (C═O). MS (EI, 70 eV): *m*/*z* (%) = 380, 382 (12) $[M]^+$, 301 (100) $[M - Br]^+$, 189 (54) $[M - Br - Th]^+$. Anal. Calcd for $C_{17}H_{17}BrOS_2$: C, 53.54; H, 4.49; Br, 20.95; S, 16.82. Found: C, 53.27; H, 4.80; Br, 20.91; S, 16.75.

6c. *5-Bromo-3-(2,5-dimethylthiophen-3-yl)-2-phenylcyclopent-2-en-1-one*. Yield: method E 0.75 g (72%), method F 0.26 g (25%), pale yellowish powder. Mp 132−133 °C (ethanol). IR (KBr), cm^{-1}: 2954 (C−H^{arom}), 2921 (CH_3, C−H^{arom}), 2853 (CH_3, C−H^{arom}), 1707 (C═O), 1613, 1594, 1496, 1444, 1376, 1305, 1290, 1171, 1142, 1116, 707 (C−H^{phenyl}), 696 (C−H^{phenyl}), 658, 595, 493. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.81 (s, 3H, Me), 2.40 (s, 3H, Me), 3.19−3.31 (m, 1H, 1/2CH_2), 3.53−3.67 (m, 1H, 1/2CH_2), 4.55−4.69 (m, 1H, CH), 6.57 (s, 1H, H^{thioph}), 7.27−7.39 (s, 4H, H^{phenyl}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.8, 15.1, 42.3, 42.5, 124.9, 128.1, 128.4, 129.0, 131.8, 132.4, 136.6, 137.57, 137.64, 162.5, 200.2. MS (EI, 70 eV): *m*/*z* (%) = 346, 348 (34) $[M]^+$, 267 (100) $[M - Br]^+$, 253 (68) $[M - CH(Br)]^+$, 211 (74) $[M - CH_2CH(Br)C(O)]^+$. Anal. Calcd for $C_{17}H_{15}BrOS$: C, 58.80; H, 4.35; Br, 23.01; S, 9.23. Found: C, 58.71; H, 4.40; Br, 23.14; S, 9.25.

6d. *5-Bromo-2-(2,5-dimethylthiophen-3-yl)-3-phenylcyclopent-2-en-1-one*. Yield: method E 0.60 g (58%), method F 0.22 g (21%), yellow powder. Mp 72−73 °C (ethanol). IR (KBr), cm^{-1}: 2918 (CH_3, C−H^{arom}), 2850 (CH_3, C−H^{arom}), 1705 (C═O), 1619, 1445, 1370, 1279, 1187, 1141, 1072, 1038, 763 (C−H^{phenyl}), 692 (C−H^{phenyl}). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.97 (s, 3H, Me), 2.42 (s, 3H, Me), 3.38 (dd, *J* = 1.5, 18.8 Hz, 1H, 1/2CH_2), 3.77 (dd, *J* = 7.0, 18.9 Hz, 1H, 1/2CH_2), 4.64 (dd, *J* = 1.8, 7.4 Hz, 1H, CH), 6.47 (s, 1H, H^{thioph}), 7.31−7.48 (m, 5H, H^{phenyl}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 15.3, 40.7, 41.6, 126.1, 127.8, 127.8, 128.0, 128.8, 128.9, 130.9, 133.4, 134.9, 135.5, 136.9, 164.4, 200.7 (C═O). MS (EI, 70 eV): *m*/*z* (%) = 346, 348 (15) $[M]^+$, 267 (100) $[M - Br]^+$, 233 (40) $[M - CH_2CH(Br) - CH_3]^+$, 211 (36) $[M - CH_2CH(Br)C(O)]^+$. HRMS−FAB: *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_{15}BrOS$: 368.9919, 370.9899; found: 368.9913, 370.9898.

6e. *5-Bromo-3-(4-bromophenyl)-2-(2,5-dimethylthiophen-3-yl)-cyclopent-2-en-1-one*. Yield: method E 0.96 g (75%), method F 0.40 g (31%), pale brown powder. Mp 151−152 °C (ethanol). IR

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(KBr), cm^{-1}: 2943 (C−H^{arom}), 2914 (CH_3, C−H^{arom}), 2853 (CH_3, C−H^{arom}), 1703 (C═O), 1614, 1368, 1072, 1008, 823 (C−H^{phenyl}), 494. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.99 (s, 3H, Me), 2.42 (s, 3H, Me), 3.34 (dd, J = 1.8, 18.8 Hz, 1H, 1/2CH_2), 3.74 (dd, J = 7.0, 18.5 Hz, 1H, 1/2CH_2), 4.62 (dd, J = 1.6, 6.8 Hz, 1H, CH), 6.43 (s, 1H, H^{thioph}), 7.26 (d, J = 8.4 Hz, 2H, H^{phenyl}), 7.48 (d, J = 8.4 Hz, 2H, H^{phenyl}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 15.3, 40.5, 41.3, 125.5, 125.9, 127.5, 129.3, 129.4, 132.1, 132.2, 133.7, 133.8, 135.7, 137.3, 162.8, 200.5 (C═O). MS (EI, 70 eV): m/z (%) = 424, 426, 428 (21) $[M]^+$, 345, 347 (58) $[M - Br]^+$, 291 (19) $[M - CH_2CH(Br)C(O)]^+$, 266 (61) $[M - 2Br]^+$, 223 (79) $[M - CH_2CH(Br) - CH_3]^+$, 211 (52) $[M - CH_2CH(Br)C(O) - Br]^+$. Anal. Calcd for $C_{17}H_{14}Br_2OS$: C, 47.91; H, 3.31; Br, 37.50; S, 7.52. Found: C, 47.63; H, 3.26; Br, 37.58; S, 7.54.

6f. *5-Bromo-2-(2,5-dimethylthiophen-3-yl)-3-naphthalen-1-ylcyclopent-2-en-1-one*. Yield: method E 0.98 g (82%), brown powder. Mp 68−69 °C (ethanol). IR (KBr), cm^{-1}: 2955 (C−H^{arom}), 2919 (CH_3, C−H^{arom}), 2850 (CH_3, C−H^{arom}), 1711 (C═O), 1460, 1439, 1376, 1260, 1102, 1022, 802 (C−H^{naph}), 777 (C−H^{naph}). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.83 (s, 3H, Me), 2.22 (s, 3H, Me), 3.39−3.51 (m, 1H, 1/2CH_2), 3.80 (dd, J = 6.1, 19.2 Hz, 1H, 1/2CH_2), 4.72 (d, J = 4.8 Hz, 1H, CH), 6.33 (s, 1H, H^{thioph}), 7.32−7.54 (m, 5H, $H^{naphtyl}$), 7.64 (d, J = 7.7 Hz,1H, $H^{naphtyl}$), 7.84−7.89 (m, 1H, $H^{naphtyl}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.4, 15.0, 42.0, 43.8, 124.9, 125.2, 125.3, 126.1, 126.4, 126.5, 126.8, 127.1, 128.7, 129.2, 129.9, 133.7, 134.3, 135.9, 136.3, 136.5, 167.0, 200.4 (C═O). MS (EI, 70 eV): m/z (%) = 396, 398 (19) $[M]^+$, 317 (82) $[M - Br]^+$, 302 (11) $[M - Br - CH_3]^+$, 274 (40) $[M - CH_2CH(Br) - CH_3]^+$, 261 (23) $[M - CH_2CH(Br)C(O)]^+$, 258 (45) $[M - CH_2CH(Br) - 2CH_3]^+$. HRMS−FAB: m/z $[M + Na]^+$ calcd for $C_{21}H_{17}BrOS$: 419.0076, 421.0056; found: 419.0069, 421.0056.

6g. *5-Bromo-3-(2,5-dimethylthiophen-3-yl)-2-naphthalen-1-ylcyclopent-2-en-1-one*. Yield: method E 1.05 g (88%), brown powder. Mp 65−66 °C (ethanol). IR (KBr), cm^{-1}: 2954 (C−H^{arom}), 2919 (CH_3, C−H^{arom}), 2850 (CH_3, C−H^{arom}), 1703 (C═O), 1605, 1439, 1401, 1309, 1142, 1044, 802 (C−H^{naph}), 779 (C−H^{naph}). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.82 (s, 3H, Me), 2.24 (s, 3H, Me), 3.34−3.53 (m, 1H, 1/2CH_2), 3.76−3.92 (m, 1H, 1/2CH_2), 4.64−4.87 (m, 1H, CH), 6.38 (s, 1H, H^{thioph}), 7.17−7.26 (m, 1H, $H^{naphtyl}$), 7.35−7.57 (m, 3H, $H^{naphtyl}$), 7.63−7.74 (m, 1H, $H^{naphtyl}$), 7.85 (d, J = 8.1 Hz, 2H, $H^{naphtyl}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.0, 15.4, 41.8, 42.7, 125.2, 125.3, 125.4, 125.9, 126.0, 126.3, 128.0, 128.4, 128.5, 129.0, 131.4, 132.2, 133.8, 136.6, 136.8, 163.7, 200.5 (C═O). MS (EI, 70 eV): m/z (%) = 396, 398 (18) $[M]^+$, 317 (58) $[M - Br]^+$, 302 (16) $[M - Br - CH_3]^+$, 261 (26) $[M - CH_2CH(Br)C(O)]^+$, 246 (24) $[M - CH_2CH(Br)C(O) - CH_3]^+$. Anal. Calcd for $C_{21}H_{17}BrOS$: C, 63.48; H, 4.31; Br, 20.11; S, 8.07. Found: C, 63.39; H, 4.28; Br, 20.05; S, 7.94.

6h. *5-Bromo-2,3-dinaphthalen-1-ylcyclopent-2-en-1-one*. Yield: method A 0.27 g (65%), white powder; Mp 195−197 °C (acetonitrile). IR (KBr), cm^{-1}: 3052 (C−H^{arom}), 1708 (C═O), 1616, 1508, 1344, 808 (C−H^{naph}), 772 (C−H^{naph}). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.49−3.71 (m, 1H, CH_2), 3.82−4.09 (m, 1H, CH_2), 4.77−4.98 (m, 1H, CH), 7.08−7.94 (m, 14H, 14CH^{naph}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 41.6 (CH_2), 44.4 (CH), 124.7, 124.9, 124.9, 125.1, 125.1, 125.9, 126.29, 126.30, 126.6, 127.8, 128.4, 128.6, 128.6, 128.94, 128.95, 129.6, 133.47, 133.48, 133.6, 133.7, 140.7, 169.6, 200.5 (C═O). MS (EI, 70 eV): m/z (%) = 412, 414 (100) $[M]^+$, 333 (30) $[M - Br]^+$, 278 (58) $[M - CH_2CH(Br)C(O)]^+$. Anal. Calcd for $C_{25}H_{17}BrO$: C, 72.65; H, 4.15. Found: C, 72.31; H, 4.08.

6i. *5-Bromo-2-(2,5-dimethylthiophen-3-yl)-3-(2-methyl-1-benzothiophen-3-yl)cyclopent-2-en-1-one*. Yield: method E 1.00 g (80%), method H 0.80 g (64%), yellow powder. Mp 67−68 °C (ethanol). IR (KBr), cm^{-1}: 2920 (CH_3, C−H^{arom}), 2853 (CH_3, C−H^{arom}), 1710 (C═O), 1619, 1432, 1379, 1281, 1259, 1139, 1074, 759, 731. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.86 (s, 3H, Me), 2.15 (s, 3H, Me), 2.31(s, 3H, Me), 3.08−4.01 (m, 2H, CH_2), 4.68 (t, J = 3.9 Hz, 1H, CH), 6.41 (s, 1H, H^{thioph}), 7.28−7.39 (m, 2H, $H^{benzthioph}$), 7.46−7.60 (m, 1H, $H^{benzthioph}$), 7.77 (d, J = 7.0 Hz, 1H, $H^{benzthioph}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.4, 15.0, 15.1, 42.0, 42.4, 121.8, 122.3, 124.3, 124.8, 126.0, 127.3, 128.3, 136.2, 136.5, 136.6, 138.0, 138.7, 139.5, 162.1, 200.4. MS (EI, 70 eV): m/z (%) = 416, 418 (1) $[M]^+$, 337 (100) $[M - Br]^+$, 367 (37) $[M - CH_2CH(Br)C(O) - CH_3]^+$. HRMS−FAB: m/z $[M + H]^+$ calcd for $C_{20}H_{17}BrOS_2$: 418.9957; found: 418.9950.

6j. *5-Bromo-3-(2,5-dimethylthiophen-3-yl)-2-(2-methyl-1-benzothiophen-3-yl)cyclopent-2-en-1-one*. Yield: method E 1.00 g (80%), gray powder. Mp 83−84 °C (ethanol). IR (KBr), cm^{-1}: 2918 (CH_3, C−H^{arom}), 2850 (CH_3, C−H^{arom}), 1706 (C═O), 1613, 1435, 1281, 1145, 757, 732. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.86−1.93 (m, 3H, Me), 2.15 (s, 1.5H, 1/2Me), 2.25 (s, 1.5H, 1/2Me), 2.31 (s, 3H, Me), 3.32−3.49 (m, 1H, 1/2CH_2), 3.75−3.89 (m, 1H, 1/2CH_2), 4.69 (dd, J = 5.5, 8.4 Hz, 1H, 1/2CH), 6.48 (s, 1H, H^{thioph}), 7.13−7.41 (m, 3H, $H^{benzthioph}$), 7.72 (d, J = 6.4 Hz, 1H, $H^{benzthioph}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.9, 15.0, 15.1, 41.8, 42.7, 121.9, 122.0, 122.2. 122.3, 123.7, 123.9, 124.0, 124.2, 124.7, 124.8, 131.5, 131.6, 132.6, 137.20, 137.24, 138.3, 138.6, 138.8, 139.5. 139.6, 139.7, 139.8, 164.3, 200.0 (C═O). MS (EI, 70 eV): m/z (%) = 416, 418 (13) $[M]^+$, 337 (100) $[M - Br]^+$, 322 (32) $[M - Br - CH_3]^+$, 277 (58) $[M - Br - SC(CH_3) - H]^+$, 225 (45) $[M - Br - Th]^+$. HRMS−FAB: m/z $[M + H]^+$ calcd for $C_{20}H_{17}BrOS_2$: 418.9957; found: 418.9956.

6k. *5-Bromo-2,3-bis(2-methyl-1-benzothiophen-3-yl)cyclopent-2-en-1-one*. Yield: method E 1.30 g (96%), brown powder. Mp 69−70 °C (ethanol). IR (KBr), cm^{-1}: 3057 (C−H^{arom}), 2917 (CH_3, C−H^{arom}), 2850 (CH_3, C−H^{arom}), 1712 (C═O), 1619, 1458, 1432, 1376, 1245, 1176, 1138, 759 (C−H^{arom}), 732 (C−H^{arom}). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.89−2.26 (m, 6H, 2Me), 3.28−3.51 (m, 1H, 1/2CH_2), 3.79−4.11 (m, 1H, 1/2CH_2), 4.67−4.90 (m, 1H, CHBr), 7.10−7.43 (m, 4H, H^{Bth}), 7.60−7.89 (m, 4H, H^{Bth}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.1, 15.2, 42.1, 42.8, 121.7, 121.8, 121.9, 123.1, 123.7, 123.8, 123.9, 124.3, 124.8, 127.9, 135.5, 135.6, 137.7, 138.2, 138.5, 140.2, 140.3, 165.0, 200.1 (C═O). MS (EI, 70 eV): m/z (%) = 452, 454 (48, $[M]^+$), 373 (76, $[M - Br]^+$). Anal. Calcd. for $C_{23}H_{17}BrOS_2$: C, 60.93; H, 3.78; Br, 17.62; S, 14.14. Found: C, 60.85; H, 3.79; Br, 17.69; S, 14.17.

6l. *5-Bromo-2-(2,5-dimethylthiophen-3-yl)-3-thiophen-2-ylcyclopent-2-en-1-one*. Yield: method E 0.79 g (75%), brown oil. IR (KBr), cm^{-1}: 3088 (C−H^{thioph}), 2916 (CH_3, C−H^{arom}), 2854 (CH_3, C−H^{arom}), 1702 (C═O), 1608, 1555, 1416, 1389, 1373, 1284, 1179, 1139, 1076, 864, 837, 713 (C−H^{thioph}), 576 (C−Br). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.15 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 3.43 (dd, J = 2.2, 18.3 Hz, 1H, CH_2), 3.83 (dd, J = 7.0, 18.3 Hz, 1H, CH_2), 4.64 (dd, J = 2.2, 7.0 Hz, 1H, CH), 6.43 (s, 1H, H^{thioph}), 7.06−7.13 (m, 1H, H^{thioph}), 7.41 (d, J = 3.3 Hz, 1H, H^{thioph}), 7.54 (d, J = 5.1 Hz, 1H, H^{thioph}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9, 15.4, 40.3, 41.6, 125.6, 127.4, 127.6, 130.4, 131.0, 133.0, 136.7, 137.4, 137.7, 158.1, 199.8 (C═O). MS (EI, 70 eV): m/z (%) = 352, 354 (10, $[M]^+$), 273 (100, $[M - Br]^+$). HRMS−FAB: m/z $[M + H]^+$ calcd for $C_{15}H_{13}BrOS_2$: 354.9663; found: 354.9637.

6m. *5-Bromo-3-(4-methoxyphenyl)-2-(3,4,5-trimethoxyphenyl)-cyclopent-2-en-1-one*. Yield: method E[61] 1.21 g (93%), orange powder. Mp 62−63 °C (ethanol). IR (KBr), cm^{-1}: 2997 (CH_3, C−H^{arom}), 2936 (CH_3, C−H^{arom}), 2838 (CH_3, C−H^{arom}), 1701 (C═O), 1602 (C═C), 1580 (C═C), 1503, 1451, 1413, 1364 (C═C), 1258 (C^{arom}-O), 1180 (CH_3), 1124 (CH_3), 1024 (C^{arom}-O), 1005, 833 ($CH^{p\text{-}phenyl}$). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.33 (dd, J = 1.8, 18.7 Hz, 1H, 1/2CH_2), 3.67−3.71 (m, 1H, 1/2CH_2), 3.73 (s, 6H, 2Me), 3.80 (s, 3H, Me), 3.86 (s, 3H, Me), 4.63 (dd, J = 2.1, 7.5 Hz, 1H, CH), 6.48 (s, 2H, H^{phenyl}), 6.82 (d, J = 8.4 Hz, 2H, H^{phenyl}), 7.35 (d, J = 8.4 Hz, 2H, H^{phenyl}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 40.7 ($CH_2^{cyclopent}$), 42.1 (CHBr), 55.5, 56.2, 61.0, 106.6, 114.1, 126.6, 127.5, 130.4, 135.5, 138.2, 153.6, 161.8, 164.2, 200.4 (C═O). MS (EI, 70 eV): m/z (%) = 432, 434 (100) $[M]^+$, 418 (50) $[M - CH_3]^+$, 353 (81) $[M - Br]^+$, 338 (45) $[M - Br - CH_3]^+$, 298 (25) $[M - C(O)CH(Br) - CH_3]^+$. HRMS−FAB: m/z $[M + Na]^+$ calcd for $C_{21}H_{21}BrO_5$: 455.0465, 457.0445; found: 455.0459, 457.0438.

7b. *5,5-Dibromo-2,3-bis(2,5-dimethylthiophen-3-yl)cyclopent-2-en-1-one*. Yield: method H 0.21 g (15%), method J 0.07 g (5%), brown powder. Mp 96−99 °C (ethanol). IR (KBr), cm^{-1}: 2952 (C−H^{thioph}), 2916 (CH_3, C−H^{thioph}), 2852 (CH_3, C−H^{thioph}), 1696 (C═O), 1604, 1496, 1440, 1284, 716, 504 (C−Br). ^1H NMR (300 MHz,

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$CDCl_3$): δ = 1.97 (s, 3H, Me), 2.01 (s, 3H, Me), 2.39 (s, 6H, 2Me), 4.10 (s, CH_2), 6.48 (s, 1H, H^{thioph}), 6.51 (s, 1H, H^{thioph}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2, 14.9, 15.1, 15.2, 54.4, 56.1, 124.7, 126.2, 127.7, 128.7, 131.9, 136.4, 136.6, 137.5, 140.0, 157.8, 194.0 (C═O). MS (EI, 70 eV): m/z (%) = 458, 460, 462 (11, $[M]^+$), 379, 381 (100, $[M - Br]^+$), 300 (50, $[M - 2Br]^+$). HRMS–FAB: m/z $[M + H]^+$ calcd for $C_{17}H_{16}Br_2OS_2$: 460.9061; found: 460.9058.

7i. *5,5-Dibromo-2-(2,5-dimethylthiophen-3-yl)-3-(2-methyl-1-benzothiophen-3-yl)cyclopent-2-en-1-one*. Yield: method H 0.15 g (10%), brown powder. Mp 96–99 °C (ethanol). IR (KBr), cm^{-1}: 3059 (C–H^{arom}), 2954 (C–H^{arom}), 2923 (CH_3, C–H^{arom}), 2854 (CH_3, C–H^{arom}), 1725 (C═O), 1613, 1456, 1433, 1378, 1286, 1256, 1201, 1139, 1066, 759 (C–$H^{benzthioph}$), 732 (C–$H^{benzthioph}$), 651. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.94 (s, 3H, CH_3), 2.16 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 3.96–4.48 (br. c, 2H, CH_2), 6.41 (c, 1H, H^{thioph}), 7.29–7.42 (m, 2H, $H^{benzthioph}$), 7.47–7.55 (m, 1H, $H^{benzthioph}$), 7.72–7.81 (m, 1H, $H^{benzthioph}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 14.9, 15.0, 54.5, 55.9, 121.6, 122.3, 124.4, 124.9, 125.7, 126.7, 127.2, 132.6, 136.3, 137.0, 137.7, 138.6, 140.5, 158.0, 193.6 (C═O). MS (EI, 70 eV): m/z (%) = 494, 496, 498 (15, $[M]^+$), 415, 417 (100, $[M - Br]^+$), 336 (71, $[M - 2Br]^+$). HRMS–FAB: m/z $[M + Na]^+$ calcd for $C_{20}H_{16}Br_2OS_2$: 516.8901; found: 516.8910.

8b. *4-Bromo-2,3-bis(2,5-dimethylthiophen-3-yl)cyclopent-2-en-1-one*. Yield: method F 0.55 g (48%), gray powder. Mp 124–127 °C (ethanol). IR (KBr), cm^{-1}: 2944 (C–H^{thioph}), 2912 (CH_3, C–H^{thioph}), 2852 (CH_3, C–H^{thioph}), 1708 (C═O), 1616, 1436, 1280, 1144, 832, 716, 492 (C–Br). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.87 (s, 3H, Me), 1.90 (s, 3H, Me), 2.38 (s, 3H, Me), 2.43 (s, 3H, Me), 3.08 (dd, J = 1.5, 19.8 Hz, 1H, 1/2CH_2), 3.35 (dd, J = 7.3, 20.5 Hz, 1H, 1/2CH_2), 5.41 (d, J = 6.6 Hz, 1H, CH), 6.48 (s, 1H, H^{thioph}), 6.66 (s, 1H, H^{thioph}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.36, 14.39, 15.27, 15.31, 46.3, 46.5, 124.4, 126.3, 127.5, 131.5, 136.3, 136.5, 137.1, 137.9, 138.7, 163.2, 202.3 (C═O). MS (EI, 70 eV): m/z (%) = 380, 382 (19, $[M]^+$), 301 (100, $[M - Br]^+$), 287 (32, $[M - CHBr - H]^+$), 246 (32, $[M - C(O)CH_2CHBr]^+$). HRMS–FAB: m/z $[M + Na]^+$ calcd for $C_{17}H_{17}BrOS_2$: 404.9776; found: 404.9756.

8c. *4-Bromo-3-(2,5-dimethylthiophen-3-yl)-2-phenylcyclopent-2-en-1-one*. Yield: method F 0.30 g (29%), brown powder. Mp 127–129 °C (ethanol). IR (KBr), cm^{-1}: 3061 (C–H^{arom}), 3064 (C–H^{arom}), 2966 (C–H^{arom}), 2943 (C–H^{arom}), 2914 (CH_3, C–H^{arom}), 2852 (CH_3, C–H^{arom}), 1698 (C═O), 1618, 1499, 1443, 1369, 1304, 1185, 1175, 1124, 772, 716 (C–H^{phenyl}), 695 (C–H^{phenyl}), 655, 579, 495 (C–Br). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.77 (s, 3H, Me), 2.45 (s, 3H, Me), 3.12 (dd, J = 1.5, 19.4 Hz, 1H, 1/2CH_2), 3.37 (dd, J = 6.6, 19.5 Hz, 1H, 1/2CH_2), 5.38 (dd, J = 1.1, 6.2 Hz, 1H, CH), 6.66 (s, 1H, H^{thioph}), 7.25–7.39 (m, 5H, H^{phenyl}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3, 15.3, 46.5, 46.5, 124.5, 128.4, 128.5, 129.0, 130.8, 131.0, 137.5, 137.6, 141.1, 163.4, 202.0 (C═O). MS (EI, 70 eV): m/z (%) = 346, 348 (16, $[M]^+$), 267 (100, $[M - Br]^+$), 211 (32, $[M - C(O)CH_2CHBr - H]^+$). HRMS–FAB: m/z $[M + Na]^+$ calcd for $C_{17}H_{15}BrOS$: 368.9919, 370.9899; found: 368.9919, 370.9895.

8d. *4-Bromo-2-(2,5-dimethylthiophen-3-yl)-3-phenylcyclopent-2-en-1-one*. Yield: method F 0.26 g (25%), brown powder. Mp 60–61 °C (ethanol). IR (KBr), cm^{-1}: 3025 (C–H^{arom}), 2917 (CH_3, C–H^{arom}), 2852 (CH_3, C–H^{arom}), 1704 (C═O), 1444, 1368, 1184, 775, 692 (C–H^{phenyl}), 493 (C–Br). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.89 (s, 3H, Me), 2.42 (s, 3H, Me), 3.14 (d, J = 19.4 Hz, 1H, 1/2CH_2), 3.39 (dd, J = 6.4, 19.2 Hz, 1H, 1/2CH_2), 5.61 (dd, J = 1.1, 6.2 Hz, 1H, CH), 6.51 (s, 1H, H^{thioph}), 7.32–7.48 (m, 5H, H^{phenyl}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2, 15.3, 44.4, 46.3, 126.2, 127.9, 128.3, 128.7, 128.8, 130.4, 133.7, 136.0, 136.9, 165.9, 202.7 (C═O). MS (EI, 70 eV): m/z (%) = 346, 348 (27, $[M]^+$), 267 (100, $[M - Br]^+$). HRMS–FAB: m/z $[M + Na]^+$ calcd for $C_{17}H_{15}BrOS$: 368.9919, 370.9899; found: 368.9916, 370.9897.

8e. *4-Bromo-3-(4-bromophenyl)-2-(2,5-dimethylthiophen-3-yl)-cyclopent-2-en-1-one*. Yield: method F 0.45 g (35%), brown powder. Mp 82–83 °C (ethanol). IR (KBr), cm^{-1}: 2919 (CH_3, C–H^{arom}), 2850 (CH_3, C–H^{arom}), 1705 (C═O), 1586, 1396, 1240, 1183, 1145, 1073, 1009, 830 (C–H^{phenyl}), 494 (C–Br). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.92 (s, 3H, Me), 2.42 (s, 3H, Me), 3.14 (dd, J = 1.6, 19.6 Hz, 1H, 1/2CH_2), 3.39 (dd, J = 6.4, 19.6 Hz, 1H, 1/2CH_2), 5.56 (dd, J = 1.4, 6.3 Hz, 1H, CH), 6.48 (s, 1H, H^{thioph}), 7.29 (d, J = 8.7 Hz, 2H, H^{phenyl}), 7.51 (d, J = 8.7 Hz, 2H, H^{phenyl}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2, 15.3, 44.0, 46.2, 124.9, 125.9, 126.9, 129.8, 132.0, 132.5, 136.1, 137.3, 138.0, 164.4, 202.4 (C═O). MS (EI, 70 eV): m/z (%) = 424, 426, 428 (37, $[M]^+$), 345, 347 (100, $[M - Br]^+$), 317, 319 (42, $[M - Br - C(O)]^+$), 266 (39, $[M - 2Br]^+$). Anal. Calcd for $C_{17}H_{14}Br_2OS$: C, 47.91; H, 3.31; Br, 37.50; S, 7.52. Found: C, 47.72; H, 3.29; Br, 37.47; S, 7.49.

2,3-Diaryl-4-methoxycyclopent-2-en-1-ones (General Procedure). *Method L*. To a solution of sodium methylate (1.20 mmol) in abs methanol (4 mL) 5-bromocyclopentenones ***6*** was added (1.00 mmol), the reaction mixture was stirred for 5 h at room temperature, the solvent was removed in vacuum, and the residue was purified by column chromatography eluting by petroleum ester/ethyl acetate 6:1.

9b. *2,3-Bis(2,5-dimethylthiophen-3-yl)-4-methoxycyclopent-2-en-1-one*. Yield: method H 0.18 g (18%), method I 0.50 g (50%), method L 0.07 g (22%), brown oil. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.89 (s, 6H, $2Me^{thioph}$), 2.38 (s, 3H, Me^{thioph}), 2.41 (s, 3H, Me^{thioph}), 2.59 (dd, J = 1.8, 16.5 Hz, 1H, 1/2CH_2), 2.91 (dd, J = 6.0, 12.4 Hz, 1H, 1/2CH_2), 3.39 (s, 3H, OMe), 4.88 (dd, J = 2.2, 3.7 Hz, 1H, CH), 6.47 (s, 1H, H^{thioph}), 6.64 (s, 1H, H^{thioph}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2, 14.6, 15.2, 15.2, 41.0, 56.7, 78.9, 125.3 (CH^{thioph}), 126.6 (CH^{thioph}), 128.2, 131.7, 136.0, 136.0, 136.6, 137.5, 138.3, 162.7, 203.3 (C═O). MS (EI, 70 eV): m/z (%) = 332 (48, $[M]^+$), 301 (30, $[M - OCH_3]^+$), 245 (33, $[M - CH_2CH(OCH_3)C(O)]^+$). HRMS–FAB: m/z $[M + Na]^+$ calcd for $C_{18}H_{20}O_2S_2$: 355.0797; found: 355.0800.

9i. *2-(2,5-Dimethylthiophen-3-yl)-4-methoxy-3-(2-methyl-1-benzothiophen-3-yl)cyclopent-2-en-1-one*. Yield: method H 0.09 g (8%), brown oil. IR (KBr), cm^{-1}: 3060 (C–H^{arom}), 2956 (CH_3, C–H^{arom}), 2925 (CH_3, C–H^{arom}), 2854 (CH_3, C–H^{arom}), 1704 (C═O), 1606, 1527, 1461, 1436, 1380, 1354, 1287, 1259, 1232, 1193, 1152, 1106 (OCH_3), 1082, 1017, 765 (C–$H^{benzthioph}$), 751 (C–$H^{benzthioph}$), 730 (C–$H^{benzthioph}$). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.83 (s, 3H, CH_3), 2.04 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 2.60–3.14 (m, 2H, CH_2), 3.22 (s, 3H, CH_3), 4.93–5.31 (m, 1H, CH), 6.36 (c, 1H, H^{thioph}), 7.24–7.48 (m, 2H, $H^{benzthioph}$), 7.61–7.85 (m, 2H, $H^{benzthioph}$). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2, 14.5, 15.1, 42.1, 57.9, 78.8, 121.3, 122.4, 124.0, 124.6, 126.2, 127.3, 136.0, 136.4, 138.6, 140.5, 140.8, 163.2, 203.2 (C═O). MS (EI, 70 eV): m/z (%) = 368 (52, $[M]^+$), 337 (25, $[M - OCH_3]^+$). HRMS–FAB: m/z $[M + Na]^+$ calcd for $C_{21}H_{20}O_2S_2$: 391.0797; found: 391.0792.

Thizoles 10 (General Procedure). The mixture of 5-bromocyclopentenones ***6*** (0.16 mmol) and thiobenzamide (0.16 mmol) in absolute ethanol (2 mL) was refluxed for 10 h, poured into ice–water (20 mL), and extracted with methylene chloride (2 × 10 mL). The combined organic phases were washed with water (2 × 10 mL), dried with magnesium sulfate and evaporated; the residue was crystallized from ethanol.

10a. *4,5-Bis(2,5-dimethylthiophen-3-yl)-2-phenyl-6H-cyclopenta-[d][1,3]thiazole*. Yield: 0.05 g (77%), gray powder. Mp 144–145 °C (ethanol). IR (KBr), cm^{-1}: 2936 (C–H^{arom}), 2912 (CH_3, C–H^{arom}), 2848 (CH_3, C–H^{arom}), 1452, 1440, 1136, 768, 688. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.95 (s, 3H, Me), 2.09 (s, 3H, Me), 2.43 (s, 3H, Me), 2.45 (s, 3H, Me), 3.76 (s, 2H, CH_2), 6.57 (s, 1H, H^{thioph}), 6.80 (s, 1H, H^{thioph}), 7.38–7.51 (m, 3H, Ph), 8.00 (d, J = 6.2 Hz, 2H, Ph). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3, 14.5, 15.3, 15.4, 37.7 ($CH_2^{cyclopent}$), 126.5, 126.5, 127.1, 128.9, 129.6, 131.4, 131.8, 132.2, 133.2, 134.4, 134.8, 134.9, 135.4, 135.7, 140.1, 167.0, 170.7. MS (EI, 70 eV): m/z (%) = 419 (100) $[M]^+$. HRMS–FAB: m/z $[M + H]^+$ calcd for $C_{24}H_{21}NS_3$: 420.0909; found: 420.0905.

10b. *4,5-Dinaphthalen-1-yl-2-phenyl-6H-cyclopenta[d][1,3]-thiazole*. Yield: 0.02 g (22%), yellow powder. Mp 205–207 °C (ethanol). IR (KBr), cm^{-1}: 3048 (C–H^{arom}), 2961 (C–H^{arom}), 2923 (CH_3, C–H^{arom}), 2853 (CH_3, C–H^{arom}), 1504, 1449, 1391, 1374, 1261, 1097, 1028, 800 (C–H^{arom}), 777 (C–H^{arom}), 763 (C–H^{arom}), 692, 685. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.11 (s, 2H, CH_2), 7.19–7.52 (m, 11H, H^{arom}), 7.65–7.73 (m, 2H, H^{arom}), 7.78 (t, J = 7.2 Hz, 2H, H^{arom}), 7.90–8.03 (m, 3H, H^{arom}), 8.08 (d, J = 8.1 Hz, 1H, H^{arom}).

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^{13}C NMR (75 MHz, $CDCl_3$): δ = 39.6 ($CH_2^{cyclopent}$), 125.25, 125.31, 125.4, 125.6, 125.7, 125.9, 125.9, 126.6, 126.8, 127.4, 127.7, 127.8, 128.1, 128.2, 128.3, 128.8, 128.9, 129.7, 131.9, 132.0, 132.4 133.0, 133.6, 133.8, 134.7, 135.4, 138.0, 145.7, 160.3, 167.3, 171.1. MS (EI, 70 eV): m/z (%) = 451 (100, $[M]^+$), 347 (36, $[M - PhC{=}N - H]^+$). HRMS–FAB: m/z $[M + H]^+$ calcd for $C_{32}H_{21}NS$: 452.1467; found: 452.1461.

Nucleophilic Substitutions of Bromine Atom by Phenol and Thiophenol (General Procedure). To a solution of phenol or thiophenol (1.20 mmol) in abs benzene (5 mL), metallic sodium (1.25 mmol) was added, and the reaction mixture was stirred at room temperature overnight (sodium was dissolved entirely); then, 5-bromoketone **6b** (1.00 mmol) was added, and reaction mixture was refluxed for 2 h, poured into cold water (70 mL), and extracted with ethyl acetate (3 × 20 mL). The combined organic phases were washed with water (30 mL), dried with magnesium sulfate, and solvent was removed under vacuum. The residue was purified by column chromatography eluting by petroleum ester/ethyl acetate 10:1.

11a. *2,3-Bis(2,5-dimethylthiophen-3-yl)-5-phenoxycyclopent-2-en-1-one.* Yield: 0.24 g (60%), brown oil. IR (KBr), cm^{-1}: 3062 (C–H^{arom}), 3039 (C–H^{arom}), 2946 (C–H^{arom}), 2916 (CH_3, C–H^{arom}), 2856 (CH_3, C–H^{arom}), 1711 (C=O), 1598, 1589, 1449, 1438, 1387, 1280, 1244, 1226, 1142, 1071, 828, 753 (C–H^{arom}), 691, 495. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.95 (s, 6H, 2Me), 2.39 (s, 6H, 2Me), 3.07 (dd, J = 2.4, 17.7 Hz, 1H, 1/2CH_2), 3.45 (dd, J = 6.3, 17.5 Hz, 1H, 1/2CH_2), 5.01 (dd, J = 2.4, 6.0 Hz, 1H, CHO), 6.53 (s, 1H, H^{thioph}), 6.56 (s, 1H, H^{thioph}), 7.01–7.13 (m, 3H, H^{Ph}), 7.28–7.39 (m, 2H, H^{Ph}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3, 14.8, 15.1, 15.2, 38.8 ($CH_2^{cyclopent}$), 75.8 (CHO), 115.4, 115.7, 121.6, 124.9, 126.4, 128.4, 129.5, 133.3, 135.7, 136.0, 138.6, 158.0, 161.6, 202.5 (C=O). MS (EI, 70 eV): m/z (%) = 394 (45, $[M]^+$), 301 (100, $[M - PhO]^+$). HRMS–FAB: m/z $[M + Na]^+$ calcd for $C_{23}H_{22}O_2S_2$: 417.0953; found: 417.0946.

11b. *2,3-Bis(2,5-dimethylthiophen-3-yl)-5-(phenylsulfanyl)-cyclopent-2-en-1-one.* Yield: 0.27 g (67%), brown oil. IR (KBr), cm^{-1}: 3057 (C–H^{arom}), 2919 (CH_3, C–H^{arom}), 2854 (CH_3, C–H^{arom}), 1698 (C=O), 1626, 1438, 1381, 1280, 1142, 1074, 831, 747, 692, 490. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.78 (s, 3H, Me), 1.79 (s, 3H, Me), 2.36 (s, 3H, Me), 2.38 (s, 3H, Me), 2.96 (dd, J = 2.5, 18.6 Hz, 1H, 1/2CH_2), 3.42 (dd, J = 7.8, 19.3 Hz, 1H, 1/2CH_2), 3.92 (dd, J = 2.9, 7.3 Hz, 1H, CHS), 6.43 (m, 2H, H^{thioph}), 7.25–7.33 (m, 2H, H^{Ph}), 7.49–7.58 (m, 3H, H^{Ph}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 14.6, 15.1, 15.3, 39.6 ($CH_2^{cyclopent}$), 48.3 (CHS), 124.8, 126.4, 127.2, 127.6, 128.1, 128.6, 129.0, 129.1, 132.6, 133.2, 133.4, 134.9, 135.4, 135.9, 136.9, 137.1, 137.7, 163.6, 203.5 (C=O). MS (EI, 70 eV): m/z (%) = 410 (9, $[M]^+$), 301 (100, $[M - SPh]^+$). HRMS–FAB: m/z $[M + Na]^+$ calcd for $C_{23}H_{22}OS_3$: 433.0725; found: 433.0709.

1-[3,4-Bis(2,5-dimethylthiophen-3-yl)-2-oxocyclopent-3-en-1-yl]-pyrrolidine-2,5-dione ***12***. The mixture of 5-bromoketone **6b** (0.26 mmol), succinimide (0.29 mmol), and potassium carbonate (0.26 mmol) in abs acetone (5 mL) was stirred at room temperature for 24 h, poured into cold water (60 mL), and extracted with ethyl acetate (3 × 20 mL). The combined organic phases were washed with water (2 × 30 mL), dried with magnesium sulfate, and solvent was removed under vacuum. The residue was purified by column chromatography eluting by petroleum ester/ethyl acetate 1:1.

Yield: 0.06 g (55%), gray powder. Mp 58–59 °C (hexane). IR (KBr), cm^{-1}: 2950 (C–H^{thioph}), 2918 (CH_3, C–H^{thioph}), 2857 (CH_3, C–H^{thioph}), 1707 (C=O), 1399, 1282, 1165, 1143, 824. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.96 (s, 3H, Me), 1.97 (s, 3H, Me), 2.38 (s, 6H, 2Me), 2.71–2.98 (m, 4H, 2CH_2^{succ}), 3.14–3.29 (m, 2H, $CH_2^{cyclopent}$), 4.81–4.95 (m, 1H, CHN), 6.45 (s, 1H, H^{thioph}), 6.54 (s, 1H, H^{thioph}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2, 14.8, 15.1, 15.2, 28.4 (2CH_2^{succ}), 35.5 (2$CH_2^{cyclopent}$), 52.5 (CHN), 125.0, 126.4, 128.5, 133.2, 134.6, 135.9, 136.0, 136.9, 138.3, 162.1, 176.4 (2C=O^{succ}), 200.3 (C=$O^{cyclopent}$). MS (EI, 70 eV): m/z (%) = 399 (100, $[M]^+$), 384 (56, $[M - CH_3]^+$), 300 (45, $[M$ – succinimide$]^+$), 285 (26, $[M$ – succinimide – $CH_3]^+$). HRMS–FAB: m/z $[M + H]^+$ calcd for $C_{21}H_{21}NO_3S_2$: 400.1036; found: 400.1035.

Introduction of Morpholine Residue into the Ethene "Bridge" (General Procedures). *Method M.* The solution of bromoketone **6b** (for compound **13**) or **9b** (for compound **15**) (0.30 mmol) in morpholine (2 mL) was stirred at room temperature for 20 min, poured into cold water (30 mL), and extracted with ethyl acetate (2 × 15 mL). The combined organic phases were washed with water (2 × 10 mL), dried with magnesium sulfate, and solvent was removed under vacuum. The residue was recrystallized from petroleum ester.

Method N. To a solution of 5-bromoketone **6b** (0.50 mmol) in abs dichloromethane (3 mL) at −70 °C, DBU (2.50 mmol) was added; after the reaction mixture stirred for 30 min at (−60 to −70) °C, morpholine (2.00 mmol) was added, and the mixture was allowed to slowly (during 2 h) heat to room temperature. The solvent was removed in vacuum and the residue was purified by flash chromatography eluting by petroleum ester/ethyl acetate 2:1→1:1.

13. *2,3-Bis(2,5-dimethylthiophen-3-yl)-5-morpholin-4-ylcyclopent-2-en-1-one.* Yield: method M 0.11 g (91%), gray powder. Mp 121–123 °C (hexane). IR (KBr), cm^{-1}: 2944 (C–H^{thioph}), 2916 (CH_3, C–H^{thioph}), 2864 (CH_3, C–H^{thioph}), 1696 (C=O), 1612, 1440, 1292, 1144 (C–N), 1116 (C–O), 856. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.91 (s, 3H, Me), 1.92 (s, 3H, Me), 2.36 (s, 3H, Me), 2.39 (s, 3H, Me), 2.57–2.71 (m, 2H, CH_2N), 2.82–2.96 (m, 2H, CH_2N), 2.99 (d, J = 5.1 Hz, 2H, $CH_2^{cyclopent}$), 3.57 (t, J = 5.0 Hz, 1H, CH), 3.76 (t, J = 4.0 Hz, 4H, 2CH_2O), 6.43 (s, 1H, H^{thioph}), 6.56 (s, 1H, H^{thioph}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3, 14.8, 15.1, 15.2, 33.4 ($CH_2^{cyclopent}$), 49.9 (2CH_2N), 67.15 (2CH_2O), 67.20 (CHN), 125.1, 126.5, 128.8, 133.7, 135.4, 135.9, 136.9, 137.9, 162.5, 205.6 (C=O). MS (EI, 70 eV): m/z (%) = 387 (2, $[M]^+$), 302 (64, $[M$ – morph$]^+$), 246 (100, $[M - CH_2CH(morph)C(O)]^+$), 190 (32, $[M$ – morph – Th$]^+$). HRMS–FAB: m/z $[M + Na]^+$ calcd for $C_{21}H_{25}NO_2S_2$: 410.1219; found: 410.1216.

15. *2,3-Bis(2,5-dimethylthiophen-3-yl)-4-morpholin-4-ylcyclopent-2-en-1-one.* Yield: method M 0.07 g (59%), method N 0.08 g (40%), brown powder. Mp 191–121 °C (hexane). IR (KBr), cm^{-1}: 2958 (C–H^{thioph}), 2918 (CH_3, C–H^{thioph}), 2853 (CH_3, C–H^{thioph}), 2816 (C–H^{thioph}), 1703 (C=O), 1616, 1495, 1446, 1346, 1280, 1257, 1142 (C–N), 1115 (C–O), 1014, 857, 827, 755, 734, 492. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.86 (s, 3H, Me), 1.92 (s, 3H, Me), 2.38 (s, 3H, Me), 2.40 (s, 3H, Me), 2.43–2.52 (m, 4H, 2CH_2N), 2.53–2.78 (m, 2H, $CH_2^{cyclopent}$), 3.54–3.69 (m, 4H, 2CH_2O), 4.38–4.45 (m, 1H, CH), 6.45 (s, 1H, H^{thioph}), 6.63 (s, 1H, H^{thioph}). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3, 14.6, 15.3 (2 signals), 34.2 ($CH_2^{cyclopent}$), 48.6 (2CH_2N), 65.2, 67.2, 125.8, 126.6, 128.4, 132.4, 135.6, 135.9, 136.0, 137.5, 138.2, 164.4, 204.7 (C=O). MS (EI, 70 eV): m/z (%) = 387 (14, $[M$ – morph$]^+$), 257 (30, $[M - CH_2C(O) - H_2]^+$). HRMS–FAB: m/z $[M + Na]^+$ calcd for $C_{21}H_{25}NO_2S_2$: 410.1219; found: 410.1215.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H, ^{13}C NMR spectra and 2D-NMR experiments of compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

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■ REFERENCES

(1) Larock, R. C. *Comprehensive Organic Transformations*, 2nd ed.; VCH Publishers Inc.: New York, 1999; pp 715–719.

(2) de Kimpe, N.; Verhe, R. *The chemistry of a -haloketones, or-haloaldehydes and a-haloimines*, Patai, S., Rappoport, Z., Eds.; ; John Wiley & Sons Ltd.: New York, 1988; pp 1−225.
(3) Dagani, M. J.; Barda, H. J.; Benya, T. J.; Sanders, D. C. *Ullmann's Encyclopedia of Industrial Chemistry: Bromine Compounds*; Wiley-WCH Verlag GmbH & Co.: Weinheim, 2002.
(4) Erian, A. W.; Sherif, S. M.; Gaber, H. M. *Molecules* **2008**, *8*, 793−865.
(5) Smith, M. B.; March, J. *March's Advanced Organic Chemistry, Reactions, Mechanisms and Structure*, 6th ed.; John Wiley & Sons: New Jersey, 2006.
(6) Mikolajczyk, M. in *Antibiotics and Antiviral Compounds*, Krohn, K., Kirst, H. A., Maag, H., Eds.; VCH: Weinheim, 1993; pp 205−213.
(7) Diaz-Maroto, M. C.; Perez-Coello, M. S.; Vinas, M. A. G.; Cabezudo., M. D. *J. Agric. Food Chem.* **2003**, *51*, 1265−1269.
(8) Kirchhoff, E. W.; Aikens, J.; Cassidy, C. *Chem. Innovation* **2000**, *30*, 52−53.
(9) Santoro, M. G. *Trends Microbiol.* **1997**, *5*, 276−281.
(10) Behrendt, J. *Microbiology* **2011**, *157*, 3435−3445.
(11) Gurjar, M. K.; Wakharkar, R. D.; Singh, A. T.; Jaggi, M.; Borate, H. B.; Shinde, P. D.; Verma, R.; Rajendran, P.; Dutt, S.; Singh, G.; Sanna, V. K.; Singh, M. K.; Srivastava, S. K.; Mahajan, V. A.; Jadhav, V. H.; Dutta, K.; Krishnan, K.; Chaudhary, A.; Agarwal, S. K.; Mukherjee, R.; Burman, A. C. *J. Med. Chem.* **2007**, *50*, 1744−1753.
(12) Mull, E.; Sattigeri, V.; Rodriguez, A.; Katzenellenbogen, J. *Bioorg. Med. Chem.* **2002**, *10*, 1381.
(13) Zhao, D.; Xu, F.; Chen, C.; Tillyer, R.; Grabowski, E.; Reider, P.; Black, C. W.; Ouimet, N.; Prasit, P. *Tetrahedron* **1999**, *55*, 6001.
(14) Brian, P.; Riggle, P. J.; Santos, R. A.; Champness, W. C. *J. Bacteriol.* **1996**, *178*, 3221−3231.
(15) Nam, N.-H.; Kim, Y.; You, Y.; Hong, D.; Kim, H.; Ahn, B. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 1955.
(16) *Proc. Natl. Acad. Sci. U.S.A.* **2001**, *98*, 12317−12319
(17) Patent WO2011073060
(18) U.S. Patent 1956 2768965
(19) Class, T. J.; Ando, T.; Casida, J. E. *J. Agric. Food. Chem.* **1990**, *38*, 529−537.
(20) Black, W. C.; Brideau, C.; Chan, C.-C.; Charleson, S.; Chauret, N.; Claveau, D.; Ethier, D.; Gordon, R.; Greig, G.; Guay, J.; Hughes, G.; Jolicoeur, P.; Leblanc, Y.; Nicoll-Griffith, D.; Ouimet, N.; Riendeau, D.; Visco, D.; Wang, Z.; Xu, L.; Prasit, P. *J. Med. Chem.* **1999**, *42*, 1274−1281.
(21) Nam, N.-H.; Kim, Y.; You, Y.-J.; Hong, D.-H.; Kim, H.-M.; Ahn, B.-Z. *Bioorg. Med. Chem.* **2003**, *11*, 1021−1029.
(22) Gurjar, M. K.; Wakharkar, R. D.; Singh, A. T.; Jaggi, M.; Borate, H. B.; Shinde, P. D.; Verma, R.; Rajendran, P.; Dutt, S.; Singh, G.; Sanna, V. K.; Singh, M. K.; Srivastava, S. K.; Mahajan, V. A.; Jadhav, V. H.; Dutta, K.; Krishnan, K.; Chaudhary, A.; Agarwal, S. K.; Mukherjee, R.; Burman, A. C. *J. Med. Chem.* **2007**, *50*, 1744−1753.
(23) Rouhi, A. M. *Chem. Eng. News* **1999**, *77* (43), 38−46.
(24) Tonari, K.; Sameshima., K. *J. Jpn. Oil Chem. Soc.* **2000**, *49*, 583.
(25) Hobbs, G.; Obanye, A. I.; Petty, J. *J. Bacteriol.* **1992**, *174*, 1487−1494.
(26) Straus, D. S.; Glass, C. K. *Med. Res. Rev* **2001**, *21*, 185−210.
(27) Shirinian, V. Z.; Shimkin, A. A.; Lonshakov, D. V.; Lvov, A. G.; Krayushkin, M. M. *J. Photochem. Photobiol. A: Chem.* **2012**, *233*, 1.
(28) Ayt, A.; Barachevsky, V.; Kobeleva, O.; Valova, T.; Gorelik, A.; Krayushkin, M.; Komlenok, M.; Kononenko, V. *Phys. Status Solidi C* **2011**, *8*, 2866.
(29) Barachevsky, V. A.; Kobeleva, O. I.; Valova, T. M.; Ait, A. O.; Dunaev, A. A.; Gorelik, A. M.; Krayushkin, M. M.; Levchenko, K. S.; Yarovenko, V. N.; Kyiko, V. V.; Grebennikov, E. H. *Proc. SPIE* **2010**, *7722*, 772225−1.
(30) Dürr, H., Bouas-Laurent, H., Eds. *Photochromism: Molecules and Systems*; Elsevier: Amsterdam, 2003.
(31) Irie, M. *Chem. Rev.* **2000**, *100*, 1685.
(32) Tian, H.; Yang, S. *Chem. Soc. Rev.* **2004**, *33*, 85.
(33) Choi, T.; Ma, E. *Molecules* **2007**, *12*, 74.
(34) Mignani, S.; Bohme, G. A.; Boireau, A.; Cheve, M.; Damour, D.; Debono, M.-W.; Genovois-Borella, A.; Imperato, A.; Jimonet, P.; Pratt, J.; Randle, J. C. R.; Ribeill, Y.; Vuilhorgne, M.; Stutzmann, J. M. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 591.
(35) Esses-Reiter, K.; Reiter, J. *J. Heterocycl. Chem.* **1996**, *33*, 879.
(36) Tandon, V. K.; Awasthi, A. K.; Singh, K. A.; Maurya, H. K.; Gautam, S. K. *Heterocycles* **2010**, *80*, 593.
(37) Boberg, F.; Deters, K.; Schulz, J.; Torges, K.-F. *Phosph., Sulf., Silic. Relat. Elem.* **1994**, *91*, 69.
(38) Benati, L.; Leardini, R.; Minozzi, M.; Nanni, D.; Spagnolo, P.; Strazzari, S; Zanardi, G.; Calestani, G. *Tetrahedron* **2002**, *58*, 3485.
(39) Prakash, O.; Aneja, D. K.; Hussain, K.; Lohan, P.; Ranjan, P.; Arora, S.; Sharma, C.; Aneja, K., R. *Eur. J. Med. Chem.* **2011**, *46*, 5065.
(40) Rorer S. A. U. S. Patent 5,902,803; 1999.
(41) Jimonet, P.; Bohme, G. A.; Bouquerel, J.; Boireau, A.; Damour, D.; Debono, M. W.; Genevois-Borella, A.; Hardy, J.-C.; Hubert, P.; Manfre, F.; Nemecek, P. *Bioorg. Med. Chem. Let.* **2001**, *11*, 127.
(42) Chatterjee, A.; Banerjee, S. *J. Ind. Chem. Soc.* **1964**, *41*, 643.
(43) Fouad, F. S.; Xi, Z.; Goldberg, I. H.; Jones, G. B. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 3337.
(44) Seeger, D. E.; Lahti, P. M.; Rossi, A. R.; Berson, J. A. *J. Am. Chem. Soc.* **1986**, *108*, 1251.
(45) Pravst, I.; Zupan, M; Stavber, S *Tetrahedron Lett.* **2006**, *47*, 4707.
(46) Pravst, I.; Zupan, M.; Stavber, S. *Tetrahedron.* **2008**, *64*, 5191.
(47) Chiba, S; Xu, Y.-J.; Wang, Y.-F. *J. Am. Chem. Soc.* **2009**, *131*, 12886.
(48) Meshram, H. M.; Reddy, P. N.; Vishnu, P.; Sadashiv, K.; Yadav, J. S. *Tetrahedron Lett.* **2006**, *47*, 991.
(49) Voets, M.; Antes, I.; Scherer, C.; Mueller-Vieira, U.; Biemel, K.; Marchais-Oberwinkler, S.; Hartmann, R. W. *J. Med. Chem.* **2006**, *49*, 2222.
(50) Fitzgerald, D. H.; Muirhead, K. M.; Botting, N. P. *Bioorg. Med. Chem.* **2001**, *9*, 983.
(51) Tillu, V. H.; Shinde, P. D.; Bedekar, A. V.; Wakharkar, R. D. *Synth. Commun.* **2003**, *33*, 1399.
(52) Zhang, R.; Dong, J.; Xu, Y.-g.; Hua, W.-y.; You, Q.-d.; Wen, N. *Eur. J. Med. Chem.* **2009**, *44*, 3771.
(53) A full version of this table includes studies in other solvents and is available in the Supporting Information.
(54) Kosower, E. M.; Cole, W. J.; Wu, G. S.; Cardy, D. E.; Meisters, G. *J. Org. Chem.* **1963**, *28*, 630.
(55) Kosower, E. M.; Wu, G. S. *J. Org. Chem.* **1963**, *28*, 633.
(56) Kojima, J.; Kawaguchi, Sh. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 1293.
(57) Kojima, J.; Usui, K.; Kawaguchi, Sh. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 3127.
(58) Rioz-Martinez, A.; De Gonzalo, G.; Gotor, V. *Synthesis* **2010**, 110.
(59) Minuti, L.; Taticchi, A.; Gacs-Baitz, E.; Marrocchi, A. *Tetrahedron.* **1995**, *51*, 8953.
(60) Gupta, R. C.; Nautiyal, P.; Jhingran, A. G.; Kamboj, V. P.; Setty, B. S.; Anand, N. *Ind. J. Chem., Sect. B: Org. Chem. Med. Chem.* **1981**, *20*, 303.
(61) The full conversion of initial compound **1m** in contrast of other cyclopentenones **1b-l** has already been attained under room temperature.