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Grob Fragmentation of Norbornyl α-Diketones: A Route to α-Ketoenols and Aromatic Compounds

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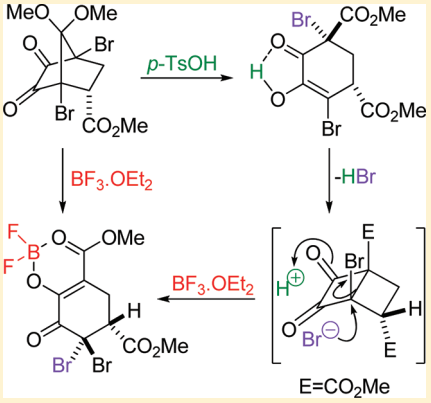
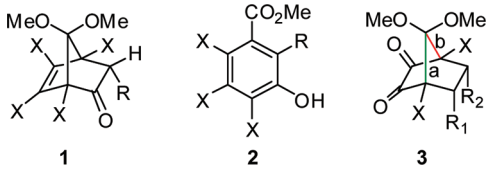
Supporting Information

ABSTRACT: An efficient acid-catalyzed Grob fragmentation of symmetrical and asymmetrically substituted norbornyl α-diketones to the corresponding six-membered α-ketoenols is reported. The regio- and stereochemical outcome of the Grob fragmentation of C2 mono- and disubstituted α-diketones was investigated. A single regioisomer resulting from a favorable half-chair intermediate was normally observed. A departure from the normal course was noticed for C2 disubstituted α-diketones possessing an *exo*-methyl and an *endo*-methoxycarbonyl derivative, giving the opposite regioisomers due to initial formation of the hemiketal. The bromo analogues of the C2 disubstituted α-diketones furnished an unusual byproduct, which appears to have been formed through highly reactive fused four-membered bicyclo[2.2.0]hexane intermediates. A plausible mechanistic proposal involving the *gem*-dihalo intermediate, which in one case was actually isolated as its BF_2-complex, is outlined. The fragmentation protocol was applied to various norbornyl substrates including bis-α-diketone derivatives. The methodology was successfully utilized for the synthesis of substituted aromatic compounds.



INTRODUCTION

Heterolytic fragmentation of a σ bond activated by electrofugal and nucleofugal groups situated in positions 1 and 3 on an aliphatic chain, known as Grob fragmentation, is an important tool in organic syntheses.[1] This strategy is particularly rewarding when fashioned in a stereoselectively constructed rigid bi- or polycyclic system to eventually unravel the target skeleton. The predictable stereochemical outcome of this fragmentation has been elegantly utilized by Mulzer and others in a variety of natural product syntheses.[2,3]



1 **2** **3**

We have reported a highly efficient Grob fragmentation of 1,4,5,6-tetrahalo-7,7-dimethoxybicyclo[2.2.1]hept-5-en-2-one **1** (R = H), occurring spontaneously upon heating, to give trihalophenol derivative **2**.[4] The alkyl- or aryl-substituted derivatives of **1** (R = alkyl or aryl) underwent transformation to **2** in presence of an acid catalyst. It occurred to us that norbornyl α-diketones **3**, prepared efficiently from the corresponding tetrahalo norbornyl derivatives,[5] would be interesting substrates to study Grob fragmentation. Particularly, for monosubstituted diketones **3** (R^2 = H), the regiochemical outcome resulting from the cleavage of either bond a or b due to two competing carbonyl nucleofuge groups would be an additional factor of curiosity.

RESULTS AND DISCUSSIONS

Initially, norbornyl α-diketone **3a** derived from Diels−Alder adduct of cyclohexene with 5,5-dimethoxy-1,2,3,4-tetrachlorocyclo-pentadiene was subjected to a variety of acid-mediated fragmentation conditions. The acids such as AcOH, 10% aq HCl, TFA, and *p*-toluenesulfonic acid (PTSA) were explored in combination with solvents such as AcOH, MeOH, 1,2-DCE, toluene, and benzene. Optimization studies revealed that PTSA in toluene gave the best results in terms of yield, reaction time, and equivalents of acid used (Table 1).

The reaction conditions optimized for **3a** were then extended to other norbornyl α-diketones, and the results are summarized in Table 1. The bromo analogue **3b** also underwent smooth transformation to give the corresponding α-ketoenol **4b** in near quantitative yield. Similarly, the chloro as well as bromo derivatives of cyclopentane- and cyclooctane-fused norbornyl α-diketones **3c,d,e,f** furnished the corresponding bicyclic α-ketoenols **4c,d,e,f** in high yield (Table 2, entries 3-6).

In order to probe the regiochemical outcome, monosubstituted norbornyl α-diketones (R^2 = H) were considered. The

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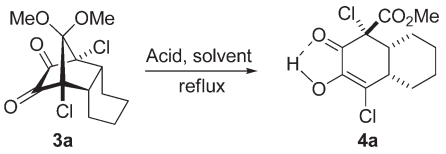
endo-phenyl substituted chloro and bromo derivatives **3g,h** upon treatment with PTSA exclusively furnished, in each case, a single regioisomer **4g,h** arising from the cleavage of bond a. The *endo*-methoxycarbonyl derivatives **3i,j** also showed a similar trend and gave excellent yields of **4i,j** (Table 2, entries 7−10).

Table 1. Solvent and Acid Screening for the Fragmentation Reaction

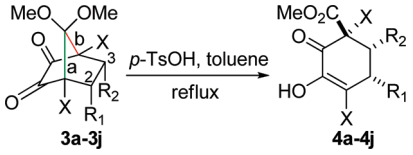


3a **4a**

no.	acid	solvent	*t* (h)	yield (%)
1	AcOH	AcOH	6	91
2	AcOH[a]	benzene	14	100
3	10% HCl[b]	MeOH	9	95
4	TFA[c]	1,2-DCE	4	100
5	*p*-TsOH (4 equiv)	benzene	3	100
6	*p*-TsOH (2 equiv)	Toluene	2.5	98

[a] Excess (40 equiv). [b] 2 mL per 1 mmol. [c] 10 equiv.

Table 2. PTSA-Mediated Grob Fragmentation of 3



3a-3j **4a-4j**

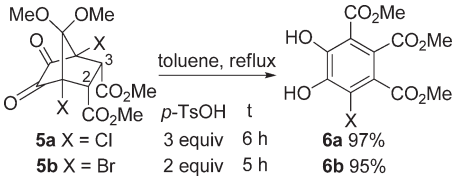
no.	R^1, R^2	X	*p*-TsOH (equiv)	*t* (h)	product (% yield)
1	$-(CH_2)_4-$	Cl	2	2.5	**4a** (98)
2	$-(CH_2)_4-$	Br	1	2.5	**4b** (98)
3	$-(CH_2)_3-$	Cl	2	1.5	**4c** (95)
4	$-(CH_2)_3-$	Br	1	0.5	**4d** (84)
5	$-(CH_2)_6-$	Cl	3	4.0	**4e** (98)
6	$-(CH_2)_6-$	Br	2	4.0	**4f** (85)
7	Ph, H	Cl	2	1.5	**4g** (100)
8	Ph, H	Br	1	1.0	**4h** (97)
9	CO_2Me, H	Cl	2	2.0	**4i** (99)
10	CO_2Me, H	Br	1	0.75	**4j** (95)

A plausible mechanism to account for the exclusive formation of a single regioisomer is depicted in Scheme 1. Protonation is equally likely at either of the two competing carbonyl nucleofuge groups 1 and 2. Protonation at carbonyl 1 of **3** triggers fragmentation of bond a leading to half-chair **X** *via* the intermediate $\mathbf{X^1}$. Since the substituent R^1 would have a *trans* 1,3-relationship to the newly formed axial CO_2Me group, it occupies sterically comfortable pseudoequatorial position. The enol moiety is well poised for intramolecular hydrogen bonding. Alternatively, protonation at carbonyl 2 followed by cleavage of bond b is expected to furnish the other possible regioisomer **Y** *via* the intermediate $\mathbf{Y^1}$. This pathway is not preferred due to unfavorable 1,2-diaxial disposition of R^1 and newly formed CO_2Me group.

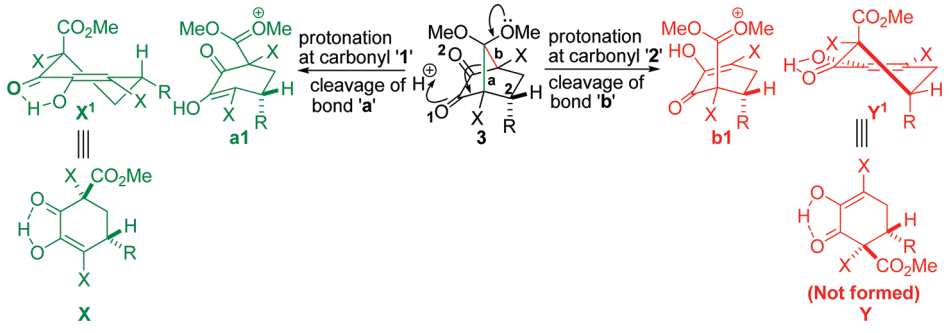
Interestingly, the diester substituted α-diketones **5a** and **5b** when subjected to acid-mediated reaction furnished substituted aromatic compounds **6a** and **6b** (Scheme 2). The electron-withdrawing ester substituent present at C-3 renders the α-hydrogen acidic, thereby facilitating elimination of HX from the initially formed enol intermediate and leading to the observed aromatic products.

We turned our attention to C2 disubstituted α-diketones in order to investigate the regio- and stereochemical outcome of the Grob fragmentation. The α-diketones **7a,b** possessing a methyl as well as an ester groups at C2 were subjected to the fragmentation reaction (Scheme 3). Intriguingly, hemiketals **8a,b** were isolated in excellent yield when the reaction was stopped after 30 min. However, continuation of the reaction or exposing the isolated hemiketals **8a,b** to the same conditions for a prolonged period furnished cleavage products (Scheme 3). Treatment of the crude reaction mixture with diazomethane followed by column purification gave a single diastereomer **9a** as a colorless viscous liquid in case of chloro analogue, whereas in case of bromo derivative two diastereomers **10a** and **10b** were obtained. Analysis of ^1H and ^{13}C NMR showed a close resemblance and consistency between **9a** and **10a**, indicating that these two belonged to the same series. The molecular connectivity in **9a** was unambiguously established through 2D NMR studies

Scheme 2. Grob Fragmentation of α-Diketone Followed by *in Situ* Aromatization of α-Ketoenol



Scheme 1. Plausible Mechanism for the Grob Fragmentation of Monosubstituted 3



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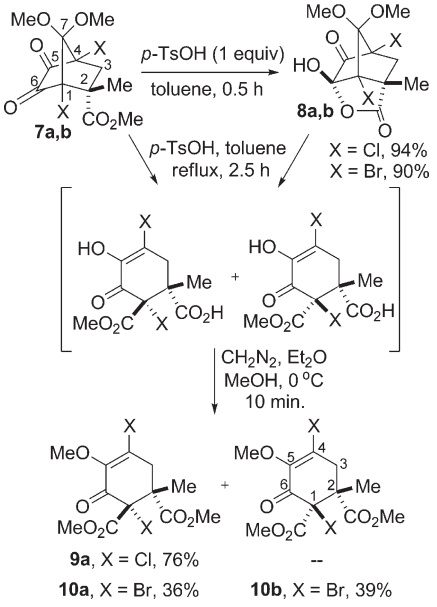
(HMBC). Contrary to C2 monosubstituted α-diketones, back-side bond b ruptured in these cases to furnish **9a** and **10a**. The isomer **10b**, formed only in the case of the bromo analogue, appeared to be unusual in the sense that the HMBC spectrum showed similar molecular connectivity as **10a** (see Supporting Information). Therefore, in order to assign the structure unequivocally, the bromo derivative **10b** was subjected to single crystal X-ray analysis.[6a] To our astonishment, the C1 center in **10b** (nonepimerizable!) got inverted.

Exclusive cleavage of back-side bond b (C4−C7) could be due to the initial formation of hemiketals **8a,b** in which carbonyl 1 is engaged thus facilitating the protonation at carbonyl 2. To confirm this premise, **12a,b** in which the ester is replaced with a phenyl group were exposed to similar cleavage conditions. Once again, chloro analogue **12a** furnished a single isomer **13a**, whereas bromo analogue **12b** resulted in a mixture of two products **14a,b** as depicted in Scheme 4. Structural assignments for **13a** and **14a** were based on internal consistency and extensive analysis of 2D NMR (HMBC, NOESY; see Supporting Information). The difficulty encountered in the purification of the minor isomer **14b** was overcome by repeated crystallization of enriched fractions obtained from preparative HPLC (hexane/dichloromethane). The structure of isomer **14b** was secured through single crystal X-ray analysis.[6b] In accordance with our proposal, all the products from **12a,b** resulted *via* cleavage of front bond a.

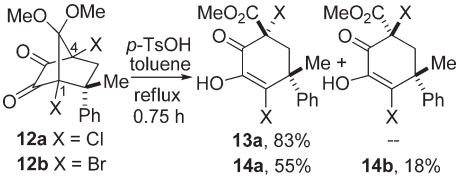
Formation of **10b** as well as **14b** is highly unexpected on the basis of the known mechanism. The inversion at the nonepimerizable C1 or C4 centers (α-bromo ester substituted carbon) in these compounds must be taking place *via* a novel pathway. To rationalize the experimental results obtained so far and particularly to account for the unusual products obtained in case of bromo analogues, a comprehensive mechanistic proposal is delineated in Scheme 5. Under acidic conditions the proton could approach either carbonyl 1 or 2. If proton approaches carbonyl 1, cleavage of bond a would lead to the formation of intermediate **a1**, where as if proton approaches carbonyl 2, cleavage of bond b would lead to the formation of intermediate **b1**.

These intermediates would then lead to highly reactive fused four-membered bicyclo[2.2.0]hexane intermediates **a2** or **b2** via intramolecular nucleophilic displacement. The HX released during this process would then trigger spontaneous opening of **a2** or **b2**, as depicted in Scheme 5, leading to *gem*-dihalo substituted products **a3** or **b3**. The *gem*-dihalo substituted intermediate **a3** or **b3** could undergo one more iteration of the

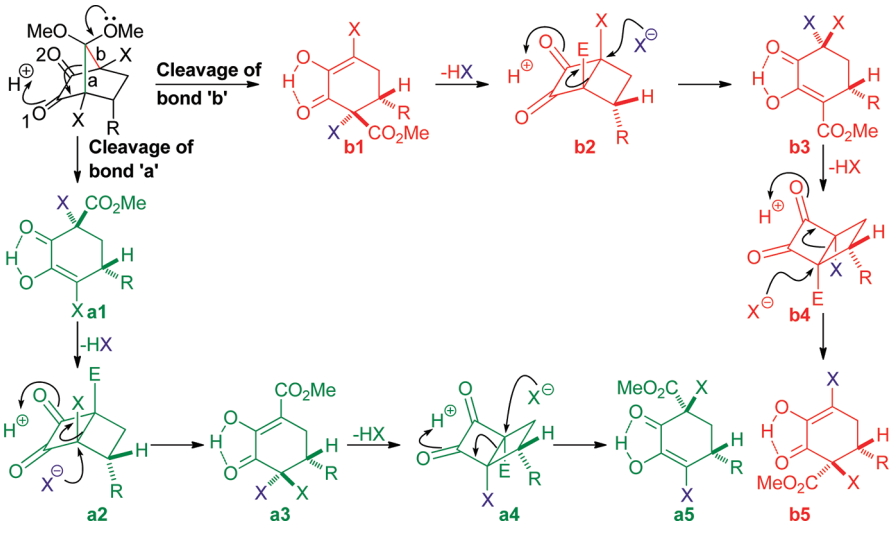
Scheme 3. Unusual Grob Fragmentation of C2 Disubstituted α-Diketones 7a,b



Scheme 4. Grob Fragmentation of α-Diketones 12a,b



Scheme 5. Plausible Mechanism for the Formation of Unusual Products



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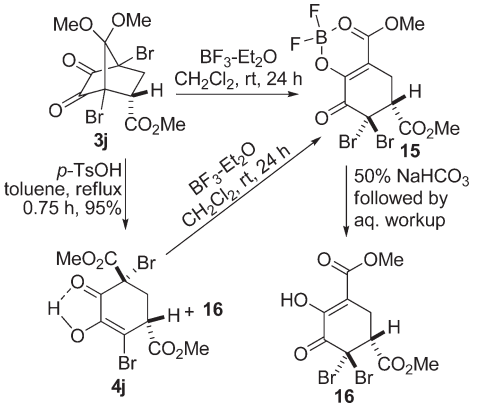
above processes via intramolecular nucleophilic displacement to **a4** or **b4** followed by HX-mediated regeneration of six-membered derivatives **a5** or **b5**.

Formation of **14b**, **10b** corresponding to **a5**, **b5** provided experimental support for the proposed mechanism in Scheme 5. Nevertheless, isolation of the *gem*-dibromo substituted product **a3** would provide additional support. In this endeavor **3j** was subjected to $BF_3 \cdot Et_2O$ in dichloromethane for 24 h. A crystalline product was obtained upon storage of the reaction mixture in deep refrigerator (−10 °C). A single crystal X-ray analysis of this sparingly soluble material revealed its structure to be a BF_2-complex of *gem*-dibromo derivative **15** (Scheme 6).[7,8a] When BF_2-complex **15** was washed with 50% aqueous sodium bicarbonate solution, decomplexed product **16** was obtained. It was also noticed that depending on the delay in recording the ^{1}H NMR spectrum of **4j**, tiny peaks corresponding to **16** popped up in the otherwise clean spectrum. Interestingly, deliberate storage of a ^{1}H NMR sample ($CDCl_3$) of freshly crystallized batch of **4j**, initially showing no detectable peaks of **16** in PMR, showed formation of a substantial amount of **16** (2:1 ratio) when analyzed after 20 days of storage in a refrigerator. In order to secure the structure of **4j** unequivocally, a single crystal X-ray analysis of a crystal picked from the above-mentioned authentic batch was performed.[8b] Further, when another authentic portion of **4j** was subjected to $BF_3 \cdot Et_2O$ reaction, the same BF_2-complex **15** was obtained (Scheme 6).

The fragmentation methodology was extended to bis-α-diketones **17** and **19**. Subjecting these derivatives to optimized conditions furnished the two regiomeric products **18a,b** and **20a, b**, respectively (Scheme 7). The products **18a** and **20a** are formed as a result of front bond−front bond fragmentation, whereas **18b**, **20b** resulted from the cleavage of front bond−back bond in the two norbornyl segments of **17** and **19**.

Scheme 6. Key Experimental Evidence for the Mechanistic Proposal



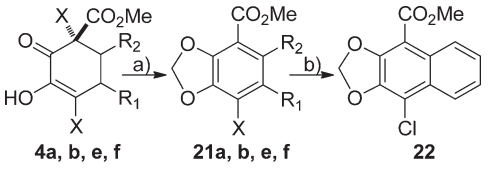
Synthesis of Highly Substituted Aromatic Compounds (Benzene, Naphthalene, Anthracene, Indane, Biphenyl Derivatives). The synthetic importance of catechol derivatives and their presence in various forms in innumerable natural products prompted us to develop a practical methodology through Grob fragmentation of abundantly available norbornyl α-diketones. Catechols, especially, protected as dioxolanes serve as flavors and fragrances.[9] Our aim was to get protected catechols directly in a one-pot protocol from Grob fragmentation products.

Grob fragmentation products **4a,b,e,f** were treated with DBU-CH_2Cl_2 to achieve aromatization as well as protection of *in situ* generated catechol derivatives by CH_2Cl_2.[10] The reaction proceeded smoothly leading to protected aromatic compounds **21a,b,e,f** in good yield (Table 3). Further, the tetrahydronaphthalene derivative **21a** obtained from the fragmented product **4a** was transformed to naphthalene derivative **22** in excellent yield *via* DDQ oxidation (Table 3).[11]

Mono-O-methylated catechol is an important structural element in many common day-to-day use natural products such as curcumin, vanillin, eugenol, gingerol, etc. Methylation of the enol moiety in Grob fragmentation products followed by aromatization would provide an easy access to mono-O-methylated catechols. In order to demonstrate this, α-ketoenols **4c,d,g,h** were exposed to an ethereal solution of diazomethane followed by DBU mediated aromatization. Excellent yields of mono-O-methylated catechols derivatives **23c,d,g,h** were obtained as shown in Table 4.

An impressive extension of this convenient methodology to a highly functionalized anthracene moiety is depicted in Scheme 8. When the bis-diketone **24** was subjected to *p*-TsOH conditions, an inseparable mixture of Grob-fragmented products **25a,b** were obtained. Methylation of enol using diazomethane followed by DBU treatment of O-methylated products **26a,b** gave a column

Table 3. Preparation of Methylene Protected Tetrahydronaphthalenes, Naphthalene, and Cyclooctane Appended Aromatic Compounds



no.	R^1, R^2	X	product (% yield)
1	-$(CH_2)_4$-	Cl	**21a** (86)
2	-$(CH_2)_4$-	Br	**21b** (85)
3	-$(CH_2)_6$-	Cl	**21e** (81)
4	-$(CH_2)_6$-	Br	**21f** (77)

[a] DBU, CH_2Cl_2, 0 °C to rt, 43 h. [b] DDQ, C_6H_6, reflux, 36 h, 91%.

Scheme 7. Demonstration of Fragmentation Protocol to Bis-α-diketone Derivatives

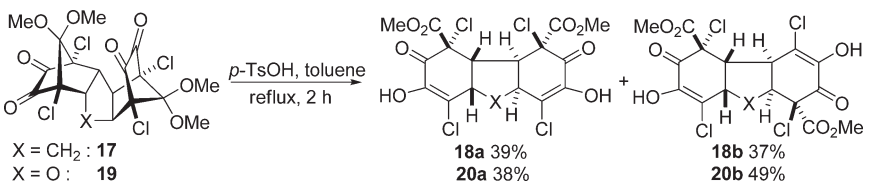


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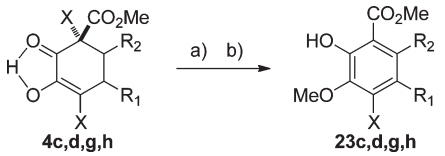
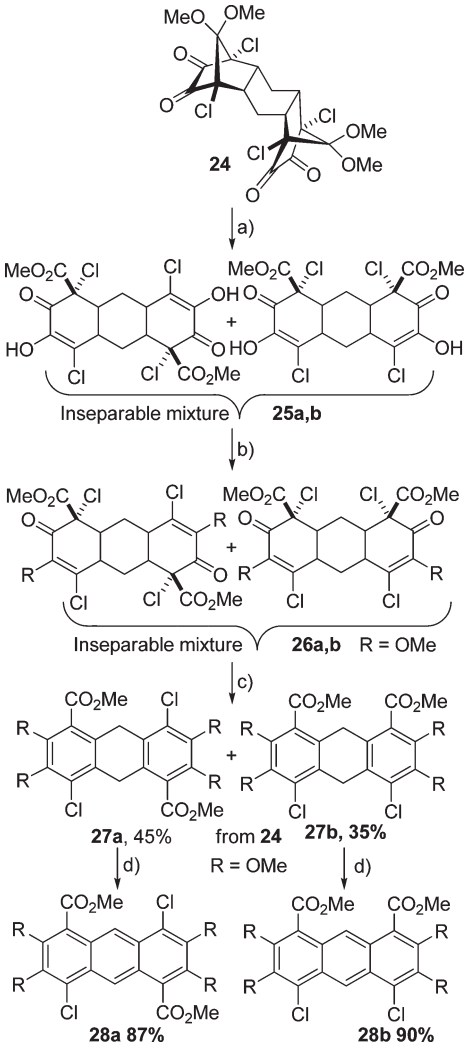
Table 4. Preparation of O-Methylated Indanols and Biphenolic Compounds



no.	R^1, R^2	X	product (% yield)
1	-$(CH_2)_3$-	Cl	**23c** (91)
2	-$(CH_2)_3$-	Br	**23d** (80)
3	Ph, H	Cl	**23g** (93)
4	Ph, H	Br	**23h** (82)

[a] CH_2N_2, Et_2O/MeOH, 0 °C, 20 min. [b] DBU, CH_2Cl_2, 0 °C, 1 h.

Scheme 8. Synthesis of Highly Substituted Anthracene Derivatives[a]



[a] Reagents and conditions: a) *p*-TsOH, toluene, reflux, 3 h, 94%; b) CH_2N_2, Et_2O-MeOH, 0 °C, 30 min.; c) DBU, MeI, CH_2Cl_2, 0 °C to rt, 24; d) DDQ, C_6H_6, reflux, 100 °C, 20 h.

chromatographically separable mixture of tetramethylated compounds **27a,b** with an impressive 45% and 35% overall yield from **24**. The central ring aromatization of **27a,b** was carried out in presence of DDQ to obtain the highly substituted anthracene derivatives **28a,b** (Scheme 8).

CONCLUSIONS

In conclusion, a facile acid-catalyzed Grob fragmentation of norbornyl α-diketone to six-membered α-ketoenols was achieved. Monosubstituted norbornyl α-diketones (R^2 = H) furnished a single regioisomer *via* cleavage of bond a. However, C2 disubstituted α-diketone possessing an *exo*-methyl and an *endo*-methoxycarbonyl derivative gave the opposite regioisomers due to initial formation of hemiketals. The selectivity reverted back when the *endo*-methoxycarbonyl group was changed to a phenyl group in the aforementioned derivatives. The bromo analogues of the aforesaid C2 disubstituted α-diketones furnished an unusual byproduct, which is probably formed *via* a highly reactive fused four-membered bicyclo[2.2.0]hexane intermediates. The *gem*-dihalo derivative described in the proposed mechanism was isolated as its BF_2-complex. The fragmentation protocol was also demonstrated to various substrates including bis-α-diketone derivatives. The methodology was successfully utilized for the synthesis of a variety of substituted aromatic compounds.

EXPERIMENTAL SECTION

General Methods. All reactions were performed in oven-dried apparatus. Commercial grade solvents were distilled before use. Melting points were obtained in open capillary tubes and are uncorrected. Infrared spectra were recorded as KBr pellets (solids), or as thin films on NaCl flats (liquids). ^{1}H NMR was recorded at 400 MHz unless otherwise mentioned 500 MHz. Proton decoupled ^{13}C NMR was recorded at 100 MHz unless otherwise mentioned 125 MHz. 2D NMR experiments were conducted for the structure confirmation of some of the compounds (see Supporting Information for HMBC of **9a**, **10b** and NOESY and HMBC for **13a**). Single crystal X-ray analysis was carried out for the structure elucidation of compounds **4d**, **10b**, **14b** and **15** (see Supporting Information for CIF data files). HRMS were recorded using electron spray ionization (ESI) or electron ionization (EI) mode.

Methyl 1,4-Dichloro-3-hydroxy-2-oxo-1,2,4a,5,6,7,8,8a-octahydronaphthalene-1-carboxylate (4a). To a stirred solution of α-diketone **3a** (200 mg, 0.652 mmol) in toluene (4 mL) was added *p*-toluenesulfonic acid (*p*-TsOH, 225 mg, 1.305 mmol), and the reaction mixture was refluxed for 2.5 h. The solvent was removed under reduced pressure. The residue was dissolved in ethyl acetate (20 mL), washed with saturated $NaHCO_3$ (5 mL) and brine (5 mL), and dried over anhydrous Na_2SO_4. After evaporation of solvent under reduced pressure, the crude reaction mixture was purified by silica gel column chromatography to afford the colorless crystalline compound with near quantitative yield. R_f (10% ethyl acetate in hexane) 0.5, colorless crystalline solid, mp 120 °C, yield 98% (187 mg, 0.639 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.20 (s, 1H), 3.83 (s, 3H), 3.11 (d, 1H, J = 3.6 Hz), 2.88 (td,1H, J = 3.8, 12.2 Hz), 2.45 (d, 1H, J = 12.2 Hz), 2.05 (dd, 1H, J = 3.4, 13.1 Hz), 1.84 (dd, 1H, J = 3.8, 7.8 Hz), 1.61−1.50 (m, 2H), 1.38−1.18 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.3, 166.5, 144.0, 130.3, 74.6, 54.2, 46.3, 38.3, 28.9, 24.7, 21.8, 21.1; IR (KBr) 3423, 2949, 2858, 1735, 1693, 1632, 1448, 1351, 1248, 1168, 855, 714 cm^{-1}; HRMS (EI) calcd for $C_{12}H_{14}O_4Cl_2$, 292.0269; found, 292.0269.

Methyl 1,4-Dibromo-3-hydroxy-2-oxo-1,2,4a,5,6,7,8,8a-octahydronaphthalene-1-carboxylate (4b). Experimental procedure is similar to that for compound **4a**. R_f (10% ethyl acetate in hexane) 0.5, colorless crystalline solid, mp 121 °C, yield 98% (193 mg,

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0.504 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.29 (s, 1H), 3.80 (s, 3H), 3.24 (s, 2H), 2.93 (td, 1H, J = 3.5, 12.7 Hz), 2.43 (d, 1H, J = 13.4 Hz), 2.06 (d, 1H, J = 13.2 Hz), 1.81 (d, 1H, J = 13.2 Hz), 1.54 (s, 2H), 1.37−1.13 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.2, 166.7, 144.8, 123.9, 69.1, 54.3, 46.9, 39.3, 31.2, 25.0, 23.2, 20.8. IR (KBr) 3420, 2965, 2910, 1745, 1695, 1635, 1450, 1430, 1350, 1170, 1015, 855 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{14}O_4Br$, 2379.9259; found, 379.9258.

Methyl 4,7-Dichloro-6-hydroxy-5-oxo-2,3,3a,4,5,7a-hexahydro-1*H*-indene-4-carboxylate (4c). Experimental procedure is similar to that for compound **4a**. R_f (10% ethyl acetate in hexane) 0.6, colorless solid, mp 104 °C, yield 95% (200 mg, 0.72 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78 (s, 3H), 3.29−3.19 (m, 2H), 2.29−2.26 (m, 1H), 2.07−1.92 (m, 2H), 1.73−1.63 (m, 2H), 1.52−1.47 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.1, 166.4, 142.8, 130.7.0, 71.9, 54.3, 47.3, 44.6, 32.6, 26.1, 22.4; IR (KBr) 3450, 2995, 1750, 1690, 1640, 1430, 1240, 1110, 1000, 810 cm^{-1}; HRMS (EI) calcd for $C_{11}H_{12}O_4Cl_2$, 278.0113; found, 278.0110.

Methyl 4,7-Dibromo-6-hydroxy-5-oxo-2,3,3a,4,5,7a-hexahydro-1*H*-indene-4-carboxylate (4d). Experimental procedure is similar to that for compound **4a**. R_f (10% ethyl acetate in hexane) 0.6, colorless solid, mp 100 °C, yield 84% (200 mg, 0.54 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.81 (s, 3H), 3.40−3.34 (m, 2H), 2.39−2.34 (m, 1H), 2.12−2.00 (m, 2H), 1.75−1.69 (m, 1H), 1.67−1.61 (m, 1H), 1.56−1.51 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.0, 166.6, 143.8, 124.0, 64.8, 54.3, 48.0, 45.8, 34.6, 27.4, 22.0; IR (KBr) 3450, 2965, 1735, 1675, 1630, 1430, 1230, 1105, 1000, 805 cm^{-1}. Anal. Calcd for $C_{11}H_{12}O_4Br_2$: C, 35.90; H, 3.29. Found: C, 35.72; H, 3.11.

Methyl 1,4-Dichloro-3-hydroxy-2-oxo-1,2,4a,5,6,7,8,9,-10,10a-decahydrobenzo[8]annulene-1-carboxylate (4e). Experimental procedure is similar to that for compound **4a**. Basic alumina column purification is essential to obtain pure product. R_f (10% ethyl acetate in hexane) 0.6, colorless solid, mp 108−109 °C, yield 98% (100 mg, 0.31 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.03 (s, 1H), 3,78 (s, 3H), 2.96 (s, 2H), 1.88−1.18 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.6, 199.9, 140.4, 129.8, 73.4, 54.2, 44.4, 41.8, 27.9, 26.1; IR (KBr) 3450, 2995, 1775, 1690, 1640, 1480, 1450, 1370, 1190, 1015, 835, 750 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{18}O_4Cl_2$ (M + H), 321.0660; found, 321.0660.

Methyl 1,4-Dibromo-3-hydroxy-2-oxo-1,2,4a,5,6,7,8,9,-10,10a-decahydrobenzo[8]annulene-1-carboxylate (4f). Experimental procedure is similar to that for compound **4a**. Basic alumina column purification is essential to obtain pure product. R_f (10% ethyl acetate in hexane) 0.5, colorless viscous liquid, yield 85% (150 mg, 0.37 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.17 (s, 1H), 3.77 (s, 3H), 3.09 (s, 2H), 1.76−1.18 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.7, 166.6, 54.4, 52.7, 45.1, 43.1, 29.7, 27.8, 26.2; IR (KBr) 3400, 2945, 1740, 1675, 1635, 1450, 1005, 795 cm^1; HRMS (ESI) calcd for $C_{14}H_{18}O_4Br_2$ (M + H), 408.9650; found, 408.9651.

Methyl 1,4-Dichloro-3-hydroxy-2-oxo-5-phenylcyclohex-3-enecarboxylate (4g). Experimental procedure is similar to that for compound **4a**. R_f (20% ethyl acetate in hexane) 0.5, colorless crystalline solid, mp 127−128 °C, yield 100% (150 mg, 0.48 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.36 (m, 3H), 7.23 (d, 2H, J = 6.8 Hz), 6.42 (s, 1H), 4.10 (dd, 1H, J = 4.9, 10.2 Hz), 3.91 (s, 3H), 3.22 (dd, 1H, J = 4.9, 13.9 Hz), 2.55 (dd, 1H, J = 10.5, 13.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.0, 168.8, 144.2, 139.9, 131.6, 129.03, 128.97, 128.1, 67.3, 54.5, 45.9, 44.3; IR (KBr) 3350, 3040, 2955, 1745, 1695, 1640, 1490, 1440, 1320, 1195, 1020, 910, 855, 810, 750, 700 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{12}O_4Cl_2$ (M + H), 315.0191; found, 315.0190.

Methyl 1,4-Dibromo-3-hydroxy-2-oxo-5-phenylcyclohex-3-enecarboxylate (4h). Experimental procedure is similar to that for compound **4a**. R_f (20% ethyl acetate in hexane) 0.5, colorless crystalline solid, mp 145−146 °C, yield 97% (160 mg, 0.40 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46−7.38 (m, 3H), 7.23 (d, 2H, J = 6.8 Hz), 6.55 (s, 1H), 4.19 (dd, 1H, J = 4.7, 10.4 Hz), 3.92 (s, 3H), 3.39 (dd, 1H, J = 4.7, 13.9 Hz), 2.70 (dd, 1H, J = 10.4, 13.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.0, 165.8, 144.2, 139.8, 131.6, 129.03, 128.2, 128.0, 67.3, 54.5, 45.9, 44.3; IR (KBr) 3320, 3040, 2955, 1745, 1695, 1640, 1490, 1440, 1320, 1195, 1020, 910, 855, 810, 750, 700 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{12}O_4Cl_2$, 401.9102; found, 401.9101.

Dimethyl 1,4-Dichloro-5-hydroxy-6-oxocyclohex-4-ene-1,3-dicarboxylate (4i). Experimental procedure is similar to that for compound **4a**. R_f (20% ethyl acetate in hexane) 0.5, colorless crystalline solid, mp 155−156 °C, yield 99% (100 mg, 0.34 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.36 (s, 1H), 3.84 (s, 3H), 3.82 (dd, 1H, J = 6.5, 7.9 Hz), 3.79 (s, 3H), 3.17 (dd, 1H, J = 5.6, 13.9 Hz), 2.83 (dd, 1H, J = 7.3, 14.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.2, 169.7, 165.7, 143.7, 125.3, 66.4, 54.5, 53.2, 45.9, 37.7; IR (KBr) 3385, 2985, 1745, 1700, 1650, 1440, 1355, 1170, 1030, 975, 900, 835, 740, 705 cm^{-1}; HRMS (EI) calcd for $C_{10}H_{10}O_6Cl_2$, 295.9854; found, 295.9857.

Dimethyl 1,4-Dibromo-5-hydroxy-6-oxocyclohex-4-ene-1,3-dicarboxylate (4j). Experimental procedure is similar to that for compound **4a**. R_f (20% ethyl acetate in hexane) 0.5, colorless crystalline solid, mp 126−127 °C, yield 95% (100 mg, 0.26 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.48 (s, 1H), 3.93 (dd, 1H, J = 5.3, 8.1 Hz),3.83 (s, 3H), 3.79 (s, 3H), 3.27 (dd, 1H, J = 5.3, 14.0 Hz), 2.92 (dd, 1H, J = 8.1, 14.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.2, 169.9, 165.8, 145.1, 116.1, 57.7, 56.4, 54.6, 53.1, 47.8, 39.1; IR (KBr) 3400, 2990, 1735, 1695, 1650, 1435, 1350, 1170, 1075, 870, 780, 735, 695 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_{10}O_6Br_2$ (M + H), 384.8922; found, 384.8926.

Trimethyl 4-Chloro-5,6-dihydroxybenzene-1,2,3-tricarboxylate (6a). Experimental procedure is similar to that for compound **4a**. R_f (20% ethyl acetate in hexane) 0.4, colorless crystalline solid, mp 140 °C, yield 97% (60 mg, 0.18 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.30 (s, 1H), 6.30 (s, 1H), 3.92 (s, 3H), 3.87 (s, 3H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 166.9, 165.2, 150.1, 143.3, 126.2, 124.2, 122.3, 108.7, 53.6, 53.0, 52.9; IR (KBr) 3300, 3028, 1738, 1722, 1690, 1598, 1436, 1220, 998, 932, 878, 830, 812, 774, 727 cm^{-1}; HRMS (EI) calcd for $C_{12}H_{11}O_8Cl$, 318.0142; found, 318.0143.

Trimethyl 4-Bromo-5,6-dihydroxybenzene-1,2,3-tricarboxylate (6b). Experimental procedure is similar to that for compound **4a**. R_f (20% ethyl acetate in hexane) 0.4, colorless crystalline solid, mp 148−149 °C, yield 95% (60 mg, 0.16 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.31 (s, 1H), 6.37 (s, 1H), 3.93 (s, 3H), 3.88 (s, 3H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 166.8, 165.9, 149.5, 144.6, 126.4, 126.1, 111.5, 109.3, 53.6, 53.57, 53.0; IR (KBr) 3300, 3025, 1740, 1720, 1680, 1590, 1430, 990, 920, 770, 730 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{11}O_8Br$, 361.9637; found, 361.9630.

Hemiketal 8a. Experimental procedure is similar to that for compound **4a** except for the time and stoichiometry of the reaction (Scheme 3). R_f (40% ethyl acetate in hexane) 0.4, colorless crystalline solid, mp 152−154 °C, yield 94% (130 mg, 0.42 mmol); ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6, 20:1) δ 4.50 (bs, 1H), 3.69 (s, 3H), 3.63 (s, 3H), 2.54 (d, 1H, J = 13.4 Hz), 2.48 (d, 1H, J = 13.4 Hz), 1.54 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6, 20:1) δ 192.7, 173.2, 102.5, 78.4, 73.9, 52.5, 51.7, 51.6, 41.3, 17.8; IR (KBr) 3150, 2900, 1760 (br), 1430, 1370 cm^{-1}; HRMS (EI) calcd for $C_{11}H_{12}Cl_2O_6$, 310.0011; found, 310.0011.

Hemiketal 8b. Experimental procedure is similar to that for compound **4a** except for the time and stoichiometry of the reaction (Scheme 3). R_f (40% ethyl acetate in hexane) 0.4, colorless crystalline solid, mp 188−189 °C, yield 90% (150 mg, 0.38 mmol); ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6, 20:1) δ 3.71 (s, 3H), 3.67 (s, 3H), 2.58 (d, 1H, J = 13.3 Hz), 2.47 (d, 1H, J = 13.3 Hz), 1.54 (s, 3H); ^{13}C NMR (100 MHz $CDCl_3$ + DMSO-d_6, 20:1) δ 193.4, 173.8, 102.5, 101.1, 72.7, 66.6, 52.6, 52.5, 51.5, 44.2, 21.1; IR (KBr) 3150, 2900, 1760 (br), 1430 cm^{-1}; HRMS (ESI) calcd for $C_{11}H_{12}Br_2O_6$ (M + H), 398.9079; found, 398.9072.

Dimethyl 2,5-Dichloro-4-methoxy-1-methyl-3-oxocyclohex-4-ene-1,2-dicarboxylate (9a). Experimental procedure is similar to that for compound **4a** except for the time and stoichiometry of the reaction (Scheme 3). R_f (15% ethyl acetate in hexane) 0.6, colorless viscous liquid, yield 76% (40 mg, 0.12 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.83 (s, 3H), 3.74 (s, 3H), 3.71 (s, 3H), 3.32 (d, 1H, J = 18.6 Hz), 2.94 (d, 1H, J = 18.6 Hz), 1.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.4, 171.5, 165.2, 146.5, 138.3, 75.5, 59.9, 54.0, 53.1, 52.6, 42.1, 21.1; IR (neat) 2975, 1745, 1720, 1700, 1630, 1445, 1050, 990, 810, 830, 750 cm^{-1}; HRMS (EI) calcd for $C_{12}H_{14}O_6Cl_2$, 324.0167; found, 324.0167.

Dimethyl 2,5-Dibromo-4-methoxy-1-methyl-3-oxocyclohex-4-ene-1,2-dicarboxylate (10a). Experimental procedure is similar to that for compound **4a** except for the time and stoichiometry of the reaction (Scheme 3) and the methylation of enol followed the diazomethane treatment protocol. R_f (15% ethyl acetate in hexane) 0.6, colorless viscous liquid, yield 36% (150 mg, 0.34 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.83 (s, 3H), 3.74 (s, 3H), 3.72 (s, 3H), 3.49 (d, 1H, J = 18.9 Hz), 3.08 (d, 1H, J = 18.9 Hz), 1.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.5, 171.6, 165.2, 147.7, 129.6, 69.9, 59.6, 54.1, 53.4, 53.1, 44.8, 21.4; IR (KBr) 2925, 1750, 1720, 1690, 1620, 1430, 1375, 1010, 890, 800, 730 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{14}O_6Br_2Na$, 434.9055, found, 434.9324.

Dimethyl 2,5-Dibromo-4-methoxy-1-methyl-3-oxocyclohex-4-ene-1,2-dicarboxylate (10b). Experimental procedure is similar to that for compound **4a** except for the time and stoichiometry of the reaction (Scheme 3). R_f (15% ethyl acetate in hexane) 0.6, colorless crystalline solid, mp 87−88 °C, yield 39% (150 mg, 0.34 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.86 (s, 3H), 3.76 (s, 3H), 3.68 (s, 3H), 3.06 (d,1H, J = 19.2 Hz), 2.88 (d, 1H, J = 19.2 Hz), 1.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.3, 171.3, 165.6, 147.9, 126.1, 68.5, 59.4, 54.2, 53.1, 51.2, 44.6, 21.2; IR (KBr) 2928, 1752, 1721, 1694, 1629, 1428, 1372, 1030, 802, 731 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{14}O_6Br_2$-Na, 434.9055; found, 434.9324.

Methyl 1,4-Dichloro-3-hydroxy-5-methyl-2-oxo-5-phenylcyclohex-3-enecarboxylate (13a). Experimental procedure is similar to that for compound **4a**. R_f (15% ethyl acetate in hexane) 0.6, colorless viscous liquid, yield 83% (100 mg, 0.30 mmol); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.34 (2H, m), 7.30−2.25 (3H, m), 3.86 (s, 3H), 3.10 (d, 1H, J = 11.8 Hz), 2.78 (d, 1H, J = 11.8 Hz), 1.70 (s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 183.0, 167.6, 144.4, 143.8, 136.3, 128.7, 127.4, 126.5, 66.3, 54.2, 50.5, 45.8, 25.5; IR (KBr) 3450, 1735, 1710, 1640, 1450, 1350, 1235, 1010, 880, 775 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{14}O_4Cl_2$ (M + H), 329.0347; found, 329.0347.

Methyl 1,4-Dibromo-3-hydroxy-5-methyl-2-oxo-5-phenylcyclohex-3-enecarboxylate (14a). Experimental procedure is similar to that for compound **4a**. R_f (15% ethyl acetate in hexane) 0.6, colorless viscous liquid, yield 55% (400 mg, 0.96 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.25 (m, 5H), 6.61 (bs, 1H), 3.85 (s, 3H) 3.25 (d, 1H, J = 14.5 Hz), 2.92 (d, 1H, J = 14.5 Hz), 1.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.0, 168.0, 145.3, 144.7, 130.7, 128.6, 127.4, 126.6, 58.0, 54.4, 51.5, 47.5, 25.1; IR (KBr) 3450, 1730, 1700, 1640, 1450, 1350, 1235, 1010, 885, 770 cm^{-1}; HRMS (EI) calcd for $C_{15}H_{14}O_4Br_2$, 415.9259; found, 415.9259.

Methyl 1,4-Dibromo-3-hydroxy-5-methyl-2-oxo-5-phenylcyclohex-3-enecarboxylate (14b). Experimental procedure is similar to that for compound **4a**. R_f (10% ethyl acetate in hexane) 0.5, colorless crystalline solid, mp 158 °C, yield 18% (400 mg, 0.96 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.22 (m, 5H), 6.68 (bs, 1H), 3.45 (d, 1H, J = 13.8 Hz), 3.04 (s, 3H), 2.91 (d, 1H, J = 13.8 Hz), 1.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.4, 166.4, 145.4, 141.3, 128.9, 128.4, 127.4, 127.1, 58.1, 53.4, 51.6, 47.2, 32.3; IR (KBr) 3450, 1735, 1695, 1635, 1450, 1355, 1240, 1010, 880, 775 cm^{-1}; HRMS (EI) calcd for $C_{15}H_{14}O_4Br_2$, 415.9259; found, 415.9259.

BF_2 Complex 15. To a stirred solution of diketone **3j** (100 mg, 0.25 mmol) in dry dichloromethane (2 mL) was added excess $BF_3 \cdot Et_2O$ (0.5 mL) at room temperature over a period of 4 min under argon. The reaction mixture was stirred for 24 h at 35 °C. After the reaction mixture cooled in a refrigerator at 0 to −10 °C over a period of 10−12 h, a colorless crystalline material (70 mg/100 mg) of **15** was separated from the reaction mixture. The mother liquor was further purified by silica gel column chromatography to obtain the pure compound. R_f (30% ethyl acetate in hexane) 0.4, colorless crystalline compound, mp 178 °C, yield 95%; ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6, 20:1) δ 3.80 (s, 3H), 3.70(t, 1H, J = 4.8 Hz), 3.67 (s, 3H), 3.02 (dd, 1H, J = 5.6, 18.5 Hz), 2.76 (dd, 1H, J = 4.0, 18.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6, 20:1) δ 178.5, 170.6, 168.9, 151.9, 147.6, 107.0, 61.2, 55.8, 52.7, 52.6, 26.1; IR (KBr) 3150, 1720, 1630, 1400, 1310, 1060, 900, 770 cm^{-1}.

Dimethyl 6,6-Dibromo-4-hydroxy-5-oxocyclohex-3-ene-1,3-dicarboxylate (16). To the homogeneous solution of BF_2 complex **15** (32 mg, 0.07 mmol) in ethyl acetate (10−15 mL), was added 50% $NaHCO_3$ solution. The mixture was vigorously shaken in a separating funnel, and the separated organic layer was washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure to obtain a viscous liquid without any further purification. R_f (30% ethyl acetate in hexane) 0.4, brown viscous liquid, yield 95%; ^{1}H NMR (400 MHz, $CDCl_3$) δ11.43 (s, 1H, OH), 3.83 (s, 3H), 3.70 (s, 4H), 3.04 (dd, 1H, J = 5.1, 18.4 Hz), 2.79 (dd, 1H, J = 3.3, 18.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.7, 171.1, 169.1, 152.6, 107.2, 61.4, 56.4, 53.1, 53.0, 26.5; IR (KBr) 2990, 1730, 1670, 1615, 1440, 870, 740 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_{10}O_6Br_2$ (M + H), 384.8922; found, 384.8926.

Dimethyl 1,4,5,8-Tetrachloro-2,7-dihydroxy-3,6-dioxo-4,4a,4b,5,6,8a,9,9a-octahydro-3*H*-fluorene-4,5-dicarboxylate (18a). Experimental procedure is similar to that for compound **4a**. R_f (30% ethyl acetate in hexane) 0.5, colorless solid, mp 222−223 °C, yield 59% (75 mg, 0.15 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.90 (d, 2H, J = 5.3 Hz), 3.81 (s, 3H), 3.28 (td, 2H, J = 5.3, 9.8 Hz), 1.94 (t, 2H, J = 9.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6 (20:1)) δ 181.7, 165.5, 145.6, 125.5, 71.4, 54.2, 49.7, 43.0, 27.1; IR (KBr) 3590, 3528, 2964, 1750, 1702, 1636, 1460, 1243, 991, 703, 542 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{14}O_8Cl_4$ (M + H), 486.9521; found, 486.9525.

Dimethyl 1,4,5,8-Tetrachloro-3,7-dihydroxy-2,6-dioxo-2,4a,4b,5,6,8a,9,9a-octahydro-1*H*-fluorene-1,5-dicarboxylate (18b). Experimental procedure is similar to that for compound **4a**. R_f (30% ethyl acetate in hexane) 0.5, colorless solid, mp 219−220 °C, yield 37% (75 mg, 0.15 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.30 (s, 1H), 6.18 (s, 1H), 3.98 (d, 1H, J = 7.3 Hz), 3.88 (s, 3H), 3.84 (d, 1H, J = 7.3 Hz), 3.80 (s, 3H), 3.43−3.34 (m, 2H), 2.54−2.47 (m, 1H), 2.18−2.09 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6, 15:1) δ 181.6, 181.4, 165.7, 145.2,143.3, 128.1, 125.5, 71.7, 54.2, 50.5, 46.8, 45.0, 41.9, 32.1; IR (KBr) 3381, 2959, 1759, 1708, 1676, 1634, 1365, 1246, 1044, 764 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{14}O_8Cl_4$ (M + H), 486.9521; found, 486.9525.

Dimethyl 1,4,6,9-Tetrachloro-3,7-dihydroxy-2,8-dioxo-1,2,4a,5a,8,9,9a,9b-octahydrodibenzo[b,d]furan-1,9-dicarboxylate (20a). Experimental procedure is similar to that for compound **4a**. R_f (30% ethyl acetate in hexane) 0.4, colorless solid, mp 178−179 °C, yield 38% (50 mg, 0.10 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.50 (bs, 2H), 4.73 (d, 2H, J = 4.2 Hz), 4.11 (d, 2H, J = 4.2 Hz), 3.80 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.7, 164.1, 144.4, 123.1, 78.9, 69.6, 55.0, 50.1; IR (KBr) 3400, 2995, 1715, 1650, 1440, 1345, 1245, 1015, 945, 870 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{12}O_9Cl_4$ (M + H), 488.9313; found, 488.9316.

Dimethyl 1,4,6,9-Tetrachloro-3,8-dihydroxy-2,7-dioxo-1,2,4a,5a,6,7,9a,9b-octahydrodibenzo[*b*,*d*]furan-1,6-dicarboxylate (20b). Experimental procedure is similar to that for compound **4a**. R_f (30% ethyl acetate in hexane) 0.4, colorless solid, mp

175−176 °C, yield 49% (50 mg, 0.10 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.41 (bs, 1H), 6.26 (bs, 1H), 5.07 (d, 1H, J = 7.3 Hz), 4.79 (d, 1H, J = 5.1 Hz), 4.10 (dd, 1H, J = 2.5, 7.3 Hz), 3.87 (s, 3H), 3.80 (s, 3H), 3.65 (dd, 1H, J = 2.5, 5.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6, 15:1) δ 180.8, 179.9, 165.5, 164.5, 146.2, 144.2, 124.0, 121.9, 78.0, 77.0, 70.2, 69.9, 54.6, 54.4, 51.6, 47.1; IR (KBr) 3400, 1750, 1695, 1640, 1430, 1345, 1245 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{12}O_9Cl_4$ (M + H), 488.9313; found, 488.9316.

Methyl 9-Chloro-5,6,7,8-tetrahydronaphtho[2,3-*d*][1,-3]dioxole-4-carboxylate (21a). To a stirred solution of substrate (150 mg, 0.512 mmol) in dichloromethane (2 mL), was added DBU (311 mg, 2.05 mmol) at ice bath temperature. The reaction mixture was allowed to rt (30 °C). After 3 days the reaction mixture was acidified with 10% aqueous HCl, and the reaction mixture was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure. The crude reaction mixture was purified by silica gel column chromatography to obtain the aromatized compound **21a**. R_f (10% ethyl acetate in hexane) 0.6, colorless solid, mp 59−60 °C, yield 86% (40 mg, 0.14 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.98 (s, 2H), 3.83 (s, 3H), 2.76 (t, 2H, J = 6.4 Hz), 2.62 (t, 2H, J = 6.4 Hz), 1.74−1.63 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 145.5, 142.7, 131.1, 128.9, 117.3, 112.4, 101.9, 52.1, 27.8, 27.0, 22.5, 22.2; IR (KBr) 2950, 1715, 1620, 1505, 1440, 940, 770 cm^{-1}; HRMS (EI) calcd for $C_{13}H_{13}O_4Cl$, 268.0502; found, 268.0503.

Methyl 9-Bromo-5,6,7,8-tetrahydronaphtho[2,3-*d*][1,3] dioxole-4-carboxylate (21b). Experimental procedure is similar to that for compound **21a**. R_f (10% ethyl acetate in hexane) 0.6, colorless solid, mp 68−69 °C, yield 85% (30 mg, 0.10 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.98 (s, 2H), 3.83 (s, 3H), 2.76 (t, 2H, J = 6.4 Hz), 2.61 (t, 2H J = 6.4 Hz), 1.73−1.60 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 144.8, 144.3, 131.1, 129.9, 113.0, 107.1, 101.5, 52.1, 29.8, 27.9, 22.6; IR (KBr) 1720, 1610, 1510, 1450, 1050, 930, 785, 770 cm^{-1}; HRMS (EI) calcd for $C_{13}H_{13}O_4Br$, 311.9997; found, 311.9994.

Compound 21e. Experimental procedure is similar to that for compound **21a**. R_f (10% ethyl acetate in hexane) 0.6, colorless solid, mp 80−82 °C, yield 81% (80 mg, 0.27 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.99 (s, 2H), 3.83 (s, 3H), 2.86−2.79 (m, 4H), 1.64−1.61 (m, 4H), 1.30 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 145.2, 142.9, 134.3, 132.8, 116.5, 113.1, 101.9, 52.3, 2.19, 31.5, 29.3, 27.9, 26.19, 26.16; IR (KBr) 2950, 1725, 1630, 1490, 1440, 1220, 940, 785 cm^{-1}; HRMS (EI) calcd for $C_{15}H_{17}O_4Cl$, 296.0815; found, 296.0818.

Compound 21f. Experimental procedure is similar to that for compound **21a**. R_f (10% ethyl acetate in hexane) 0.6, colorless solid, mp 72 °C, yield 77% (80 mg, 0.23 mmol); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.04 (s, 2H), 3.89 (s, 3H), 2.93 (t, 2H, J = 5.0 Hz), 2.88 (t, 2H, J = 4.8 Hz), 1.68 (dd, 4H J = 4.2, 10.8 Hz), 1.35 (t, 4H, J = 2.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 144.6, 134.2, 134.0, 113.7, 106.2, 101.6, 52.4, 31.7, 30.5, 29.8, 29.4, 26.3, 26.1; IR (neat) 2950, 1720, 1490, 1440, 1060, 940, 740 cm^{-1}; HRMS (EI) calcd for $C_{15}H_{17}O_4Br$, 340.0310; found, 340.0315.

Methyl 9-Chloronaphtho[2,3-*d*][1,3]dioxole-4-carboxylate (22). To a stirred solution of compound **21a** (20 mg, 0.074 mmol) in benzene (2 mL) was added 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ, 33.6 mg, 0.148 mmol). The reaction mixture was refluxed for 36 h and then passed through a Celite pad and washed with ethyl acetate. The solvent was removed under reduced pressure. The crude reaction mixture was purified by silica gel column chromatography to afford light brown color solid compound **22**. R_f (5% ethyl acetate in hexane) 0.5, colorless solid, mp 124 °C, yield 91%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (dd, 1H, J = 2.7, 5.0 Hz), 8.10 (dd, 1H, J = 2.7, 5.2 Hz), 7.49 (dd, 2H, J = 2.7, 5.2 Hz), 6.20 (s, 2H), 4.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 148.8, 143.9, 128.2, 127.8, 126.6, 125.8, 125.4, 123.3, 112.2, 106.1, 102.5, 52.3; IR (KBr) 2950, 1700, 1650, 1605, 1500, 1450, 1225, 1160, 955, 770 cm^{-1}; HRMS (EI) calcd for $C_{13}H_9O_4Cl$, 264.0189; found, 264.0186.

Methyl 6-Chloro-4-hydroxy-5-methoxybiphenyl-3-carboxylate (23g). To a stirred solution of substrate (50 mg, 0.16 mmol) in methanol (2 mL) was added the ethereal solution of diazomethane at ice bath temperature, which was prepared freshly from its precursor (*N*-methyl, *N*-nitroso-urea, 50 mg) in 50% KOH solution in ether layer (10 mL). The excess diazomethane was quenched with a drop of AcOH. The solvent was removed under reduced pressure, and the crude reaction mixture was purified by silica gel column chromatography. A portion of methylated compound (0.08 mmol) was dissolved in dichloromethane (1 mL), and DBU (121 mg, 0.79 mmol) was added at ice bath temperature. The reaction mixture was allowed to rt (30 °C). After 6 h the reaction mixture was acidified with 10% aqueous HCl, and the reaction mixture was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure. The crude reaction mixture was purified by silica gel column chromatography to obtain the aromatized compound **23g**. R_f (10% ethyl acetate in hexane) 0.6, colorless solid, mp118−119 °C, yield 93%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.98 (s, 1H), 7.59 (s, 1H), 7.41−7.36 (m, 5H), 3.96 (s, 3H), 3.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 155.0, 145.1, 138.5, 133.6, 132.4, 129.6, 128.1, 127.6, 126.0, 111.8, 60.5, 52.6; IR (KBr) 2900, 1670, 1600, 1445, 1335, 1030, 800, cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{13}O_4Cl$, 293.0580; found, 293.0586.

Methyl 6-Bromo-4-hydroxy-5-methoxybiphenyl-3-carboxylate (23h). Experimental procedure is similar to that for compound **23g**. R_f (10% ethyl acetate in hexane) 0.6, colorless solid, mp 110−112 °C, yield 74% (50 mg, 0.15 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.98 (s, 1H), 7.57 (s, 1H), 7.42−7.33 (m, 5H), 3.95 (s, 3H), 3.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 154.6, 146.2, 140.3, 134.3, 129.6, 128.0, 127.6, 125.9, 125.5, 112.3, 60.4, 52.6; IR (KBr) 2900, 1720, 1680, 1600, 1445, 1340, 1035, 910, 800 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{13}O_4Br$ (M + H), 337.0075; found, 337.0074.

Methyl 7-Chloro-5-hydroxy-6-methoxy-2,3-dihydro-1*H*-indene-4-carboxylate (23c). Experimental procedure is similar to that for compound **23g**. R_f (10% ethyl acetate in hexane) 0.6, colorless solid, mp 90 °C, yield 91% (75 mg, 0.29 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.30 (s, 1H), 3.93 (s, 3H), 3.87 (s, 3H), 3.19 (t, 2H, J = 7.4 Hz), 2.87 (t, 2H, J = 7.6 Hz), 2.03 (t, 2H, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 155.3, 143.1, 141.3, 133.8, 130.9, 109.1, 60.4, 52.1, 36.2, 31.9, 23.8; IR (KBr) 2900, 1665, 1600, 1570, 1420, 1095, 995, 895, 805, 770 cm^{-1}; HRMS (EI) calcd for $C_{12}H_{13}O_4Cl$, 256.0502; found, 256.0507.

Methyl 7-Bromo-5-hydroxy-6-methoxy-2,3-dihydro-1*H*-indene-4-carboxylate (23d). Experimental procedure is similar to that for compound **23g**. R_f (10% ethyl acetate in hexane) 0.6, colorless solid, mp 78−80 °C, yield 82% (50 mg, 0.15 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.30 (s, 1H), 3.92 (s, 3H), 3.86 (s, 3H), 3.22 (t, 2H, J = 7.7 Hz), 2.87 (t, 2H, J = 7.7 Hz), 2.03 (t, 2H, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 154.9, 144.2, 141.1, 135.7, 121.9, 109.7, 60.3, 52.3, 36.5, 34.3, 23.6; IR (KBr) 2900, 1675, 1600, 1575, 1425, 1330, 1095, 895, 805,770 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{13}O_4BrNa$, 322.9895; found, 322.9851.

Compounds 25a,b (Mixture). Experimental procedure is similar to that for compound **4a**. R_f (30% ethyl acetate in hexane) 0.4, colorless liquid, yield 94% (282 mg, 0.56 mmol); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.14 (bs, 4H), 3.86 (s, 6H), 3.82 (s, 6H), 3.28−3.10 (m, 8H), 2.73−2.69 (m, 2H), 2.42−2.32 (m, 4H), 2.21−2.17 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$+DMSO−D_6, 15:1) δ 181.5, 181.4, 165.5, 165.4, 143.2, 142.9, 128.7, 128.2, 73.5, 72.9, 53.9, 38.2, 37.4, 36.7, 29.6, 24.8, 19.2; IR (KBr) 2950, 1760, 1730, 1700, 1620, 1440, 1240, 1010, 920, 840 cm^{-1}.

Compounds 26a,b (Mixture). R_f (30% ethyl acetate in hexane) 0.5, colorless solid, mp 200−202 °C, quantitative yield; ^{1}H NMR

(400 MHz, $CDCl_3$) δ 3.86 (s, 6H), 3.82 (s, 6H), 3.73 (s, 6H), 3.71 (s, 6H), 3.26−3.07 (m, 8H), 2.58−2.39 (m, 4H), 1.59−1.31 (m, 4H); HRMS (ESI) calcd for $C_{20}H_{20}Cl_4O_8$ (M + H), 528.9990; found, 528.9998.

Dimethyl 4,8-Dichloro-2,3,6,7-tetramethoxy-9,10-dihydroanthracene-1,5-dicarboxylate (27a). Experimental procedure is similar to that for compound **23g** except that MeI was added during the DBU reaction. R_f (30% ethyl acetate in hexane) 0.5, colorless solid, mp 158−160 °C, yield 45% (130.5 mg, 0.269 mmol, from **24**); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.99 (s, 6H), 3.94 (s, 4H), 3.89 (s, 6H), 3.87 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.3, 149.6, 148.1, 129.3, 129.2, 128.2, 126.8, 62.0, 60.9, 52.7, 30.1; IR (KBr) 2900, 1730, 1570, 1460, 1420, 1280, 1100, 980, 810, 770 cm^{-1}; HRMS (EI) calcd for $C_{22}H_{22}O_8Cl_2$, 484.0692; found, 484.0697.

Dimethyl 4,5-Dichloro-2,3,6,7-tetramethoxy-9,10-dihydroanthracene-1,8-dicarboxylate (27b). Experimental procedure is similar to that for compound **23g** except that MeI was added during the DBU reaction. R_f (30% ethyl acetate in hexane) 0.5, yellow color solid, mp 114−115 °C, yield 35% (101.5 mg, 0.209 mmol, from **24**); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.08 (t, 2H, J = 1.8 Hz), 3.94 (s, 6H), 3.90 (s, 6H), 3.88 (s, 6H), 3.80 (t, 2H, J = 1.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.2, 149.6, 148.1, 129.6, 129.4, 128.3, 126.5, 61.9, 60.9, 52.5, 30.5, 30.0; IR (KBr) 2900, 1730, 1600, 1460, 1420, 1280, 1100, 980, 810, 770 cm^{-1}; HRMS (EI) calcd for $C_{22}H_{22}O_8Cl_2$, 484.0692; found, 484.0697.

Dimethyl 4,8-Dichloro-2,3,6,7-tetramethoxyanthracene-1,5-dicarboxylate (28a). Experimental procedure is similar to that for compound **22**. R_f (15% ethyl acetate in hexane) 0.5, yellow color solid, mp 148 °C, yield 87% (30 mg, 0.06 mmol); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (s, 2H), 4.07 (s, 6H), 3.98 (s, 6H), 3.95 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 151.0, 149.0, 127.3, 125.9, 125.8, 122.6, 120.8, 62.2, 61.2, 52.8; IR (KBr) 2950, 1735, 1535, 1450, 1410, 1360, 1230, 1030, 895, 820, 770 cm^{-1}; HRMS (EI) calcd for $C_{22}H_{20}O_8Cl_2$, 482.0535; found, 482.0536.

Dimethyl 4,5-Dichloro-2,3,6,7-tetramethoxyanthracene-1,8-dicarboxylate (28b). Experimental procedure is similar to that for compound **22**. R_f (15% ethyl acetate in hexane) 0.5, yellow color solid, mp 135 °C yield 90% (25 mg, 0.05 mmol); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.09 (s, 1H) 8.27 (s, 1H), 4.09 (s, 6H), 4.03 (s, 6H), 4.02 (s, 6H); IR (KBr) 2950, 1735, 1535, 1450, 1410, 1360, 1230, 1030, 895, 820, 770 cm^{-1}; HRMS (EI) calcd for $C_{22}H_{20}O_8Cl_2$, 482.0535; found, 482.0536.

■ ASSOCIATED CONTENT

Supporting Information. ^{1}H and ^{13}C NMR spectra, HRMS, and crystallographic data files in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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