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Synthesis of *cis*-Oriented Vicinal Diphenylethylenes through a Lewis Acid-Promoted Annulation of Oxotriphenylhexanoates

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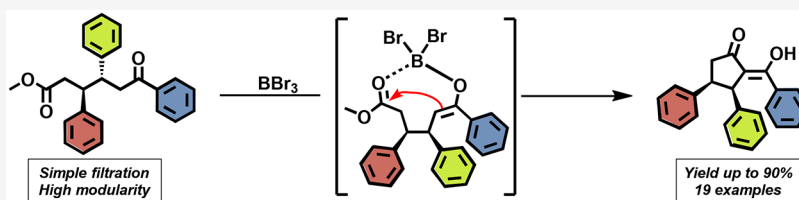
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ABSTRACT: This study explores the synthesis of cyclic *cis*-vicinal phenyl ethylenes from oxotriphenylhexanoates. The reaction is a BBr_3 -promoted cyclization of 1,6-ketoesters (**1**) to five-membered diketo compounds (**2**). The synthesis is interesting as it constitutes one of the few examples of modular stereoselective synthesis of structures with a *cis*-oriented vicinal diphenylethylene. The core structure of **2** can be smoothly derivatized, which makes it a promising synthetic building block for further stereoselective synthetic applications.

INTRODUCTION

Cyclic compounds possessing adjacent $\text{C}(\text{sp}^3)$ -aryl moieties are widely present in nature. While in most cases these compounds have a *trans*-vic-diphenylethylene moiety such as indanone^{1–7} and resveratrol-based natural products,^{8–19} the *cis*-vic-diphenylethylene motif has been explored less. Nevertheless, these interesting substances still show biological activity, and representative examples include both pharmaceuticals²⁰ and natural products (Figure 1a).^{21–34} For example, the rocaglates, rocaglamide, and silvestrol have received widespread attention as they have been investigated for

therapeutic targets such as cancer^{21,34,35} and recently viruses like the coronavirus,³⁶ the Ebola virus,³⁷ and the hepatitis E virus.³⁸ Thus, synthetic strategies leading to the formation the *cis*-vic-diphenylethylene are attractive. However, there are only a limited number of general methods for direct stereoselective formation of cyclic compounds possessing the *cis*-vic-diphenylethylene moiety. It is also worth noting that a majority of these syntheses are devoted to the diphenyl dihydrobenzofuran moiety found in the rocaglates.^{21,23,24,34,39–51}

A practical way to prepare the *cis*-vic-configured $\text{C}(\text{sp}^3)$ -aryl could potentially be a ring closure of an acyclic starting material with a preset configuration on the carbons bearing the aryl substituents. We envisioned that a Dieckmann type condensation of a 1,6-ketoester such as the oxotriphenylhexanoate (OTHO)^{52–56} would be ideal for this type of transformation. The OTHO has an enolizable ketone and an ester moiety and can, after cyclization, generate a five-membered diketo compound. Furthermore, one very interesting feature of the OTHO is that the synthesis of the OTHO proceeds with exclusive formation of the *trans*-vic-diphenylethylene. Used as a starting material in the Dieckmann condensation would thus ensure total control of the *cis*-vic-diphenylethylene buildup (Figure 1b).

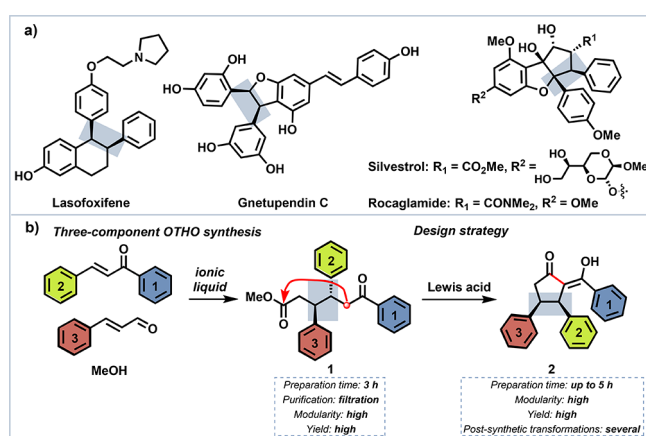


Figure 1. (a) Examples of biologically active compounds with a *cis*-oriented diphenylethylene moiety. (b) Design approach for the synthesis of the desired carbocycle.

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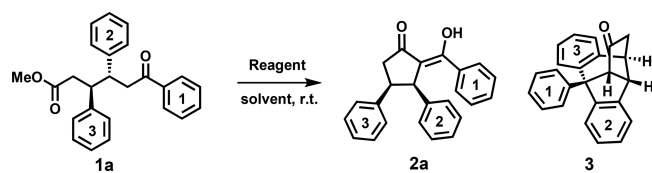
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RESULTS AND DISCUSSION

Our studies commenced with screening of different Lewis acids for the cyclization of **1a** (Table 1) because Lewis acids were

Table 1. Conditions for the Intramolecular Cyclization of **1a**^a



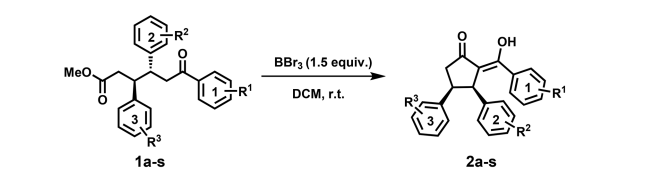
entry	reagent	solvent	time (h)	conversion (%)	yield of 2a/3 (%) ^b
1	BF ₃ ·OEt ₂ (1.0 equiv)	DCM	168	0	0/0
2	BBr ₃ (1.0 equiv)	DCM	24	100	67/0
3	BCl ₃ (1.0 equiv)	DCM	48	100	60/0
4	AgOAc (1.0 equiv)	DCM	168	0	—
5	SnCl ₄ (1.0 equiv)	DCM	168	0	—
6	TiCl ₄ (1.0 equiv)	DCM	168	0	—
7	AlCl ₃ (4.0 equiv)	DCM	168	0	—
8	FeCl ₃ (4.0 equiv)	DCM	168	0	—
9	(C ₆ F ₅) ₃ B (1.0 equiv)	DCM	168	0	—
10	NaH (1.5 equiv)	THF	6	50	45
11	BBr ₃ (1.5 equiv)	DCM	3	100	80/0
12	BBr ₃ (2.0 equiv)	DCM	5	100	30/21
13	BBr ₃ (3.0 equiv)	DCM	5	100	11/28
14	BBr ₃ (0.25 equiv)	DCM	168	25	15/0
15	BBr ₃ (1.5 equiv)	CHCl ₃	20	100	50/0
16	BBr ₃ (1.5 equiv)	toluene	16	100	63/0

^aReactions were carried out on a 0.25 mmol scale of **1a** in DCM (3 mL) in a sealed reaction vessel at room temperature. ^bIsolated yield.

already reported to be useful promoters in the Dieckmann type cyclization.⁵⁷ Initial attempts showed that the cyclization reaction was highly dependent on the Lewis acid used. Only BBr₃ and BCl₃ delivered the corresponding cyclized product **2a** in good yield after 24 and 48 h, respectively (Table 1, entries 2 and 3, respectively). Single-crystal X-ray analysis of compound **2a** confirmed that the vicinal aromatic rings were in the *cis* orientation (Table 2, entry 2a). Other Lewis acids failed even after prolonged reaction times (Table 1, entries 1 and 4–9). Generally basic conditions were not efficient in promoting the cyclization; only NaH in THF as a solvent successfully afforded **2a** in 45% yield (Table 1, entry 10). Investigating the loading of BBr₃ showed that 1.5 equiv of BBr₃ is sufficient to reach full conversion within 3 h and produce a yield of 80% (Table 1, entry 11). Higher loadings of BBr₃ (2–3 equiv) resulted in a significant decrease in the level of formation of **2a**, and the polycyclization reaction of **1a** afforded tricyclic compound **3** (Table 1, entries 12 and 13).⁵⁸ At substoichiometric loadings of BBr₃, the cyclization reaction does not proceed efficiently. For instance, in the presence of 0.25 equiv of BBr₃, the reaction reaches 25% conversion and stops (Table 1, entry 14). The reaction performs best in chlorinated solvents such as dichloromethane and chloroform; additionally, toluene is shown to promote the reaction efficiently (Table 1, entries 11, 15, and 16).

With our optimized conditions in hand, we first decided to verify the effectiveness of the reaction on a larger scale. It was shown that the reaction of **1a** on a 1 mmol scale proceeds with

Table 2. Substrates in BBr₃-Promoted Intramolecular Cyclization of **1a–s**^a



Substrate	Yield (%)
2a	80/76 ^b
2b (F)	90
2c (Cl)	80
2d (Br)	81
2e (Br)	69
2f (Br)	67
2g (H ₃ C)	90
2h (H ₃ C)	76
2i (MeO)	50
2j (MeO ₂ C)	50
2k (Cl)	59
2l (Br)	72
2m (CH ₃)	70
2n (CN)	79
2o (Cl)	56
2p (Br)	75
2q (CH ₃)	58
2r (CO ₂ Me)	41
2s (CN)	60

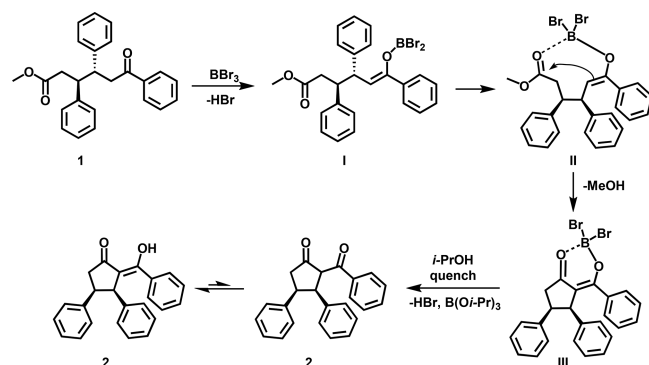
^aReactions were carried out on a 0.25 mmol scale of **1** in DCM (3 mL) in a sealed reaction vessel at room temperature. ^b1 mmol reaction scale.

only small decrease in the yield and the corresponding compound **2a** could be isolated in 76% yield. Next, we turned our attention to the scope of the reaction (Table 2). The effect of aromatic ring 3 (Ar₃) on the course of cyclization was investigated first. This revealed that the reaction tolerates a broad scope of substituents. For example, OTHOs substituted with halogens in the *para* position delivered the corresponding products **2b–d** in good yields (81–90%). Similarly, OTHOs with a sterically demanding bromine in the *meta* and *ortho* positions on Ar₃ could also be employed in the cyclization reaction. However, a decrease in the yield could be observed for compounds **2e** and **2f** (69% and 67%, respectively) compared to that *para*-substituted derivative **2d** (81%). Substrates with an electron rich Ar₃ are tolerated by the reaction, as well. For instance, OTHO with a methyl group at the *para* position on Ar₃ provides the corresponding product **2g** in high yield (90%). A slight decrease in the yield was observed when OTHO substituted with methyl groups at both Ar₂ and Ar₃ was used. Corresponding derivative **2h** was

isolated in a good yield (76%). Introduction of a methoxy group at the *para* position of Ar3 decreased the yield of the corresponding product **2i** to 50%. The lower yield can be explained by the formation of a demethylated OTHO (**1i'**) as a side product in 25% yield. The influence of a strong electron-withdrawing group was also verified, and BBr₃ applied on OTHO substituted with a methyl ester group at the *para* position of Ar3 led to the formation of product **2j** in 50% yield. Next, we investigated the effect of aromatic ring 2 (Ar2) in the cyclization reaction. The results showed lower reactivity compared to that of OTHOs substituted at Ar3. This was demonstrated on OTHOs substituted with chlorine or bromine at the *para* position on Ar2 where the corresponding diketones **2k** and **2l** could be isolated in 59% and 72% yields, respectively. OTHO substituted with a methyl at the *para* position of Ar2 led to the formation of **2m**; however, the isolated yield was lower (70%) than that of derivative **2g** (90%). Also, the effect of the electron-withdrawing cyano group at the *para* position of OTHO on Ar2 was successfully investigated, isolating the corresponding product **2n** in 79% yield. Finally, substituent effects at Ar1 of the OTHOs were investigated. Both *p*-chloro and *p*-bromo are well tolerated, and the corresponding diketones **2o** and **2p** were isolated in good yields (56–75%). A comparable result was obtained with OTHO substituted with a methyl group yielding derivative **2q** in 58% yield. In addition, OTHOs substituted with electron-withdrawing methyl ester and cyano groups at the *para* position on Ar1 were successfully employed in the cyclization reaction; however, the yields of corresponding compounds **2r** and **2s** were lower (41% and 60%, respectively) than those of derivatives **2j** and **2n**. Notably, the ester group and the cyano group can be readily transferred to carboxylic acid and amide or amine, respectively, and thus, these substrates open up for the preparation of potentially biologically active compounds with hydrogen bond donor and acceptor capabilities. Expanding the scope by replacing the aryl moieties with an alkyl group is difficult as the synthesis of **1** is not compatible with alkyl substituents.

Mechanistically, we propose that the reaction starts with enolization of OTHO **1** promoted by BBr₃ leading to intermediate **I** (Scheme 1). In the next step, the ester carbonyl is intramolecularly activated by boron leading to the boron-tethered species (**II**). In intermediate **II**, the enol reacts with the ester in an intramolecular fashion, resulting in boron-containing cyclic transition intermediate **III**.⁵⁹ At the end of the reaction, an excess of isopropanol is added to quench

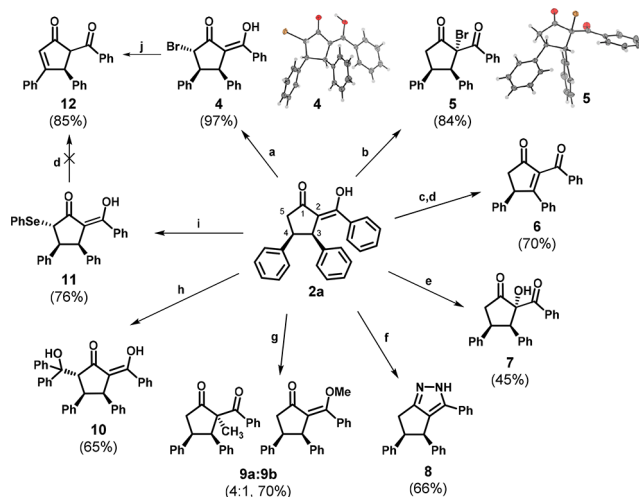
Scheme 1. Proposed Mechanism of Intramolecular Cyclization of OTHOs (**1**) to Diketo Compounds **2**



intermediate **III**, generating compound **2**, which is stabilized in the enol form.

To demonstrate the versatility of this methodology, we used **2a** as a building block in various transformations (Scheme 2).

Scheme 2. Synthetic Transformation of **2a** into Different Derivatives **4–12**^a



^aConditions: (a) pyridinium tribromide, DCM, rt; (b) NBS, DCM, rt; (c) *N*-(phenylseleno)phthalimide, DCM, rt; (d) H₂O₂, EtAOC, rt; (e) *m*-CPBA, NaHCO₃, DCM, rt; (f) N₂H₄, EtOH, reflux; (g) K₂CO₃, MeI, DMF, 60 °C; (h) DIPA, *n*-BuLi, benzophenone, 0 °C to rt; (i) DIPA, *n*-BuLi, *N*-(phenylseleno)phthalimide, DCM, 0 °C to rt; (j) DABCO, THF, rt.

At first, we focused on bromination reactions. When **2a** was subjected to *N*-bromosuccinimide,⁶⁰ α -bromo derivative **5** was isolated in 84% yield as a single diastereoisomer. Interestingly, when **2a** was treated with pyridinium tribromide, δ -brominated regioisomer **4** was isolated in high yield (97%). This bromination strategy offers a route toward compounds that can be used as building blocks in, for example, the Reformatsky type cyanation reaction mediated by samarium salts⁶¹ or in organocatalytic cyclopropanation reactions.⁶² Remarkably, compound **4** was like derivative **5** isolated as a single diastereoisomer with an *anti* orientation of bromine and both aromatic rings. This relative configuration of substituents on the cyclopentanone ring was confirmed by X-ray diffraction of both derivatives **4** and **5** (see the Supporting Information).

Apart from bromination, we also showed that **2a** can be regioselectively substituted with phenylselenium on either C-2 or C-5 of cyclopentanone based on the used conditions. When **2a** was subjected to *N*-(phenylseleno)phthalimide in the presence of 2 equiv of LDA, prepared in situ, selenylated product **11** was isolated in 76% yield as a single diastereoisomer, whereas selenylation with *N*-(phenylseleno)phthalimide without a base led to the selenylation on C-2 of **2a**. The corresponding intermediate was unstable upon isolation, but after the crude mixture had been treated with hydrogen peroxide, the elimination reaction took place and unsaturated derivative **6** was isolated in 70% overall yield. The same reaction conditions were also used on compound **11**. Unfortunately, elimination did not proceed, and decomposition of the starting material was observed. On the contrary, corresponding unsaturated derivative **12** was isolated in good yield (85%) after treatment of **4** with 1,4-diazabicyclo[2.2.2]-

octane (DABCO) in THF at room temperature. Furthermore, diastereoselective hydroxylation of **2a** was developed in the presence of *m*-CPBA and hydroxylated diketone **7** could be isolated in 45% yield. Next, the possibility of C–C bond formation on C-2 and C-5 of **2a** was investigated. When **2a** was treated with iodomethane in the presence of potassium carbonate, methylated product **9** was isolated as a single diastereoisomer in a good yield of 70%, however, as a mixture of regioisomers (4:1 keto:enol). On the contrary, when 2 equiv of in situ-generated LDA was used in the presence of **2a** and benzophenone as an electrophile,⁶³ the corresponding product **10** was isolated in 65% yield as a single diastereomer. These examples nicely illustrate the influence of both *cis*-oriented aromatic rings on stereoselective addition of electrophiles to both C-2 and C-5 to the unhindered side of the cyclic keto ester. We were also able to show that **2a** can be transformed into pyrazole derivative **8** upon being treated with hydrazine hydrate in ethanol under reflux conditions.⁶⁴

To validate whether our diastereoselective synthesis of *cis*-*vic*-diphenylethylene dicarbonyl compounds could be useful for the synthesis of compounds that are structurally similar to rocaglamide or silvestrol, a superimposition was made between compound **2t** and rocaglamide. As it turns out, the superimposition shows an unambiguous match between both *cis*-oriented neighboring Ar of **2t** and the rocaglamide aromatic rings (Figure 2). This provides evidence that the geometry of

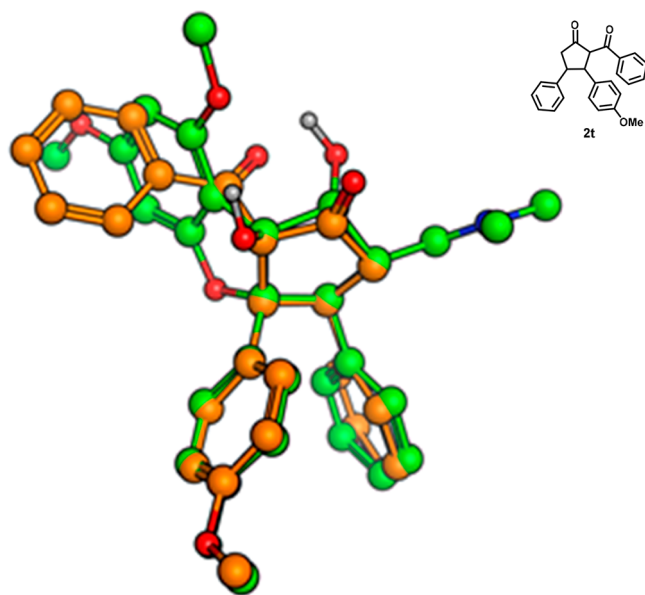


Figure 2. Superimposition of the global minima conformation of rocaglamide (green) and a low-energy conformation ($\Delta E = 0.7$ kcal mol⁻¹) of **2t** (orange).

the diphenylethylene moiety found in the series of compound **2** mimics the diphenylethylene found in natural products such as rocaglamide and silvestrol.

CONCLUSION

We have developed an intramolecular cyclization reaction of 1,6-ketoesters using boron tribromide as a Lewis acid promoter. This methodology provides straightforward access to 1,3-diketo compounds with a cyclopentane moiety having a *cis*-oriented vicinal diphenylethylene that is unique and difficult to obtain by known synthetic methods. We have also shown

that the defined orientation of both vicinal aromatic rings has a directing effect on stereoselectivity in subsequent substitution reactions with bromine, selenium, or a carbon electrophile on C-2 or C-5 of the 1,3-diketones (Scheme 2). Also, regioselective elimination procedures were developed on the basis of the substitution at C-2 or C-5 providing access to two types of α,β -unsaturated carbonyl compounds. Moreover, successful transformation of a 1,3-diketo compound to a heterocyclic pyrazole derivative has been demonstrated showing the importance of 1,3-diketones as potential building blocks for druglike architectures. Additionally, the matching superimposition of **2t** and rocaglamide indicates that the substructure found in compound **2** is a good starting point for the synthesis of a molecular library for probing biological activity. Compounds including *cis*-*vic*-diphenylethylene-oriented motifs such as rocaglamide and silvestrol have attracted considerable pharmaceutical interest, e.g., in cancer treatment and as antiviral agents.^{21,36–38} The synthesis protocol presented here can easily be fine-tuned to achieve a wanted pharmacological profile and thus opens up new opportunities to further explore new analogues for the therapies mentioned above.

EXPERIMENTAL SECTION

Molecular Modeling. To verify the hypothesis that the aromatic rings in **2t** can mimic the corresponding rings in rocaglamide, molecular mechanics calculations were used. A conformational search was performed on both compounds using the Amber10:EHT force field, the Born aqueous solvation model, and the LowModeMD search methodology. The standard settings were applied, and the energy cutoff was set to 5 kcal/mol from their global minima. An ensemble of conformations of the two compounds (24 of rocaglamide and 14 of **2t**) was achieved, and these were crosswise superimposed (336 combinations). The conclusion was that superimposition of **2t** mimics rocaglamide very well, and among the top-scoring combinations were the global minima of rocaglamide and a low-energy conformation of **2t**, i.e., $\Delta E = 0$ and 0.7 kcal mol⁻¹ (Figure 2). The superimposition queries were aromatic rings 2 and 3, the methoxy oxygen, and C-3 and C-4 in the five-membered ring (see Scheme 2 for numbering). All molecular calculations were performed using tools implemented in MOE modeling software.⁶⁵

General Experimental Information. Column chromatography was performed on automated column chromatography Biotage Isolera Spektra One with Biotage SNAP-10g KP-sil columns. Thin layer chromatography (TLC) was performed on Merck TLC plates precoated with silica gel 60 F254 (Art 5715, 0.25 mm) and visualized with ultraviolet light (254 nm). The ¹H NMR (400 MHz) and ¹³C NMR (101 MHz) spectra were recorded on a Varian 400 instrument, and ¹⁹F NMR (470 MHz) spectra were recorded on a Varian 500 spectrometer. The chemical shifts are reported in parts per million (δ) relative to the residual solvent peak CDCl₃: ¹H NMR at δ 7.26 and ¹³C NMR at δ 77.16. Coupling constants (*J*) are reported in hertz. Infrared (IR) spectra were recorded on a PerkinElmer series FT-IR spectrometer and are reported in wavenumbers (cm⁻¹). Melting points were recorded on a Stuart Scientific Melting Point SMP1 instrument. Gas chromatographic studies were performed using an Agilent 7820A instrument equipped with a flame ionization detector and an Agilent HP-5 19091J-413 column. Crystallographic data were obtained using a Bruker D8 VENTURE Kappa Duo PHOTONIII instrument. The 1-ethyl-3-methylimidazolium acetate (EMIMAc) was purchased from Sigma-Aldrich (Stockholm, Sweden), produced by BASF $\geq 95\%$, and dried in vacuo with heating prior to use. All other solvents and reagents were purchased from commercial sources and used without further treatments.

Synthesis of the Starting Material, OTHOs (1). OTHOs **1a–d**, **1g**, **1i–l**, **1n**, **1o**, **1e**, **1f**, **1h**, **1m**, and **1p–s** were synthesized according to previously published procedures.^{52,58}

Methyl 4-(4-Cyanophenyl)-6-oxo-3,4-diphenylhexanoate (1n). Isolated as a white solid (450 mg, 53% yield); mp 167–169 °C (from MeOH); ¹H NMR (400 MHz, CDCl₃) δ 7.67–7.57 (m, 4H), 7.52–7.42 (m, 3H), 7.39–7.22 (m, 7H), 3.70 (td, *J* = 10.8 Hz, *J'* = 3.2 Hz, 1H), 3.48–3.39 (s, 4H), 3.28 (dd, *J* = 17.2 Hz, *J'* = 10.5 Hz, 1H), 2.96 (dd, *J* = 17.3 Hz, *J'* = 3.2 Hz, 1H), 2.50 (dd, *J* = 15.6 Hz, *J'* = 10.2 Hz, 1H), 2.34 (dd, *J* = 15.6 Hz, *J'* = 4.5 Hz, 1H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 197.8, 172.2, 148.4, 141.3, 136.7, 133.3, 132.6 (2C), 129.4 (2C), 129.1 (2C), 128.7 (2C), 128.2 (2C), 127.9 (2C), 127.6, 118.9, 111.0, 51.7, 47.4, 46.7, 43.4, 39.8; ATR-FTIR ν 2951, 2228, 1726, 1718, 1679, 1609, 1597, 1436, 1237, 1157 cm⁻¹; HRMS (ESI) *m/z* calcd for C₂₆H₂₄NO₃ [M + H]⁺ 398.1751, found 398.1751.

General Procedure for the BBr₃-Promoted Synthesis of 2. To a flask equipped with a magnetic stir bar were added OTHO 1a–s (0.25 mmol, 1 equiv) and DCM (3 mL). The solution was stirred at room temperature under nitrogen and syringed with a solution of BBr₃ (375 μL, 1 M in DCM, 1.5 equiv). The mixture was stirred until full conversion was reached (monitored by TLC), then the reaction quenched with *i*-PrOH (2 mL), and the mixture evaporated to dryness. The crude material was separated by flash chromatography with a petroleum ether/EtOAc mixture, yielding the corresponding compound 2a–s.

Procedure for the BBr₃-Promoted Synthesis of 2a on a 1 mmol Scale. To a flask equipped with a magnetic stir bar were added OTHO 1a (0.372 mmol, 1 equiv) and DCM (12 mL). The solution was stirred at room temperature under nitrogen and syringed with a solution of BBr₃ (1.5 mL, 1 M in DCM, 1.5 equiv). The mixture was stirred until full conversion was reached (monitored by TLC), then the reaction quenched with *i*-PrOH (8 mL), and the mixture evaporated to dryness. The crude material was separated by flash chromatography in a petroleum ether/EtOAc mixture yielding corresponding compound 2a as a yellow solid (204 mg, 76%).

(2Z)-2-[Hydroxy(phenyl)methylidene]-3,4-diphenylcyclopentan-1-one (2a). Purified in 92:8 petroleum ether/EtOAc; 68 mg yield as a yellow solid (80%); mp 121–123 °C (from MeOH); 1:10 keto:enol. Enol: ¹H NMR (400 MHz, CDCl₃) δ 7.55–7.49 (m, 2H), 7.40–7.34 (m, 1H), 7.28–7.24 (m, 3H), 7.12–7.06 (m, 6H), 6.78–6.74 (m, 3H), 4.36 (d, *J* = 7.4 Hz, 1H), 3.87 (dt, *J* = 14.0 Hz, *J'* = 7.2 Hz, 1H), 3.09 (dd, *J* = 17.4 Hz, *J'* = 13.5 Hz, 1H), 2.62 (dd, *J* = 17.3 Hz, *J'* = 7.1 Hz, 1H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 209.3, 170.8, 140.5, 138.9, 133.9, 131.2, 128.6 (2C), 128.4 (2C), 128.3 (2C), 128.2 (4C), 127.9 (2C), 126.8, 126.7, 113.3, 52.0, 48.3, 39.8. Keto: ¹H NMR (400 MHz, CDCl₃) δ 8.04–7.96 (m, 2H), 7.62–7.56 (m, 1H), 7.50–7.48 (m, 2H), 7.17–7.13 (m, 3H), 7.11–7.06 (m, 3H), 6.82–6.76 (m, 4H), 4.83 (d, *J* = 8.3 Hz, 1H), 4.57–4.44 (m, 1H), 4.07 (q, *J* = 7.0 Hz, 1H), 3.01–2.92 (m, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 212.3, 194.5, 139.6, 138.6, 136.6, 133.7, 129.6, 128.7 (2C), 128.3 (2C), 128.2 (3C), 128.1 (4C), 127.0, 126.9, 61.2, 51.1, 45.5, 44.8; ATR-FTIR ν 1758, 1642, 1608, 1593, 1570, 1357, 1268, 1222, 1146, 1099 cm⁻¹; HRMS (ESI) *m/z* calcd for C₂₄H₂₁O₂ [M + H]⁺ 341.1537, found 341.1536.

(2Z)-4-(4-Fluorophenyl)-2-[hydroxy(phenyl)methylidene]-3-phenylcyclopentan-1-one (2b). Purified in 99:1 to 97:3 petroleum ether/EtOAc; 81 mg yield as a thick orange oil (90%); 1:10 keto:enol. Enol: ¹H NMR (400 MHz, CDCl₃) δ 7.55–7.51 (m, 2H), 7.41–7.34 (m, 1H), 7.26 (s, 2H), 7.17–7.09 (m, 3H), 6.83–6.66 (m, 6H), 4.33 (d, *J* = 7.4 Hz, 1H), 3.85 (dt, *J* = 14.0 Hz, *J'* = 7.2 Hz, 1H), 3.02 (dd, *J* = 17.3 Hz, *J'* = 13.5 Hz, 1H), 2.62 (dd, *J* = 17.3 Hz, *J'* = 7.1 Hz, 1H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 208.9, 171.1, 161.7 (d, *J* = 245.2 Hz), 140.4, 134.7 (d, *J* = 3.1 Hz), 133.9, 131.3, 129.6 (d, *J* = 8.0 Hz, 2C), 128.6 (2C), 128.4 (6C), 126.9, 114.8 (d, *J* = 21.2 Hz, 2C), 113.1, 52.0, 47.6, 40.1; ¹⁹F NMR (470 MHz, CDCl₃) δ -115.9 (ddd, *J* = 13.7 Hz, *J'* = 8.3 Hz, *J''* = 5.4 Hz). Keto: ¹H NMR (400 MHz, CDCl₃) δ 8.07–7.96 (m, 2H), 7.62–7.57 (m, 1H), 7.50–7.45 (m, 2H), 7.28–7.24 (m, 1H), 7.17–7.09 (m, 2H), 6.88–6.74 (m, 6H), 4.82 (d, *J* = 7.7 Hz, 1H), 4.46 (t, *J* = 7.3 Hz, 1H), 4.08 (q, *J* = 7.2 Hz, 1H), 2.93 (d, *J* = 7.8 Hz, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 212.0, 194.4, 161.8 (d, *J* = 245.6 Hz), 138.6, 136.4, 135.3 (d, *J* = 3.3 Hz), 133.9, 133.9, 129.7 (2C), 129.5 (d, *J* = 8.0 Hz, 2C), 128.8 (2C),

128.2 (2C), 127.2, 115.1 (d, *J* = 21.2 Hz, 2C), 61.4, 51.1, 44.9, 44.6; ¹⁹F NMR (470 MHz, CDCl₃) δ -115.8 (tt, *J* = 8.5 Hz, *J'* = 5.5 Hz); ATR-FTIR ν 2905, 1746, 1636, 1592, 1565, 1510, 1492, 1448, 1352, 1219, 1150, 1096 cm⁻¹; HRMS (ESI) *m/z* calcd for C₂₄H₂₀FO₂ [M + H]⁺ 359.1442, found 359.1437.

(2Z)-4-(4-Chlorophenyl)-2-[hydroxy(phenyl)methylidene]-3-phenylcyclopentan-1-one (2c). Purified in 98:2 to 97:3 petroleum ether/EtOAc; 74 mg yield as a thick orange oil (80%); 1:10 keto:enol. Enol: ¹H NMR (400 MHz, CDCl₃) δ 7.57–7.47 (m, 2H), 7.43–7.34 (m, 1H), 7.26 (s, 2H), 7.18–7.11 (m, 3H), 7.09–7.02 (m, 2H), 6.82–6.76 (m, 2H), 6.67 (d, *J* = 8.4 Hz, 2H), 4.34 (d, *J* = 7.4 Hz, 1H), 3.83 (dt, *J* = 14.0 Hz, *J'* = 7.2 Hz, 1H), 3.03 (dd, *J* = 17.3 Hz, *J'* = 13.4 Hz, 1H), 2.61 (dd, *J* = 17.3 Hz, *J'* = 7.1 Hz, 1H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 208.7, 171.1, 140.3, 137.6, 133.9, 132.5, 131.4, 129.5 (2C), 128.6 (2C), 128.5 (2C), 128.4 (4C), 128.1 (2C), 127.0, 113.1, 51.8, 47.7, 39.9. Keto: ¹H NMR (400 MHz, CDCl₃) δ 8.02 (dd, *J* = 8.4 Hz, *J'* = 1.3 Hz, 2H), 7.64–7.55 (m, 1H), 7.50–7.46 (m, 2H), 7.28–7.24 (m, 3H), 7.16–7.10 (m, 4H), 6.82–6.76 (m, 2H), 6.76–6.71 (m, 2H), 4.82 (d, *J* = 7.6 Hz, 1H), 4.47 (t, *J* = 7.3 Hz, 1H), 4.08 (q, *J* = 7.3 Hz, 1H), 2.92 (d, *J* = 7.6 Hz, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 211.8, 194.3, 138.4, 138.1, 136.4, 132.7, 131.4, 129.7 (2C), 129.4 (2C), 128.8 (2C), 128.5 (2C), 128.3 (2C), 128.2 (2C), 127.3, 61.5, 51.0, 45.0, 44.4; ATR-FTIR ν 3026, 1743, 1595, 1570, 1493, 1447, 1362, 1266, 1226, 1091, 1016 cm⁻¹; HRMS (ESI) *m/z* calcd for C₂₄H₂₀ClO₂ [M + H]⁺ 375.1146, found 375.1160.

(2Z)-4-(4-Bromophenyl)-2-[hydroxy(phenyl)methylidene]-3-phenylcyclopentan-1-one (2d). Purified in 98:2 to 97:3 petroleum ether/EtOAc; 85 mg yield as a thick orange oil (81%); 1:10 keto:enol. Enol: ¹H NMR (400 MHz, CDCl₃) δ 7.55–7.49 (m, 2H), 7.42–7.35 (m, 1H), 7.29–7.19 (m, 4H), 7.17–7.10 (m, 3H), 6.81–6.77 (m, 2H), 6.65–6.57 (m, 2H), 4.35 (d, *J* = 7.4 Hz, 1H), 3.81 (dt, *J* = 14.0 Hz, *J'* = 7.2 Hz, 1H), 3.02 (dd, *J* = 17.3 Hz, *J'* = 13.5 Hz, 1H), 2.61 (dd, *J* = 17.3 Hz, *J'* = 7.1 Hz, 1H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 208.7, 171.1, 140.2, 138.1, 133.9, 131.3, 131.0 (2C), 129.9 (2C), 128.6 (2C), 128.5 (2C), 128.4 (4C), 127.0, 120.7, 113.1, 51.8, 47.8, 39.9. Keto: ¹H NMR (400 MHz, CDCl₃) δ 8.07–7.99 (m, 2H), 7.62–7.57 (m, 1H), 7.50–7.46 (m, 1H), 7.26 (s, 1H), 7.17–7.09 (m, 4H), 6.82–6.75 (m, 2H), 6.68 (d, *J* = 8.4 Hz, 2H), 4.82 (d, *J* = 7.6 Hz, 1H), 4.47 (t, *J* = 7.3 Hz, 1H), 4.06 (q, *J* = 7.3 Hz, 1H), 2.95–2.89 (m, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 211.7, 194.2, 138.6, 138.4, 136.4, 133.9, 131.3 (2C), 129.7 (4C), 128.8 (2C), 128.5 (2C), 128.1 (2C), 127.3, 120.8, 61.4, 50.9, 45.1, 44.3; ATR-FTIR ν 3028, 1746, 1596, 1567, 1490, 1365, 1263, 1225, 1077, 1011 cm⁻¹; HRMS (ESI) *m/z* calcd for C₂₄H₂₀BrO₂ [M + H]⁺ 419.0641, found 419.0635.

(2Z)-4-(3-Bromophenyl)-2-[hydroxy(phenyl)methylidene]-3-phenylcyclopentan-1-one (2e). Purified in 97:3 to 95:5 petroleum ether/EtOAc; 72 mg yield as a thick orange oil (69%); 1:10 keto:enol. Enol: ¹H NMR (400 MHz, CDCl₃) δ 7.56–7.51 (m, 2H), 7.42–7.35 (m, 1H), 7.30–7.22 (m, 3H), 7.16–7.13 (m, 3H), 6.96–6.89 (m, 2H), 6.81–6.77 (m, 2H), 6.67–6.63 (m, 1H), 4.35 (d, *J* = 7.4 Hz, 1H), 3.81 (dt, *J* = 14.1 Hz, *J'* = 7.3 Hz, 1H), 3.03 (dd, *J* = 17.3 Hz, *J'* = 13.4 Hz, 1H), 2.62 (dd, *J* = 17.3 Hz, *J'* = 7.2 Hz, 1H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 208.5, 171.2, 141.5, 140.2, 133.8, 131.5, 131.4, 129.9, 129.5, 128.5 (2C), 128.4 (6C), 127.1, 126.7, 122.1, 113.0, 51.9, 48.0, 39.7. Keto: ¹H NMR (400 MHz, CDCl₃) δ 8.06–8.00 (m, 2H), 7.62–7.57 (m, 1H), 7.51–7.47 (m, 1H), 7.29–7.22 (m, 3H), 7.16–7.13 (m, 3H), 7.03–6.99 (m, 1H), 6.83–6.77 (m, 2H), 6.76–6.72 (m, 1H), 4.82 (d, *J* = 7.1 Hz, 1H), 4.46 (t, *J* = 7.1 Hz, 1H), 4.08 (q, *J* = 7.4 Hz, 1H), 2.92 (dd, *J* = 7.8 Hz, *J'* = 1.1 Hz, 1H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 211.6, 194.2, 141.9, 138.4, 136.3, 133.9, 131.3, 130.0, 129.7 (3C), 128.8 (2C), 128.4 (2C), 128.1 (2C), 127.4, 126.5, 122.4, 61.7, 51.0, 45.3, 43.9; ATR-FTIR ν 3024, 2917, 1744, 1637, 1592, 1569, 1494, 1475, 1357, 1265, 1225, 1152, 1098, 1075 cm⁻¹; HRMS (ESI) *m/z* calcd for C₂₄H₂₀BrO₂ [M + H]⁺ 419.0641, found 419.0631.

(2Z)-4-(2-Bromophenyl)-2-[hydroxy(phenyl)methylidene]-3-phenylcyclopentan-1-one (2f). Purified in 97:3 to 95:5 petroleum ether/EtOAc; 70 mg yield as a thick orange oil (67%); 1:24 keto:enol; ¹H NMR (400 MHz, CDCl₃) δ 7.62–7.49 (m, 3H), 7.42–7.34 (m, 1H),

7.30–7.26 (m, 2H), 7.12–7.04 (m, 3H), 6.99–6.94 (m, 1H), 6.92–6.79 (m, 3H), 6.41 (dd, $J = 7.9$ Hz, $J' = 1.7$ Hz, 1H), 4.73 (d, $J = 7.4$ Hz, 1H), 4.29 (dt, $J = 14.1$ Hz, $J' = 7.2$ Hz, 1H), 3.13 (dd, $J = 17.2$ Hz, $J' = 13.7$ Hz, 1H), 2.59 (dd, $J = 17.2$ Hz, $J' = 7.1$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 208.4, 171.5, 140.8, 138.0, 133.9, 132.7, 131.4, 128.5 (2C), 128.4 (5C), 128.3, 128.0 (2C), 126.9, 126.8, 125.5, 112.6, 48.4, 47.1, 39.1; ATR-FTIR ν 3067, 3024, 1596, 1567, 1494, 1471, 1367, 1230, 1023 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{20}\text{BrO}_2$ $[\text{M} + \text{H}]^+$ 419.0641, found 419.0630.

(2Z)-2-[Hydroxy(phenyl)methylidene]-4-(4-methylphenyl)-3-phenylcyclopentan-1-one (**2g**). Purified in 98:2 to 97:3 petroleum ether/EtOAc; 80 mg yield as a thick yellow oil (90%); 1:7 keto:enol. Enol: ^1H NMR (400 MHz, CDCl_3) δ 7.57–7.54 (m, 2H), 7.40–7.35 (m, 1H), 7.29–7.26 (m, 2H), 7.14–7.11 (m, 3H), 6.93–6.91 (m, 2H), 6.85–6.78 (m, 2H), 6.67–6.65 (m, 2H), 4.36 (d, $J = 7.4$ Hz, 1H), 3.84 (dt, $J = 14.1$ Hz, $J' = 7.2$ Hz, 1H), 3.08 (dd, $J = 17.3$ Hz, $J' = 13.6$ Hz, 1H), 2.61 (dd, $J = 17.3$ Hz, $J' = 7.1$ Hz, 1H), 2.27 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 209.5, 170.7, 140.6, 136.3, 135.8, 134.0, 131.2, 128.7 (2C), 128.6 (2C), 128.4 (2C), 128.3 (2C), 128.2 (2C), 128.1 (2C), 126.7, 113.4, 51.9, 48.1, 40.1, 21.1. Keto: ^1H NMR (400 MHz, CDCl_3) δ 8.05–8.00 (m, 2H), 7.52–7.48 (m, 2H), 7.30–7.26 (m, 2H), 7.15–7.08 (m, 3H), 7.00–6.96 (m, 2H), 6.84–6.78 (m, 1H), 6.72 (d, $J = 8.1$ Hz, 2H), 4.86 (d, $J = 8.6$ Hz, 1H), 4.51 (dd, $J = 8.6$ Hz, $J' = 6.8$ Hz, 1H), 4.05 (q, $J = 6.9$ Hz, 1H), 2.96 (d, $J = 6.9$ Hz, 1H), 2.27 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 212.5, 194.6, 172.1, 142.2, 138.7, 136.4, 134.0, 133.7, 129.6, 128.9 (2C), 128.7 (2C), 128.6 (2C), 128.2 (2C), 128.0 (2C), 127.9 (2C), 61.1, 51.9, 45.1, 22.0; ATR-FTIR ν 3024, 1744, 1608, 1592, 1571, 1515, 1492, 1448, 1365, 1261, 1227, 1150, 1098, 1078, 1030 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{23}\text{O}_2$ $[\text{M} + \text{H}]^+$ 355.1693, found 355.1677.

(2Z)-2-[Hydroxy(phenyl)methylidene]-3,4-bis(4-methylphenyl)-cyclopentan-1-one (**2h**). Purified in 98:2 petroleum ether/EtOAc; 70 mg yield as a thick yellow oil (76%); 1:5 keto:enol. Enol: ^1H NMR (400 MHz, CDCl_3) δ 7.58–7.51 (m, 2H), 7.40–7.33 (m, 1H), 7.28–7.25 (m, 2H), 6.91 (d, $J = 7.8$ Hz, 4H), 6.71–6.61 (m, 4H), 4.29 (d, $J = 7.2$ Hz, 1H), 3.79 (dt, $J = 14.0$ Hz, $J' = 7.1$ Hz, 1H), 3.04 (dd, $J = 17.3$ Hz, $J' = 13.7$ Hz, 1H), 2.57 (dd, $J = 17.3$ Hz, $J' = 7.0$ Hz, 1H), 2.26 (s, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 209.7, 170.4, 137.4, 136.3 (2C), 136.2, 136.0, 131.2, 129.0 (2C), 128.6 (2C), 128.6 (2C), 128.5 (2C), 128.3 (2C), 128.2 (2C), 113.8, 51.5, 48.2, 40.1, 21.2 (2C). Keto: ^1H NMR (400 MHz, CDCl_3) δ 8.02–7.96 (m, 2H), 7.59–7.55 (m, 1H), 7.51–7.42 (m, 3H), 7.29–7.24 (m, 2H), 6.97 (d, $J = 7.8$ Hz, 2H), 6.74–6.68 (m, 3H), 4.79 (d, $J = 8.5$ Hz, 1H), 4.43 (dd, $J = 8.5$ Hz, $J' = 6.8$ Hz, 1H), 4.00 (q, $J = 6.9$ Hz, 1H), 2.93 (d, $J = 6.9$ Hz, 2H), 2.26 (s, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 212.8, 194.8, 136.7, 136.6, 136.5, 136.4, 135.6, 133.7, 129.6 (2C), 128.9 (4C), 128.7 (2C), 128.1 (4C), 61.4, 50.8, 45.2, 45.1, 21.1 (2C); ATR-FTIR ν 3020, 2913, 1744, 1573, 1513, 1494, 1361, 1223 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{26}\text{H}_{25}\text{O}_2$ $[\text{M} + \text{H}]^+$ 369.1849, found 369.1862.

(2Z)-2-[Hydroxy(phenyl)methylidene]-4-(4-methoxyphenyl)-3-phenylcyclopentan-1-one (**2i**). Purified in 98:2 petroleum ether/EtOAc; 46 mg yield as a thick yellow oil (50%); 1:5 keto:enol. Enol: ^1H NMR (400 MHz, CDCl_3) δ 7.61–7.51 (m, 2H), 7.39–7.33 (m, 1H), 7.28–7.24 (m, 2H), 7.15–7.06 (m, 3H), 6.82–6.75 (m, 2H), 6.65–6.63 (m, 3H), 4.32 (d, $J = 7.4$ Hz, 1H), 3.82 (dt, $J = 14.0$ Hz, $J' = 7.2$ Hz, 1H), 3.73 (s, 3H), 3.04 (dd, $J = 17.3$ Hz, $J' = 13.6$ Hz, 1H), 2.59 (dd, $J = 17.3$ Hz, $J' = 7.1$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 209.5, 170.7, 158.4, 140.7, 134.0, 131.2, 129.6, 129.2 (2C), 128.7 (2C), 128.4 (2C), 128.3 (4C), 126.7, 113.6, 113.4 (2C), 55.3, 52.0, 47.7, 40.2. Keto: ^1H NMR (400 MHz, CDCl_3) δ 8.04–7.96 (m, 2H), 7.61–7.56 (m, 1H), 7.50–7.45 (m, 2H), 7.14–7.09 (m, 3H), 6.82–6.75 (m, 2H), 6.70 (d, $J = 2.8$ Hz, 2H), 6.64 (d, $J = 3.2$ Hz, 2H), 4.81 (d, $J = 8.5$ Hz, 0H), 4.46 (dd, $J = 8.4$, 6.8 Hz, 1H), 4.02 (q, $J = 6.9$ Hz, 1H), 3.75 (s, 2H), 2.96–2.90 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 212.6, 195.0, 138.8, 136.6, 133.8, 131.6, 131.0 (2C), 129.6, 129.1 (2C), 128.8 (2C), 128.3 (4C), 127.0, 113.4 (2C), 61.2, 56.3, 51.2, 45.1, 44.8; ATR-FTIR ν 2840, 1744, 1610, 1515,

1365, 1248, 1180, 1032 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{23}\text{O}_3$ $[\text{M} + \text{H}]^+$ 371.1642, found 371.1638.

Characterization of Demethylated OTHO (1i'). Methyl 4-(4-Hydroxyphenyl)-6-oxo-3,4-diphenylhexanoate (1i'). Purified in 3:1 pentane/EtOAc; 25 mg yield (25%) as a white solid; mp 180–182 °C (from MeOH); ^1H NMR (400 MHz, CDCl_3) δ 7.64 (d, $J = 7.6$ Hz, 2H), 7.45 (t, $J = 7.3$ Hz, 1H), 7.34–7.27 (m, 6H), 7.21–7.12 (m, 3H), 6.72 (d, $J = 7.7$ Hz, 2H), 3.55 (td, $J = 11.3$ Hz, $J' = 10.2$ Hz, $J'' = 6.6$ Hz, 1H), 3.47–3.21 (m, 5H), 2.93 (dd, $J = 16.6$ Hz, $J' = 3.2$ Hz, 1H), 2.67–2.30 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 199.3, 173.2, 155.0, 142.6, 137.1, 133.8, 133.0, 129.4 (2C), 128.8 (2C), 128.5 (2C), 128.4 (2C), 128.0 (2C), 127.0, 115.8 (2C), 51.7, 47.3 (2C), 44.0, 40.3; ATR-FTIR ν 2204, 2160, 2190, 1726, 1680, 1514, 1231, 1153 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{25}\text{O}_4$ $[\text{M} + \text{H}]^+$ 389.1747, found 389.1748.

Methyl 4-((3Z)-3-[Hydroxy(phenyl)methylidene]-4-oxo-2-phenylcyclopentyl)benzoate (2j). Purified in 94:6 to 93:7 petroleum ether/EtOAc; 50 mg yield as a thick yellow oil (50%); 1:8 keto:enol 1:8. Enol: ^1H NMR (400 MHz, CDCl_3) δ 7.79–7.73 (m, 2H), 7.53–7.50 (m, 2H), 7.39–7.35 (m, 1H), 7.28–7.24 (s, 3H), 7.13–7.05 (m, 3H), 6.87–6.81 (m, 2H), 6.78–6.75 (m, 2H), 4.39 (d, $J = 7.4$ Hz, 1H), 3.96–3.86 (m, 4H), 3.11 (dd, $J = 17.3$ Hz, $J' = 13.4$ Hz, 1H), 2.64 (dd, $J = 17.4$ Hz, $J' = 7.1$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 208.6, 171.3, 167.0, 144.6, 140.2, 133.9, 131.4, 129.3 (2C), 128.5 (4C), 128.4 (5C), 128.2 (2C), 127.0, 113.0, 52.1, 51.9, 48.3, 39.6. Keto: ^1H NMR (400 MHz, CDCl_3) δ 8.02 (dt, $J = 9.0$ Hz, $J' = 1.5$ Hz, 2H), 8.00–7.94 (m, 2H), 7.82–7.79 (m, 2H), 7.62–7.57 (m, 1H), 7.51–7.47 (m, 2H), 7.13–7.03 (m, 2H), 6.94–6.86 (m, 2H), 6.78–6.75 (m, 2H), 4.83 (d, $J = 7.5$ Hz, 1H), 4.51 (t, $J = 7.3$ Hz, 1H), 4.16 (q, $J = 7.3$ Hz, 1H), 3.87 (s, 3H), 3.05–2.92 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 211.6, 194.2, 145.0, 138.3, 136.3, 130.0, 129.7 (2C), 129.5 (2C), 128.8 (2C), 128.6 (3C), 128.1 (4C), 127.3, 61.6, 51.0, 45.6, 44.1, 35.3, 31.0; ATR-FTIR ν 3062, 2951, 1717, 1677, 1607, 1570, 1493, 1367, 1277, 1097, 1019 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{26}\text{H}_{23}\text{O}_4$ $[\text{M} + \text{H}]^+$ 399.1591, found 399.1607.

(2Z)-3-(4-Chlorophenyl)-2-[hydroxy(phenyl)methylidene]-4-phenylcyclopentan-1-one (**2k**). Purified in 99:1 to 95:5 petroleum ether/EtOAc; 55 mg yield as a thick transparent oil (59%); 1:4 keto:enol. Enol: ^1H NMR (400 MHz, CDCl_3) δ 7.52–7.44 (m, 2H), 7.42–7.35 (m, 1H), 7.30–7.26 (m, 1H), 7.22–7.16 (m, 1H), 7.16–7.09 (m, 3H), 7.09–7.02 (m, 2H), 6.85–6.74 (m, 2H), 6.74–6.64 (m, 2H), 4.35 (d, $J = 7.4$ Hz, 1H), 3.93–3.82 (m, 1H), 3.09–2.94 (m, 1H), 2.67–2.57 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 212.1, 171.7, 139.5, 138.9, 131.8, 130.2 (2C), 130.0, 128.8 (2C), 128.7 (2C), 128.6 (2C), 128.5 (4C), 128.4, 127.4, 113.2, 51.7, 48.5, 39.9. Keto: ^1H NMR (400 MHz, CDCl_3) δ 8.01–7.96 (m, 2H), 7.62–7.56 (m, 1H), 7.52–7.44 (m, 1H), 7.30–7.26 (m, 1H), 7.22–7.16 (m, 2H), 7.16–7.09 (m, 3H), 6.85–6.74 (m, 2H), 6.74–6.64 (m, 2H), 4.76 (d, $J = 9.1$ Hz, 1H), 4.56–4.47 (m, 1H), 4.06–3.99 (q, $J = 6.7$ Hz, 1H), 3.09–2.94 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 212.1, 194.5, 139.7, 137.5, 134.2, 134.2, 132.9, 130.0, 129.8, 129.1, 128.8, 128.8 (2C), 128.7(2C), 128.6 (2C), 128.4 (2C), 127.5, 61.3, 50.7, 45.6, 45.4; ATR-FTIR ν 2956, 2915, 1546, 1566, 1489, 1351, 1257, 1227, 1088, 1014 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{20}\text{ClO}_2$ $[\text{M} + \text{H}]^+$ 375.1146, found 375.1145.

(2Z)-3-(4-Bromophenyl)-2-[hydroxy(phenyl)methylidene]-4-phenylcyclopentan-1-one (**2l**). Purified in 99:1 to 97:3 petroleum ether/EtOAc; 75 mg yield as a thick yellow oil (72%); 1:10 keto:enol. Enol: ^1H NMR (400 MHz, CDCl_3) δ 7.54–7.46 (m, 2H), 7.44–7.36 (m, 1H), 7.29–7.25 (m, 2H), 7.24–7.19 (m, 2H), 7.16–7.10 (m, 3H), 6.82–6.74 (m, 2H), 6.69–6.58 (m, 2H), 4.34 (d, $J = 7.4$ Hz, 1H), 3.94–3.81 (m, 1H), 3.04 (dd, $J = 17.4$ Hz, $J' = 13.5$ Hz, 1H), 2.63 (dd, $J = 17.4$ Hz, $J' = 7.1$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 208.9, 171.3, 139.6, 138.5, 133.8, 131.4, 131.3 (2C), 130.2 (2C), 128.4 (2C), 128.3 (2C), 128.2 (2C), 128.1 (2C), 127.1, 120.7, 112.7, 51.4, 48.1, 39.5. Keto: ^1H NMR (400 MHz, CDCl_3) δ 8.04–7.97 (m, 2H), 7.64–7.56 (m, 1H), 7.53–7.45 (m, 1H), 7.30–7.24 (m, 1H), 7.24–7.18 (m, 2H), 7.16–7.11 (m, 3H), 6.84–6.79 (s, 2H), 6.68–6.62 (m, 2H), 4.77 (d, $J = 9.2$ Hz, 1H), 4.51 (dd, $J = 9.2$ Hz, $J' = 6.9$ Hz, 1H), 4.03 (q, $J = 6.7$ Hz, 1H), 2.97 (d, $J = 6.6$ Hz, 1H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 211.6, 194.1, 139.3, 137.7, 136.5, 133.9, 131.3, 129.8 (2C), 129.6 (2C), 128.8 (2C), 128.4 (2C), 128.1 (2C), 127.1 (2C), 121.0, 60.8, 50.4, 45.2, 45.0; ATR-FTIR ν 2959, 1742, 1644, 1592, 1565, 1486, 1351, 1230 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{20}\text{BrO}_2$ $[\text{M} + \text{H}]^+$ 419.0641, found 419.0641.

(2Z)-2-[Hydroxy(phenyl)methylidene]-3-(4-methylphenyl)-4-phenylcyclopentan-1-one (**2m**). Purified in 98:2 to 97:3 petroleum ether/EtOAc; 62 mg yield as a thick yellow oil (70%); 1:10 keto:enol. Enol: ^1H NMR (400 MHz, CDCl_3) δ 7.61–7.54 (m, 2H), 7.43–7.34 (m, 1H), 7.30–7.26 (s, 2H), 7.16–7.07 (m, 3H), 6.95–6.89 (m, 2H), 6.84–6.76 (m, 2H), 6.71–6.64 (m, 2H), 4.35 (d, $J = 7.3$ Hz, 1H), 3.85 (dt, $J = 14.0$ Hz, $J' = 7.1$ Hz, 1H), 3.10 (dd, $J = 17.3$ Hz, $J' = 13.7$ Hz, 1H), 2.62 (dd, $J = 17.2$ Hz, $J' = 7.0$ Hz, 1H), 2.26 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 209.5, 170.5, 139.0, 137.3, 136.2, 134.0, 131.2, 128.9 (2C), 128.5 (2C), 128.4 (2C), 128.3 (2C), 128.2 (2C), 127.9 (2C), 126.7, 113.6, 51.6, 48.4, 39.8, 21.1. Keto: ^1H NMR (400 MHz, CDCl_3) δ 8.07–7.99 (m, 2H), 7.52–7.45 (m, 2H), 7.30–7.26 (s, 2H), 7.20–7.17 (m, 3H), 6.95–6.89 (m, 1H), 6.88–6.82 (m, 2H), 6.72–6.62 (m, 2H), 4.83 (d, $J = 8.3$ Hz, 1H), 4.48 (dd, $J = 8.3$ Hz, $J' = 6.9$ Hz, 1H), 4.07 (q, $J = 7.0$ Hz, 1H), 3.02–2.91 (m, 2H), 2.24 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 212.5, 194.7, 139.7, 136.6, 136.5, 135.5, 133.7, 129.6 (2C), 128.9 (2C), 128.7 (2C), 128.2 (2C), 128.1 (2C), 128.0 (2C), 126.8, 61.4, 50.8, 45.5, 44.8, 21.1; ATR-FTIR ν 2917, 1740, 1606, 1569, 1494, 1369, 1265 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{23}\text{O}_2$ $[\text{M} + \text{H}]^+$ 355.1693, found 355.1701.

4-[(2Z)-2-[Hydroxy(phenyl)methylidene]-3-methylidene-5-phenylcyclopentyl]benzointrile (**2n**). Purified in 9:1 to 4:1 pentane/EtOAc; 72 mg yield as a thick pink oil (79%); >1:7 keto:enol. Enol: ^1H NMR (400 MHz, CDCl_3) δ 7.48–7.41 (m, 2H), 7.36 (dd, $J = 9.5$ Hz, $J' = 7.8$ Hz, 3H), 7.28–7.24 (m, 2H), 7.12 (dt, $J = 5.4$ Hz, $J' = 2.7$ Hz, 3H), 6.87 (d, $J = 8.1$ Hz, 2H), 6.76 (dd, $J = 7.1$ Hz, $J' = 2.4$ Hz, 2H), 4.48 (d, $J = 7.6$ Hz, 1H), 3.95 (dt, $J = 12.9$ Hz, $J' = 7.4$ Hz, 1H), 3.03 (dd, $J = 17.5$ Hz, $J' = 13.0$ Hz, 1H), 2.69 (dd, $J = 17.5$ Hz, $J' = 7.2$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 208.2, 172.2, 146.4, 138.1, 133.6, 131.9 (2C), 131.6, 129.1 (2C), 128.6, 128.4 (2C), 128.3 (2C), 128.1 (2C), 127.9 (2C), 127.3, 111.9, 110.6, 52.0, 47.9, 39.4. Keto: ^1H NMR (400 MHz, CDCl_3) δ 8.06–7.97 (m, 2H), 7.61 (t, $J = 7.4$ Hz, 1H), 7.50 (t, $J = 7.7$ Hz, 2H), 7.21–7.17 (m, 3H), 6.89–6.86 (m, 3H), 6.81–6.78 (m, 3H), 4.82 (d, $J = 9.6$ Hz, 1H), 4.64 (dd, $J = 9.6$ Hz, $J' = 6.9$ Hz, 1H), 4.06 (td, $J = 7.1$ Hz, $J' = 5.1$ Hz, 1H), 3.06–2.96 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 210.7, 193.5, 144.3, 139.0, 136.3, 134.0, 132.0 (2C), 129.7 (2C), 128.9, 128.8 (2C), 128.6 (2C), 128.4 (2C), 128.3 (2C), 127.4, 118.8, 110.9, 60.2, 50.7, 45.1; ATR-FTIR ν 3029, 2228, 1743, 1607, 1570, 1493, 1361, 1227, 1151 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{20}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 366.1489, found 366.1489.

(2Z)-2-[Hydroxy(4-methylphenyl)methylidene]-3,4-diphenylcyclopentan-1-one (**2o**). Purified in 99:1 to 95:5 petroleum ether/EtOAc; 52 mg yield as a thick transparent oil (56%); >1:20 keto:enol. Enol: ^1H NMR (400 MHz, CDCl_3) δ 7.51–7.45 (m, 2H), 7.27–7.21 (m, 2H), 7.17–7.04 (m, 6H), 6.80–6.73 (m, 4H), 4.33 (d, $J = 7.4$ Hz, 1H), 3.94–3.83 (m, 1H), 3.59–3.03 (m, 1H), 2.68–2.59 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 212.6, 212.3, 209.7, 193.5, 169.9, 140.7, 140.6, 139.8, 139.1, 138.8, 137.8, 135.2, 132.7, 131.4, 130.1, 129.4, 129.0, 128.9, 128.7, 128.5, 128.3, 127.4, 127.2, 113.4, 77.2, 61.6, 52.3, 48.6, 45.8, 45.2, 40.1; ATR-FTIR ν 3027, 1591, 1487, 1360, 1259, 1090, 1011 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{20}\text{ClO}_2$ $[\text{M} + \text{H}]^+$ 375.1139, found 375.1146.

(2Z)-2-[(4-Bromophenyl)(hydroxy)methylidene]-3,4-diphenylcyclopentan-1-one (**2p**). Purified in 98:2 to 96:4 petroleum ether/EtOAc; 79 mg yield as a thick yellow oil (75%); 1:18 keto:enol. Enol: ^1H NMR (400 MHz, CDCl_3) δ 7.42–7.38 (m, 4H), 7.14–7.06 (m, 6H), 6.81–6.72 (m, 4H), 4.33 (d, $J = 7.4$ Hz, 1H), 3.88 (dt, $J = 14.1$ Hz, $J' = 7.3$ Hz, 1H), 3.10 (dd, $J = 17.4$ Hz, $J' = 13.6$ Hz, 1H), 2.64 (dd, $J = 17.4$ Hz, $J' = 7.1$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 209.4, 169.6, 140.2, 138.7, 132.8, 131.6 (2C), 129.9 (2C), 128.5 (2C), 128.4 (2C), 128.2 (2C), 128.0 (2C), 126.9, 126.9, 126.0, 113.5, 51.9, 48.2, 39.8. Keto: ^1H NMR (400 MHz, CDCl_3) δ 7.89 (d, $J = 8.7$ Hz, 2H), 7.62 (d, $J = 8.5$ Hz, 2H), 7.56–7.52 (m, 1H), 7.35–

7.29 (m, 1H), 7.18–7.07 (m, 6H), 6.84–6.73 (m, 2H), 4.77 (d, $J = 8.4$ Hz, 1H), 4.52 (dd, $J = 8.6$ Hz, $J' = 6.9$ Hz, 1H), 4.06 (q, $J = 7.0$ Hz, 1H), 3.01–2.94 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 211.9, 193.3, 139.4, 138.5, 135.3, 132.1 (2C), 131.2 (2C), 128.3 (2C), 128.2 (2C), 128.1 (4C), 127.1, 127.0, 126.0, 61.2, 50.9, 45.4, 44.8; ATR-FTIR ν 1588, 1485, 1359, 1257, 1234, 1071, 1007 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{20}\text{BrO}_2$ $[\text{M} + \text{H}]^+$ 419.0641, found 419.0638.

(2Z)-2-[Hydroxy(4-methylphenyl)methylidene]-3,4-diphenylcyclopentan-1-one (**2q**). Purified in 99:1 to 95:5 petroleum ether/EtOAc; 51 mg yield as a thick transparent oil (58%); 1:10 keto:enol. Enol: ^1H NMR (400 MHz, CDCl_3) δ 7.49–7.44 (m, 2H), 7.14–7.05 (m, 8H), 6.85–6.69 (m, 4H), 4.38 (d, $J = 7.4$ Hz, 1H), 3.87 (dt, $J = 13.6$ Hz, $J' = 7.2$ Hz, 1H), 3.09 (dd, $J = 17.3$ Hz, $J' = 13.6$ Hz, 1H), 2.62 (dd, $J = 17.3$ Hz, $J' = 7.1$ Hz, 1H), 2.32 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 209.0, 171.2, 141.9, 140.6, 139.0, 131.1, 129.1 (2C), 128.6 (2C), 128.5 (2C), 128.2 (4C), 128.0 (2C), 126.8, 126.7, 112.8, 52.1, 48.4, 39.7, 21.6. Keto: ^1H NMR (400 MHz, CDCl_3) δ 7.93 (d, $J = 8.3$ Hz, 2H), 7.28 (dt, $J = 8.0$ Hz, $J' = 0.8$ Hz, 3H), 7.18–7.14 (m, 3H), 7.11–7.04 (m, 2H), 6.90–6.88 (m, 2H), 6.83–6.81 (m, 4H), 4.82 (d, $J = 8.2$ Hz, 1H), 4.51 (dd, $J = 8.2$ Hz, $J' = 7.0$ Hz, 1H), 4.08 (q, $J = 7.0$ Hz, 1H), 3.01–2.91 (m, 1H), 2.42 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 212.5, 194.0, 144.8, 139.7, 138.8, 134.1, 129.8 (2C), 129.5 (2C), 128.2 (6C), 128.1 (2C), 127.0, 126.9, 61.2, 51.1, 45.5, 44.7 21.8; ATR-FTIR ν 3022, 1744, 1632, 1595, 1495, 1364, 1225, 1149, 1098 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{23}\text{O}_2$ $[\text{M} + \text{H}]^+$ 355.1693, found 355.1698.

Methyl 4-[Hydroxy[(1Z)-5-oxo-2,3-diphenylcyclopentylidene]methyl]benzoate (**2r**). Purified in 99:1 to 95:5 petroleum ether/EtOAc; 41 mg yield as a thick transparent oil (41%); >1:20 keto:enol. Enol: ^1H NMR (400 MHz, CDCl_3) δ 8.06–7.77 (m, 2H), 7.68–7.48 (m, 2H), 7.16–7.00 (m, 6H), 6.82–6.69 (m, 4H), 4.34 (d, $J = 7.4$ Hz, 1H), 3.88 (s, 3H), 3.10 (dd, $J = 17.5$ Hz, $J' = 13.5$ Hz, 1H), 2.65 (dd, $J = 17.4$ Hz, $J' = 7.1$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 209.9, 169.2, 166.4, 140.3, 138.7, 138.0, 132.1, 129.5 (2C), 128.6 (2C), 128.4 (2C), 128.3 (2C), 128.2 (2C), 128.0 (2C), 126.9, 114.3, 77.2, 52.5, 51.9, 48.2, 39.9; ATR-FTIR ν 2957, 1712, 1636, 1593, 1426, 1371, 1283, 1112, 1018 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{26}\text{H}_{23}\text{O}_4$ $[\text{M} + \text{H}]^+$ 399.1591, found 399.1597.

4-[Hydroxy[(1Z)-5-oxo-2,3-diphenylcyclopentylidene]methyl]benzointrile (**2s**). Purified in 9:1 to 4:1 pentane/EtOAc; 55 mg yield as an orange solid (60%); mp 122–125 $^{\circ}\text{C}$; >1:10 keto:enol. Enol: ^1H NMR (400 MHz, CDCl_3) δ 7.61 (d, $J = 8.5$ Hz, 2H), 7.53 (d, $J = 8.5$ Hz, 2H), 7.15–7.05 (m, 6H), 6.75 (td, $J = 7.5$ Hz, $J' = 2.0$ Hz, 4H), 4.32 (d, $J = 7.4$ Hz, 1H), 3.89 (dt, $J = 13.0$ Hz, $J' = 7.2$ Hz, 1H), 3.10 (dd, $J = 17.5$ Hz, $J' = 13.4$ Hz, 1H), 2.67 (dd, $J = 17.5$ Hz, $J' = 7.1$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 210.1, 167.7, 139.9, 138.4, 138.1, 132.0 (2C), 128.8 (2C), 128.5 (2C), 128.4 (2C), 128.1 (4C), 127.1, 127.0, 114.7, 114.4 (2C), 51.7, 48.1, 39.9. Keto: ^1H NMR (400 MHz, CDCl_3) δ 8.10 (d, $J = 8.2$ Hz, 2H), 7.78 (d, $J = 8.2$ Hz, 2H), 7.18–7.13 (m, 6H), 6.84–6.74 (m, 4H), 4.79 (d, $J = 8.9$ Hz, 1H), 4.53 (dd, $J = 8.9$ Hz, $J' = 6.9$ Hz, 1H), 4.05 (q, $J = 6.8$ Hz, 1H), 2.99 (dd, $J = 6.7$ Hz, $J' = 4.6$ Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 211.4, 193.1, 139.5, 139.2, 138.2, 132.5 (2C), 130.0 (2C), 128.3 (4C), 128.0 (4C), 127.2, 127.1, 116.9, 114.4, 61.5, 50.8, 45.4, 45.0; ATR-FTIR ν 3030, 1637, 1585, 1495, 1345, 1261, 1224, 1148, cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{20}\text{NO}_2$ $[\text{M} + \text{H}]^+$ 366.1489, found 366.1494.

(Z)-2-[Hydroxy(phenyl)methylene]-3-(4-methoxyphenyl)-4-phenylcyclopentan-1-one (**2t**). Purified in 8:1 to 4:1 pentane/EtOAc; 43 mg yield as a yellow semisolid (46%); >1:10 keto:enol. Enol: ^1H NMR (400 MHz, CDCl_3) δ 7.55–7.53 (m, 2H), 7.41–7.33 (m, 1H), 7.31–7.22 (m, 2H), 7.14–7.05 (m, 3H), 6.79–6.76 (m, 2H), 6.72–6.59 (m, 4H), 4.31 (d, $J = 7.2$ Hz, 1H), 3.89–3.78 (m, 1H), 3.73 (s, 3H), 3.06 (dd, $J = 17.3$ Hz, $J' = 13.6$ Hz, 1H), 2.60 (dd, $J = 17.3$ Hz, $J' = 7.0$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ (101 MHz, CDCl_3) δ 209.5, 170.7, 158.4, 139.1, 132.6, 131.3, 129.6 (3C), 128.5 (2C), 128.4 (2C), 128.3 (2C), 128.0 (2C), 126.8, 113.7 (2C), 113.6, 55.3, 51.2, 48.4, 39.8. Keto: ^1H NMR (400 MHz, CDCl_3) δ 8.00–7.98 (m, 1H), 7.49–7.46 (m, 3H), 7.26–7.24 (m, 2H), 7.18–7.15 (m, 3H), 6.84–6.80 (m, 2H), 6.72–

6.62 (m, 4H), 4.76 (d, $J = 8.4$ Hz, 1H), 4.44 (dd, $J = 8.4$ Hz, $J' = 6.9$ Hz, 1H), 4.02 (q, $J = 6.8$ Hz, 1H), 3.71 (s, 3H), 2.98–2.91 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 212.6, 194.8, 139.8, 136.7, 133.8, 130.7, 129.6 (2C), 129.2 (2C), 128.8 (2C), 128.4, 128.3 (2C), 128.2 (2C), 128.0, 126.9, 113.7 (2C), 61.6, 50.5, 45.5, 44.9; ATR-FTIR ν 2934, 1741, 1608, 1570, 1509, 1246 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{22}\text{O}_3\text{Na}$ [$\text{M} + \text{Na}$] $^+$ 393.1461, found 393.1467.

Bromination of 2a with Pyridinium Tribromide. Diketo compound **2a** (210 mg, 0.62 mmol, 1 equiv) was dissolved in DCM (18 mL) and cooled to 0 °C. Then $\text{PyrHBr}\cdot\text{Br}_2$ (220 mg, 90%, 0.62 mmol, 1 equiv) was added at once while the reaction mixture was vigorously stirred. The reaction mixture was then stirred overnight at room temperature. A saturated solution of NaHCO_3 was added; the organic phase was extracted and washed with water and dried, and the solvent was removed in vacuo. The crude mixture was purified by automated column chromatography with a 98:2 petroleum ether/EtOAc eluent, yielding product **4** as a pale orange solid.

(5Z)-2-Bromo-5-[hydroxy(phenyl)methylidene]-3,4-diphenylcyclopentan-1-one (4). Yield 250 mg (97%); mp 120–122 °C (from MeOH); >1:20 keto:enol; ^1H NMR (400 MHz, CDCl_3) δ 7.58–7.52 (m, 2H), 7.45–7.38 (m, 1H), 7.30–7.26 (m, 2H), 7.20–7.09 (m, 6H), 6.77–6.74 (m, 4H), 5.22 (dd, $J = 12.3$ Hz, $J' = 1.2$ Hz, 1H), 4.43 (d, $J = 7.6$ Hz, 1H), 3.99 (dd, $J = 12.3$ Hz, $J' = 7.6$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 200.8, 173.2, 139.5, 136.0, 133.1, 131.9, 128.6 (2C), 128.5 (4C), 128.3 (2C), 128.2 (4C), 127.4, 127.2, 110.3, 58.4, 52.3, 51.2; ATR-FTIR ν 3058, 1637, 1591, 1567, 1491, 1447, 1356, 1142, 1076 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{20}\text{BrO}_2$ [$\text{M} + \text{H}$] $^+$ 419.0641, found 419.0635.

Bromination of 2a with N-Bromosuccinimide. According to the published procedure,⁵² a solution of NBS (26 mg, 0.15 mmol, 1 equiv) in DCM (2 mL) was added to a solution of 1,3-diketone **2a** (50 mg, 0.15 mmol, 1 equiv) at rt. The reaction mixture was allowed to stir at room temperature for 6 h until full conversion was achieved. Then the reaction mixture was directly purified by automated column chromatography with a petroleum ether/EtOAc gradient (98:2 to 97:3), yielding the desired compound **5** as a single diastereoisomer as an off-white oil that was crystallized from methanol to give a pale off-white solid.

2-Benzoyl-2-bromo-3,4-diphenylcyclopentan-1-one (5). Yield 52 mg (84%); mp 112–115 °C (from MeOH); ^1H NMR (400 MHz, CDCl_3) δ 7.93–7.82 (m, 2H), 7.45–7.36 (m, 1H), 7.30–7.26 (s, 2H), 7.11–7.08 (m, 3H), 6.98–6.81 (m, 5H), 6.64–6.56 (m, 2H), 4.64–4.52 (m, 1H), 4.41 (dd, $J = 6.5$ Hz, $J' = 1.3$ Hz, 1H), 3.11 (dd, $J = 19.1$ Hz, $J' = 13.3$ Hz, 1H), 2.92 (ddd, $J = 19.1$ Hz, $J' = 7.9$ Hz, $J'' = 1.4$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 204.4, 190.9, 137.2, 135.5, 135.1, 132.9, 129.4, 129.1, 128.2, 128.0, 127.9, 127.4, 127.1, 77.2, 63.3, 61.6, 42.6, 39.1; ATR-FTIR ν 3029, 1757, 1664, 1596, 1447, 1252, 1234, 1142, 1072 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{20}\text{BrO}_2$ [$\text{M} + \text{H}$] $^+$ 419.0641, found 419.0631.

Synthesis of 6. To diketo compound **2a** (60 mg, 0.176 mmol, 1 equiv) in DCM (3 mL) was added at rt a solution of *N*-(phenylseleno)phthalimide (90 mg, 90%, 0.26 mmol, 1.5 equiv). The reaction mixture stirred for 3 h until full conversion was achieved, and the solvent was removed in vacuo. The crude mixture was then dissolved in EtOAc (6 mL), and hydrogen peroxide (2 mL of 30% in water) was added. After 3 h, full conversion was achieved, the reaction mixture was diluted with water (1 mL), and the organic phase was collected and washed with saturated NaHCO_3 and water and dried over MgSO_4 . After filtration and evaporation of the solvent, the crude product was separated by automated column chromatography with a petroleum ether/EtOAc gradient (93:7 to 85:15), yielding product **6** as a transparent oil.

2-Benzoyl-3,4-diphenylcyclopent-2-en-1-one (6). Yield 42 mg (70%); ^1H NMR (400 MHz, CDCl_3) δ 7.94–7.84 (m, 1H), 7.59–7.49 (m, 1H), 7.44–7.40 (m, 2H), 7.31–7.13 (m, 10H), 4.80 (dd, $J = 7.4$ Hz, $J' = 2.3$ Hz, 1H), 3.30 (dd, $J = 19.0$ Hz, $J' = 7.4$ Hz, 1H), 2.67 (dd, $J = 19.0$ Hz, $J' = 2.3$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 204.2, 194.6, 172.8, 141.5, 136.1, 134.4, 134.2, 130.8, 129.5 (2C), 129.3 (2C), 128.9 (2C), 128.7 (4C), 127.5 (2C), 127.3, 123.7, 47.3, 46.3; ATR-FTIR ν 3057, 1690, 1654, 1597, 1579, 1497, 1331,

1236, 1174, 1052 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{19}\text{O}_2$ [$\text{M} + \text{H}$] $^+$ 339.1385, found 339.1389.

Hydroxylation of 2a. To the mixture of **2a** (120 mg, 0.35 mmol, 1 equiv) and 0.5 M aqueous NaHCO_3 (0.7 mL, 1 equiv) in DCM (4 mL) was added *m*-CPBA (198 mg, 77%, 0.88 mmol, 2.5 equiv) portionwise at ambient temperature. After 3 h, full conversion was achieved according to TLC analysis. The excess of peracid was quenched by adding 15% aqueous Na_2SO_3 (3 mL), and the resulting mixture was stirred for an additional 1 h at room temperature. The organic layer was then separated, washed with brine (5 mL), dried over MgSO_4 , and filtered and concentrated in vacuo. The residue was purified by automated column chromatography with a petroleum ether/EtOAc gradient (98:2 to 85:15), yielding product **7** as a single diastereoisomer as a thick transparent oil.

2-Benzoyl-2-hydroxy-3,4-diphenylcyclopentan-1-one (7). Yield 56 mg (45%); ^1H NMR (400 MHz, CDCl_3) δ 7.94–7.63 (m, 2H), 7.42–7.34 (m, 1H), 7.27–7.19 (m, 2H), 7.15–7.04 (m, 3H), 7.00–6.97 (m, 2H), 6.87–6.84 (m, 3H), 6.76–6.73 (m, 2H), 4.32 (dt, $J = 14.3$ Hz, $J' = 7.6$ Hz, 1H), 4.19 (dd, $J = 8.0$ Hz, $J' = 1.2$ Hz, 1H), 3.50 (dd, $J = 17.8$ Hz, $J' = 13.7$ Hz, 1H), 2.95 (ddd, $J = 17.8$ Hz, $J' = 7.3$ Hz, $J'' = 1.4$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 213.5, 198.4, 138.1, 135.1, 135.1, 133.1, 130.4 (2C), 129.9 (2C), 128.2 (2C), 128.0 (4C), 127.9 (2C), 127.0, 126.7, 87.8, 60.3, 42.8, 41.6; ATR-FTIR ν 3396, 3029, 1748, 1665, 1596, 1448, 1251, 1039 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{21}\text{O}_3$ [$\text{M} + \text{H}$] $^+$ 357.1485, found 357.1499.

Reaction of 2a with Hydrazine Hydrate. According to the published procedure,⁵⁶ to a sealed vial with **2a** (168 mg, 0.49 mmol, 1 equiv) in EtOH (4 mL) was added hydrazine hydrate (37 μL , 65% in water, 1 equiv). The reaction mixture was then heated on an oil bath to reflux until full conversion was achieved as indicated by TLC. The solvent was then removed in vacuo, and the reaction mixture was then purified by automated column chromatography with a petroleum ether/EtOAc gradient (80:20 to 67:33), yielding pyrazole derivative **8** as a yellow thick oil (110 mg, 66%).

3,4,5-Triphenyl-2H,4H,5H,6H-cyclopenta[c]pyrazole (8). Yield 110 mg (66%); ^1H NMR (400 MHz, CDCl_3) δ 10.19 (bs, 1H), 7.54–7.37 (m, 2H), 7.28–7.19 (m, 3H), 7.13–7.06 (m, 3H), 7.03–6.99 (m, 3H), 6.88–6.86 (m, 2H), 6.74–6.65 (m, 2H), 4.57 (d, $J = 7.8$ Hz, 1H), 4.47 (dtd, $J = 10.2$ Hz, $J' = 7.7$ Hz, $J'' = 2.1$ Hz, 1H), 3.24 (dd, $J = 15.3$ Hz, $J' = 10.9$ Hz, 1H), 3.07 (ddd, $J = 15.4$ Hz, $J' = 7.7$, $J'' = 2.0$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 140.2, 140.2, 130.3, 129.0 (4C), 128.7 (2C), 128.6 (2C), 128.0 (2C), 127.9 (2C), 127.8 (2C), 126.5, 126.4, 125.8, 125.8, 58.1, 49.4, 29.1; ATR-FTIR ν 3026, 2898, 1602, 1493, 1452, 1314, 1233, 1180, 1109 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{21}\text{N}_2$ [$\text{M} + \text{H}$] $^+$ 337.1699, found 337.1704.

Methylation of 2a. To the starting **2a** (0.85 mmol, 290 mg, 1 equiv) in DMF (5 mL) under argon was added K_2CO_3 (0.94 mmol, 180 mg, 1.5 equiv), and then methyl iodide (0.94 mmol, 60 μL , 1.1 equiv) was slowly added. The reaction mixture was then stirred overnight at 60 °C (oil bath). The next day, the reaction was quenched with water (5 mL) and the mixture washed with EtOAc (3 \times 50 mL). The combined organic layer was washed with brine (2 \times 30 mL) and dried over MgSO_4 . After filtration, the solvent was evaporated in vacuo and the crude material was separated by automated column chromatography with a pentane/EtOAc gradient (85:15 to 4:1), yielding product **9** as a thick transparent oil.

2-Benzoyl-2-methyl-3,4-diphenylcyclopentan-1-one and 2-[Methoxy(phenyl)methylidene]-3,4-diphenylcyclopentan-1-one (9a:9b). Yield 210 mg (70%); 4:1 keto:enol ether. Keto: ^1H NMR (400 MHz, CDCl_3) δ 7.68–7.56 (m, 2H), 7.35–7.31 (m, 1H), 7.29–7.19 (m, 2H), 7.13–7.05 (m, 4H), 6.94–6.87 (m, 4H), 6.77–6.75 (m, 2H), 4.15–4.11 (m, 1H), 4.08 (t, $J = 6.9$ Hz, 1H), 3.28 (dd, $J = 18.0$ Hz, $J' = 13.5$ Hz, 1H), 2.73 (dd, $J = 18.5$ Hz, $J' = 6.2$ Hz, 1H), 1.85 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 214.1, 199.2, 137.9, 137.2, 136.2, 132.0, 129.5, 128.7 (2C), 128.0 (6C), 127.9 (2C), 127.6 (2C), 126.7, 65.8, 60.2, 43.2, 40.6, 24.7. Enol: ^1H NMR (400 MHz, CDCl_3) δ 7.77–7.69 (m, 2H), 7.47–7.44 (m, 1H), 7.40–7.37 (m, 2H), 7.03–6.97 (m, 3H), 6.87 (s, 4H), 4.58 (d, $J = 8.2$ Hz,

1H), 4.01 (q, $J = 8.8$ Hz, 1H), 3.77 (s, 3H), 3.22–3.15 (m, 1H), 3.01 (dd, $J = 16.8$ Hz, $J' = 8.1$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 192.4, 167.6, 140.3, 140.1, 139.7, 131.3, 128.6 (2C), 128.2 (2C), 127.7 (4C), 126.7 (4C), 126.3, 126.1, 116.2, 58.0, 54.4, 46.7, 35.3; ATR-FTIR ν 3026, 1745, 1669, 1596, 1454, 1246 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{23}\text{O}_2$ $[\text{M} + \text{H}]^+$ 355.1698, found 355.1700.

Aldol Reaction of 2a with Benzophenone. According to the modified procedure,⁵⁵ diisopropylamine (91 μL , 2.20 equiv) was dissolved in dry tetrahydrofuran (5 mL), and after the mixture had cooled to 0 °C, *n*-butyllithium (260 μL , 2.20 equiv, 2.5 M solution in *n*-hexane) was added. The reaction mixture was stirred at rt for 30 min followed by further cooling to 0 °C. Diketone 2a (100 mg, 0.29 mmol, 1 equiv) was dissolved in dry tetrahydrofuran (3 mL) and slowly added to the solution of diisopropylamine and *n*-butyllithium, and the mixture was stirred. After 15 min, benzophenone (65 mg, 0.35 mmol, 1.20 equiv) was added and the reaction mixture stirred at 0 °C for 30 min and then at rt overnight. After 16 h, TLC revealed full conversion; the reaction was then quenched by the addition of a saturated aqueous solution of ammonium chloride (1 mL) and water (10 mL), and EtOAc was then added. The organic phase was separated, and the aqueous phase extracted with EtOAc (2 \times 20 mL). The combined organic phases were washed with brine and dried over MgSO_4 , and the solvent was evaporated in vacuo. The crude material was purified by automated column chromatography with a petroleum ether/EtOAc gradient (95:5 to 92:8), yielding product 10 as a transparent oil.

(2Z)-2-[Hydroxy(phenyl)methylidene]-5-(hydroxydiphenylmethyl)-3,4-diphenylcyclopentan-1-one (10). Yield 100 mg (65%); >1:20 keto/enol; ^1H NMR (400 MHz, CDCl_3) δ 7.50 (ddd, $J = 15.3$ Hz, $J' = 8.2$ Hz, $J'' = 1.2$ Hz, 4H), 7.39–7.31 (m, 1H), 7.28–7.18 (m, 6H), 7.05–6.93 (m, 5H), 6.86–6.60 (m, 5H), 6.33 (bs, 2H), 4.36 (d, $J = 10.6$ Hz, 1H), 4.25 (d, $J = 8.2$ Hz, 1H), 4.04 (dd, $J = 10.6$ Hz, $J' = 8.1$ Hz, 1H), 3.87 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 208.7, 172.9, 146.1, 143.9, 141.4, 139.5, 133.8, 131.4, 128.6 (4C), 128.2 (4C), 128.1 (2C), 127.9 (2C), 127.5 (2C), 127.3 (2C), 127.2, 127.0 (4C), 126.8, 126.5, 125.4, 113.5, 79.7, 57.7, 51.0, 50.8; ATR-FTIR ν 3061, 3028, 2956, 1738, 1603, 1568, 1492, 1447, 1365, 1269, 1218, 1154 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{37}\text{H}_{29}\text{O}_3$ $[\text{M} - \text{H}]^-$ 521.2117, found 521.2119.

Selenylation of 2a. According to the modified procedure,⁵⁵ diisopropylamine (91 μL , 2.20 equiv) was dissolved in dry tetrahydrofuran (5 mL). After the mixture had cooled to 0 °C, *n*-butyllithium (260 μL , 2.20 equiv, 2.5 M solution in *n*-hexane) was added and the reaction mixture was stirred at room temperature for 30 min. Then after the mixture had again cooled to 0 °C, diketone 2a (100 mg, 0.29 mmol, 1 equiv) was dissolved in dry tetrahydrofuran (3 mL) and slowly added to the solution of diisopropylamine and *n*-butyllithium. The reaction mixture was stirred for 15 min followed by an addition of *N*-(phenylseleno)phthalimide (120 mg, 1.20 equiv); the subsequent mixture was stirred at 0 °C for 30 min and then at rt for an additional 60 min when, according to TLC, full conversion was achieved. The reaction was then quenched by the addition of a saturated aqueous solution of NH_4Cl (1 mL) and water (10 mL), and EtOAc (20 mL) was then added. The organic phase was separated, and the aqueous phase extracted with EtOAc (2 \times 20 mL). The combined organic phases were washed with brine and dried over MgSO_4 , and the solvent was evaporated in vacuo. The crude material was purified by automated column chromatography with a petroleum ether/EtOAc gradient (98:2 to 92:8), yielding product 11 as single diastereoisomer in the form of a thick yellow oil.

(2Z)-2-[Hydroxy(phenyl)methylidene]-3,4-diphenyl-5-(phenylselenanyl)cyclopentan-1-one (11). Yield 110 mg (76%) as a thick yellow oil; 1:20 keto/enol. Enol: ^1H NMR (400 MHz, CDCl_3) δ 7.62–7.53 (m, 2H), 7.52–7.49 (m, 2H), 7.39–7.26 (m, 2H), 7.28–7.18 (m, 4H), 7.14–7.01 (m, 6H), 6.75–6.68 (m, 2H), 6.67–6.59 (m, 2H), 4.42 (d, $J = 12.1$ Hz, 1H), 4.33 (d, $J = 7.6$ Hz, 1H), 3.66 (dd, $J = 12.1$ Hz, $J' = 7.6$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 205.2, 172.3, 140.2, 137.6, 136.50 (2C), 133.7, 131.5, 129.0 (2C), 128.6, 128.5 (6C), 128.3 (4C), 128.0 (2C), 126.9 (2C), 126.8, 111.6, 54.5, 51.3, 50.5. Keto: ^1H NMR (400 MHz, CDCl_3) δ 8.10–

8.04 (m, 2H), 7.76 (dd, $J = 8.2$ Hz, $J' = 1.3$ Hz, 1H), 7.68–7.61 (m, 4H), 7.35–7.28 (m, 2H), 7.26–7.20 (m, 2H), 7.18–7.12 (m, 3H), 7.08–7.04 (m, 2H), 6.80–6.75 (m, 4H), 4.86 (dd, $J = 8.1$ Hz, $J' = 1.2$ Hz, 1H), 4.70 (t, $J = 7.6$ Hz, 1H), 4.29 (dd, $J = 5.6$ Hz, $J' = 1.3$ Hz, 1H), 3.97–3.89 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 206.9, 192.4, 136.5 (2C), 136.1 (2C), 133.7, 131.5, 130.0, 129.3, 129.0 (2C), 128.6 (2C), 128.5 (2C), 128.5 (4C), 128.3 (2C), 128.2 (2C), 127.1 (2C), 126.9, 60.6, 52.2, 48.91; ATR-FTIR ν 3059, 3028, 1719, 1604, 1592, 1568, 1493, 1360, 1260, 1221, 1150, 1071 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{30}\text{H}_{25}\text{O}_2\text{Se}$ $[\text{M} + \text{H}]^+$ 497.1014, found 497.1019.

Elimination of Brominated Diketo Compound 4. 1,4-Diazabicyclo[2.2.2]octane (DABCO) (0.49 mmol, 55 mg, 2 equiv) was added to a stirred solution of brominated diketone 4 (0.24 mmol, 100 mg, 1 equiv) in THF (5 mL) at rt. Full conversion was achieved after 2 h (TLC monitoring). The reaction mixture was evaporated and purified by automated column chromatography with a pentane/EtOAc gradient (9:1 to 5:1), yielding product 12 as a thick orange oil.

5-Benzoyl-3,4-diphenylcyclopent-2-en-1-one (12). Yield 70 mg (85%); >2:1 keto/enol. Keto: ^1H NMR (400 MHz, CDCl_3) δ 8.13–8.01 (m, 2H), 7.66–7.57 (m, 2H), 7.55–7.44 (m, 3H), 7.41–7.24 (m, 4H), 7.25–7.16 (m, 3H), 7.00–6.89 (m, 1H), 6.69 (d, $J = 1.4$ Hz, 1H), 5.34 (t, $J = 1.7$ Hz, 1H), 4.61 (d, $J = 2.0$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 200.9, 193.2, 175.9, 141.3, 136.2, 133.7, 132.9, 131.4, 130.6, 130.2 (2C), 129.4 (2C), 128.9 (2C), 128.7 (2C), 128.4 (2C), 127.6 (2C), 126.5, 67.1, 50.4. Enol: ^1H NMR (400 MHz, CDCl_3) δ 8.12–8.08 (m, 2H), 7.60–7.57 (m, 2H), 7.55–7.50 (m, 2H), 7.41–7.24 (m, 5H), 7.24–7.18 (m, 2H), 7.00–6.91 (m, 2H), 6.87 (d, $J = 1.2$ Hz, 0H), 5.26 (d, $J = 1.3$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 199.8, 169.9, 168.7, 138.8, 134.2, 133.2, 130.5, 128.8 (2C), 128.3 (4C), 128.1 (2C), 128.0 (2C), 127.9 (2C), 127.5 (2C), 126.8, 116.8, 50.8; ATR-FTIR ν 3060, 1690, 1666, 1596, 1570, 1493, 1446, 1176, 1148, 1000 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{19}\text{O}_2$ $[\text{M} + \text{H}]^+$ 339.1380, found 339.1380.

General Procedure for Sample Preparation and Crystal Measurement. Single crystals of products 2a, 4, and 5 were prepared by volatilization using a mixture of methanol and dichloromethane as a solvent. Suitable crystals were selected and collected on a Bruker D8 VENTURE Kappa Duo PHOTONIII instrument by a μS microfocussed sealed tube with Mo $K\alpha$ ($\lambda = 0.71073$) (5) or Cu $K\alpha$ ($\lambda = 1.54178$ Å) (2a and 4) radiation at a low temperature of 120 K.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.joc.1c00445>.

NMR spectra for all new compounds (PDF)

Accession Codes

CCDC 2063174–2063176 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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