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Samarium Diiodide Induced Reactions of Cyclopropyl Ketones: Reductive Ring Cleavage and Dimerization Leading to 1,8-Diketones – Scope, Limitations, Mechanisms

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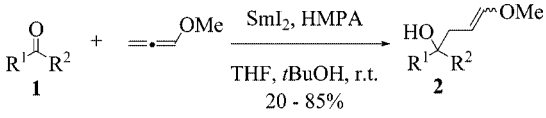
Reactions of the samarium diiodide/HMPA complex with alkyl cyclopropyl ketones such as **3**, **5**, and **7** provided dimers incorporating a 1,8-diketone moiety. The products **4**, **6**, and **8** were isolated in moderate to good yields. The aryl-substituted cyclopropyl ketones afforded a broader product spectrum, which results from the attack of samarium intermediates to the aryl group. Cyclopropyl phenyl ketone (**13**) gave dimer **14**, where one cyclopropane ring was reductively cleaved, whereas the second one is still present. The reductive dimerization of cyclopropyl 2-thienyl ketone (**21**) furnished the product **22**, which still contains two cyclopropyl groups. Further examples demonstrate the diversity of samarium diiodide induced reductions of cyclopropyl ketones. Plausible reaction mechanisms involving samarium ketyl intermediates are presented.

Introduction

We recently reported that the samarium diiodide induced[1] coupling of the carbonyl compounds **1** to methoxyallene affords the 4-hydroxy-1-enol ethers **2** in moderate to good yields,[2] thus providing a new route to these useful intermediates[3] (Scheme 1). Although other allenes[2,4] could also be coupled with carbonyl compounds, methoxyallene proved to be the most suitable substrate. In order to investigate further the substrate dependency of this novel reaction, cyclopropyl methyl ketone (**3**) was also employed as the carbonyl component.[5] However, instead of the expected enol ether of type **2**, the 1,8-diketone **4** was isolated in good yield (Scheme 2) – probably, as a result of a reductive cyclopropane cleavage, followed by a dimerization process. This observation motivated us to study in more detail the behavior of a series of cyclopropyl ketones employing samarium diiodide as reducing reagent, which disclosed the high diversity of products and mechanistic pathways herein described.



Scheme 1.

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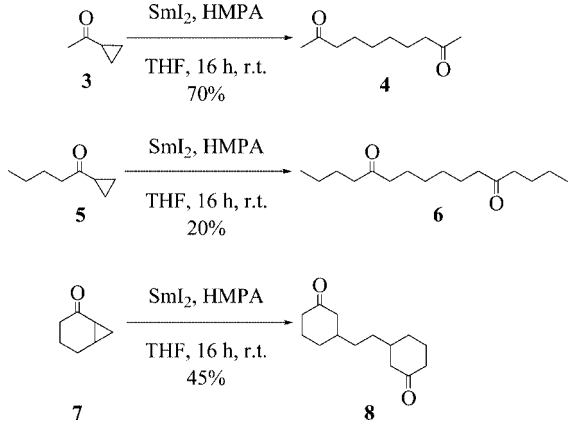


Scheme 2.

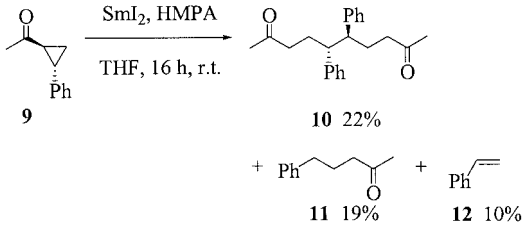
Results

Upon treatment of simple alkyl cyclopropyl ketones with 2.2 equiv. of the samarium diiodide/HMPA complex, the corresponding diketone dimers were always isolated in low to good yields (Scheme 2). The reductive coupling of cyclopropyl methyl ketone (**3**) – the simplest among the substrates tested – afforded decane-2,9-dione (**4**) in a satisfying 70% yield. The increase of the length of the aliphatic moiety – as in the case of ketone **5** – led to an impoverished efficacy of the coupling process, hence the 1,8-diketone **6** was isolated in only 20%. No other coupling products could be identified in the reaction mixture. The expected dimer was also obtained when bicyclo[4.1.0]heptan-2-one (**7**) was subjected to the standard conditions, providing the

diketone **8** in 45% yield as a 1:1 mixture of diastereomers. Disappointingly, the lower homologue bicyclo[3.1.0]hexan-2-one led to a complex mixture of unidentified compounds.[6]

Studies of the role of proton sources, amount of reductive reagent and co-solvents on the outcome of the reaction (carried out on ketone **3**), indicated that the absence of a proton source – such as *tert*-butyl alcohol – does not significantly influence the yield of the diketone, whereas a decrease of the amount of samarium diiodide to 1.1 equiv. lowered the yield to 30%. In the absence of HMPA[7] the reaction is completely inhibited.

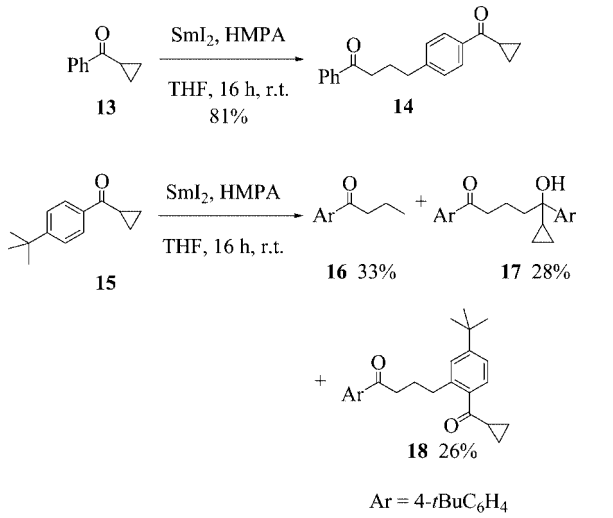
Whereas the reactions of alkyl cyclopropyl ketones occurred in an apparently uniform manner, as illustrated in Scheme 2, the coupling of the aryl-substituted cyclopropyl ketones proceeded in a more complex fashion. In the case of ketone **9** – bearing a phenyl group at C-2 of the cyclopropane ring – the dimerization product **10** (isolated in 22% yield as a single diastereomer) was accompanied by 5-phenylpentan-2-one (**11**) and styrene (**12**) in 19% and 10% yield, respectively (Scheme 3). The formation of **11** can be rationalized as the result of a simple reductive opening of **9** without dimerization, whilst an unclear fragmentation reaction might lead to **12**. We cannot exclude that similar side reactions also took place during the transformations of **3**, **5** and **7** (Scheme 2) generating volatile products, and hence explaining the reduced mass balances of these reactions.



Scheme 3.

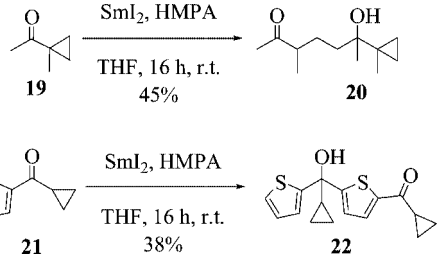
Upon the treatment of cyclopropyl phenyl ketone (**13**) with the samarium diiodide/HMPA complex, a dimerization product **14** was indeed formed as the sole product in very good yield (Scheme 4). However, in this case, the dimer was the result of the reductive cleavage of one cyclopropyl ring only, and subsequent attack of this species at the *para* position of the phenyl ring of a second molecule. When the *para* position was blocked by the bulky *tert*-butyl group (precursor **15**), the related coupling product **18** was formed from the attack of the ring-opened intermediate at the *ortho* position of the aryl moiety. However, together with the ketone **18**, the tertiary alcohol **17** and 1-(4-*tert*-butylphenyl)-butan-1-one (**16**) were also formed in similar yields.

The reaction of methyl 1-methylcyclopropyl ketone (**19**) with the samarium diiodide/HPMA complex furnished the δ-hydroxy ketone **20** as a mixture of diastereomers (Scheme 5) in moderate yield – a compound analogous to the tertiary alcohol **17**. It is generated by the attack of a ring-opened intermediate to the carbonyl group of a second



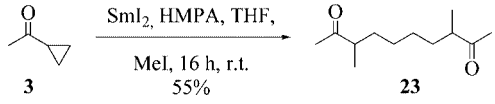
Scheme 4.

molecule. The reductive coupling of cyclopropyl 2-thienyl ketone (**21**) disclosed another manner of dimerization, wherein the product **22** retained the two cyclopropyl groups.



Scheme 5.

Finally, we carried out some experiments in order to trap possible intermediates of this reductive dimerization reaction. As during the reductive coupling of cyclopropyl methyl ketone (**3**) the most likely intermediate – before aqueous workup – is a samarium dienolate species (see Scheme 7), we performed the reaction in the presence of methyl iodide. Indeed, we were very pleased to isolate the dialkylated product **23** in a satisfying 55% yield (Scheme 6).[8] Other trapping experiments, performed on ketone **3** in the presence of allyl bromide, chlorotrimethylsilane, acetone or benzaldehyde, were not successful; instead, complex mixtures of products were observed. Experiments employing cyclopropyl phenyl ketone (**13**) as a precursor were also carried out in the presence of potential trapping reagents (acetophenone, benzonitrile, anisole, toluene). However, none of these compounds were incorporated into the products isolated; instead, the regular dimerization product **14** was formed, albeit in strongly reduced yields (14 to 36%).



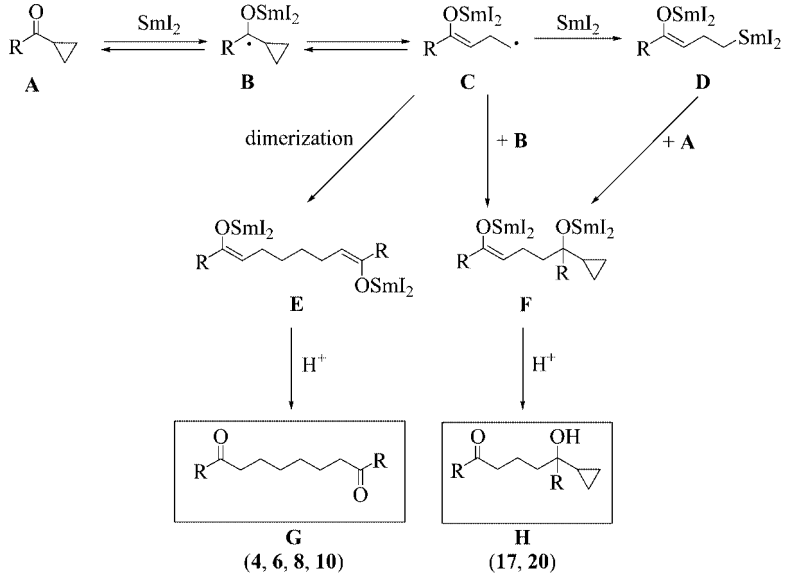
Scheme 6.

Discussion

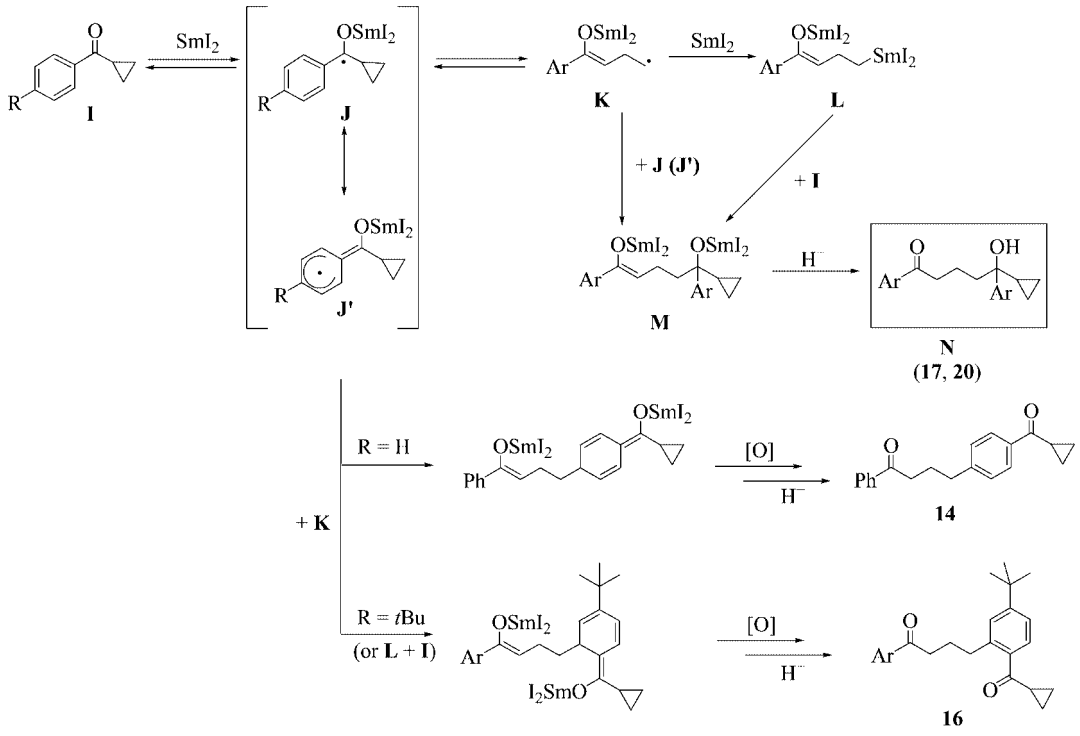
Since the spectrum of products generated under these coupling conditions is remarkably broad, and the mass balances of several transformations are low to moderate, the mechanistic discussion is complex and in part speculative. Nevertheless, examples of samarium diiodide induced reactions reported in the literature,[9,10] lend support to our mechanistic suggestions. A plausible pathway is presented in Scheme 7 that explains the formation of the dimers **4**, **6**, **8**, and **10** as well as that of **17** and **20**. Addition of 1 equiv. of samarium diiodide (the HMPA ligands in Schemes 7, 8 and 9 are omitted for clarity and simplicity) to the cyclopropyl ketone **A** furnishes the expected samarium ketyl **B** which can undergo a fast ring cleavage,[11] that leads to the homoallylic radical **C**, which incorporates a samarium enolate moiety. A simple dimerization of this radical **C** to dienolate **E**, followed by protonation of this intermediate should afford the 1,8-diketones **G**. Because the dienolate **E** could be trapped by methyl iodide (Scheme 6), we consider this mechanism conceivable. However, we cannot strictly exclude that a Lewis acid assisted ring opening[12] of cyclopropyl ketone **A** [samarium(II) or samarium(III) species being the activator] with the samarium species **D** as nucleophile, formed by reaction of the radical **C** with a second equivalent of samarium diiodide, may also furnish **E**. Whereas we believe that the involvement of **D** in the formation of **E** is rather unlikely, this species can add to the carbonyl group of **A** to produce intermediate **F**, which, after protonation, provides compounds of general structure **H**. Alternatively, **F** may be generated by addition of the samarium ketyl **B** to homoallyl radical **C**. All these coupling reactions require only 1 equiv. of samarium diiodide; however, we believe that the improved efficacy of the coupling process in the presence of 2 equiv. of samarium diiodide is because of the higher concentration of the intermediates **B**, **C**, or **D**, which shifts the equilibria to the product sides, thus favoring the progress of the reactions. We can not exclude that dimeric species bridged by O–Sm–O moieties are involved in the C–C bond-forming processes. This (speculative) template effect may lead to the observed, surprisingly high efficacy of several of the radical dimerization reactions, and it may also influence the stereoselectivity (see below).

The regiochemistry of the cyclopropane ring cleavage is also a remarkable feature of these reactions. The formation of the 1,8-diketone **8** from the bicyclic compound **7** proceeds via the primary radical generated by the cleavage of the "external" proximal cyclopropane C–C bond. The conceivable secondary cycloheptyl radical – derived from **7** by the cleavage of the "internal" cyclopropane bond – is either not formed, or it is not sufficiently reactive for a dimerization to occur, as a consequence of its higher steric hindrance.[10] Most probably, the radical derived from **9** is stabilized by the phenyl group, hence delivering dimer **10** and compound **11**, either by protonation of the samarium intermediate **D**, or by hydrogen abstraction of the benzylic radical equivalent to **C**. The pathway that in this experiment leads to the formation of styrene is not yet clear.

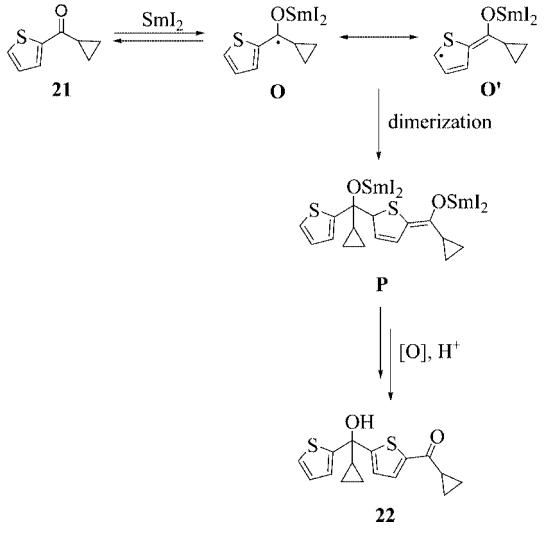
More speculative are the mechanistic routes that – from aryl-substituted cyclopropyl ketone of type **I** – lead to the formation of the products **14**, **16**, **17** and **20**. In contrast with the case of alkyl cyclopropyl ketones of type **A**, the considerably higher stability of the ketyl radical **J** (also represented by the mesomeric formula **J′**) in comparison with that of the homoallylic radical **K**, shifts the equilibrium towards the first, hence rendering this radical species more abundant. The combination of **J** with **K** may provide **M**, and finally coupling products **N**, found in two cases (**17** and **20**). However, intermediate **K** can also be further transformed into the disamarium species **L**, whose nucleophilic addition to **I** may also provide the intermediate **M**. Although the experiments aimed at confirming the proposed



Scheme 7.



Scheme 8.



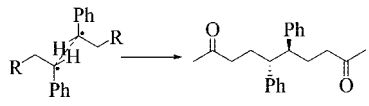
Scheme 9.

mechanism – by trapping of the intermediates – failed to afford the expected products, we believe that this last mechanistic route is the most likely to take place.

The formation of **14** and **16** could be explained by the addition of the homoallylic radical **K** to the aromatic ring of the ketyl **J**. This addition occurs preferentially at the sterically less congested *para* position or – when this is not available – at the less favorable *ortho* position. The intermediates thus formed – incorporating samarium enolate moieties in conjugation with cyclohexadiene subunits – have to be rearomatized. This event occurs probably during the workup of the reaction mixtures by oxygenation and protonation. Similar observations have been made in the samarium diiodide induced dimerization of aromatic aldehydes, from which rearomatized addition products are also isolated, or in related cyclizations of γ-aryl ketones.[10,13]

The samarium ketyl **O**, derived from cyclopropyl 2-thienyl ketone (**21**), is particularly stable, and the corresponding homoallylic radical is apparently not formed or not participating in the coupling reaction. "Head-to-tail" dimerization of **O**/**O**′ leads to the intermediate **P** which, after protonation and oxidation during workup, furnishes the adduct **22**. Similar reactions of ketyls derived from 2-thiophenecarbaldehyde are literature-known.[14]

The formation of dimer **8** occurs apparently without stereoselection (1:1) as the two possible approaches of the primary radicals are essentially identical. On the other hand, the conversion of **9** into **10** proceeds apparently with perfect stereoselectivity. The resulting product should be the D/L diastereomer because a dimerization of the stabilized secondary radical would probably involve more steric repulsions of the larger substituents (Scheme 10). However, this assignment is tentative and literature precedence is not conclusive for comparable cases.[15] Compound **20** was formed unselectively as a mixture of two diastereomers. This is to be expected as the stereogenic center next to the carbonyl group is too far from the reactive carbon atom to influence the C–C bond-forming step.



Scheme 10.

Conclusion

In this report we demonstrate that several reaction pathways are opened for samarium ketyl intermediates derived from cyclopropyl ketones. Whereas the alkyl cyclopropyl ketones provide compounds with 1,8-diketone moieties by ring cleavage of both participating cyclopropane rings, the reductive dimerizations of the aryl-substituted cyclopropyl ketones strongly depend on the substitution pattern. Products with one or two intact cyclopropyl rings are formed by a so far unpredictable reaction pathway.

Experimental Section

General Experimental Procedures: Reactions were generally performed under argon in flame-dried flasks, and solvents and reagents were added by syringes. The reagents used in the trapping experiments were purified and stored under argon: acetone and allyl bromide were distilled from calcium hydride and stored over molecular sieves (4 Å). 1,2-Diiodoethane was purified by sublimation under vacuum (0.2 mbar, 50 °C). Tetrahydrofuran (THF) was freshly distilled from sodium/benzophenone under argon for all reactions. Hexamethylphosphoramide (HMPA) was distilled from calcium hydride (130 °C, 12 mbar) and stored over molecular sieves (4 Å) under argon. Argon was purged through the solution to eliminate residual oxygen prior to use. Products were purified by flash chromatography on silica gel (230–400 mesh, Merck) or neutral alumina (activity III, Fluka). Preparative HPLC was carried out on a nucleosil 50-5 column and detected with a Knauer variable UV detector (λ = 255 nm) and a Knauer refractometer. Unless otherwise stated, yields refer to analytically pure samples. The starting materials bicyclo[4.1.0]heptan-2-one,[16] butyl cyclopropyl ketone,[17] 1-(2-phenylcyclopropyl)ethanone[16,18] were synthesized according to literature procedures. Other reagents were purchased and were used as received without purification unless otherwise stated. ^{1}H [$CHCl_3$ (δ = 7.25 ppm) or TMS (δ = 0.00 ppm) as internal standard] and ^{13}C NMR spectra [$CDCl_3$ (δ = 77.0 ppm) as internal standard] were recorded with Bruker AC 250 (250 MHz), AC 500 (500 MHz) and Joel Eclipse 500 (500 MHz) instruments in $CDCl_3$ solutions. Integrals are in accordance with assignments; coupling constants are given in Hz. IR spectra were measured with an FT-IRD spectrometer Nicolet 5 SXC. MS and HRMS analyses were performed with Finnigan MAT 711 (EI, 80 eV, 8 kV), MAT CH7A (EI, 80 eV, 3 kV) instruments. Elemental analyses were carried out with an "Elemental-Analyzer" (Perkin–Elmer). Melting points were measured with a Reichert apparatus and are uncorrected.

General Procedure for SmI_2-Induced Coupling Reactions: Samarium (2.4–2.5 equiv.) and 1,2-diiodoethane (2.2 equiv.) were suspended in THF (25 mL/2.20 mmol SmI_2) under argon and stirred at room temperature until the color of the suspension turned into dark blue (approximately 2 h). The flask was then evacuated, purged with argon and HMPA (18 equiv.) was added. The cyclopropyl ketone (1 equiv.) was dissolved in THF (15 mL/mmol of cyclopropyl ketone), argon was purged through for 10 min, and the solution was then added to the deep violet solution of SmI_2 in THF/HMPA. The mixture was stirred at room temperature for 16 h and then quenched by addition of a satd. aq. $NaHCO_3$ solution (15 mL). The aqueous phase was extracted with diethyl ether (3 × 20 mL), and the combined organic layers were washed once with distilled water and twice with brine, then dried with $MgSO_4$, filtered and the solvent was removed under reduced pressure to give the crude mixture.

Coupling of Cyclopropyl Methyl Ketone (3) To Afford Decane-2,9-dione (4): According to the general procedure above, cyclopropyl methyl ketone (**3**) (84 mg, 1.00 mmol) afforded **4** as a colorless solid (60 mg, 70%) after column chromatography on neutral alumina (hexane/ethyl acetate, 5:1), m.p. 51–53 °C (ref.[19] 56–58 °C). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.26–1.32 (m, 4 H, 5-H, 6-H), 1.51–1.62 (m, 4 H, 4-H, 7-H), 2.13 (s, 6 H, 1-H, 10-H), 2.42 (t, ^3J = 7.4 Hz, 4 H, 3-H, 8-H) ppm. ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 23.4 (t, C-5, C-6), 28.7 (t, C-4, C-7), 29.7 (t, C-3, C-8), 43.4 (q, C-1, C-10), 208.8 (s, C-2, C-9) ppm. IR (KBr): $\tilde{\nu}$ = 2930, 2905, 2850 (C–H), 1700 (C=O) cm^{-1}. Decane-2,9-dione (**4**) was then converted into the corresponding bis(2,4-dinitrophenylhydrazone) derivative, m.p. 195–197 °C (ref.[20] 199 °C).

Coupling of 1-Cyclopropylpentan-1-one (5) To Afford Hexadecane-5,12-dione (6): According to the general procedure above, ketone **5** (252 mg, 2.00 mmol) afforded **6** as a colorless solid (50 mg, 20%) after column chromatography on neutral alumina (hexane/ethyl acetate, 5:1), m.p. 77–79 °C (ref.[21] 73 °C). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.89 (t, ^3J = 7.4 Hz, 6 H, CH_3), 1.24–1.33 (m, 8 H, 2-H, 8-H, 9-H, 15-H), 1.50–1.57 (m, 8 H, 3-H, 7-H, 10-H, 14-H), 2.37 (t, ^3J = 7.4 Hz, 8 H, 4-H, 6-H, 11-H, 13-H) ppm. ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 13.8 (q, CH_3), 22.4 (t, C-8, C-9), 23.6 (t, C-2, C-15), 25.9 (t, C-7, C-10), 29.0 (t, C-3, C-14), 42.5 (t, C-4, C-13), 42.6 (t, C-6, C-11), 211.4 (s, C-5, C-12) ppm. IR (KBr): $\tilde{\nu}$ = 2995, 2930, 2900, 2865 (C–H), 1705 (C=O) cm^{-1}. MS (EI, 80 eV, 60 °C): *m/z* (%) = 254 (3) $[M]^+$, 197 (8) $[M - C_4H_9]^+$, 85 (100) $[C_5H_9O]^+$, 57 (71) $[C_4H_9]^+$. HRMS (EI, 80 eV, 60 °C): calcd. for $C_{16}H_{30}O_2$ 254.22458; found 254.22533.

Coupling of Bicyclo[4.1.0]heptan-2-one (7) To Afford 3-[2-(3-Oxocyclohexyl)ethyl]cyclohexanone (8): According to the general procedure above, ketone **7** (110 mg, 1.00 mmol) afforded **8** as a colorless solid, as a 1:1 mixture of diastereomers (50 mg, 45%) after column chromatography on silica gel (gradient elution: hexane/ethyl acetate from 9:1 to 7:3), m.p. 62–64 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.23–1.33 (m, 6 H, 4-H, 6′′-H, 1′-H_a, 2′-H_a), 1.62 (m_c, 2 H, 5-H_a, 5′′-H_a), 1.71 (m_c, 2 H, 1′′-H, 3-H), 1.87 (br. d, ^3J ≈ 13.3 Hz, 2 H, 1′-H_b, 2′-H_b), 1.95–2.20 (m, 4 H, 2-H_a, 2′′-H_a, 5-H_b, 5′′-H_b), 2.23 (dt, ^3J = 5.9 Hz, ^2J = 13.8 Hz, 2 H, 4′′-H_a, 6-H_a), 2.33 (br. d, ^2J ≈ 13.8 Hz, 2 H, 4′′-H_b, 6-H_b), 2.39 (br. d, ^2J ≈ 13.7 Hz, 2 H, 2-H_b, 2′′-H_b) ppm. ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 25.1 (t, C-4, C-6′′), 31.2 (t, C-5, C-5′′), 33.5 (t, C-1′, C-2′), 33.6 (t, C-1′, C-2′), 39.0, 39.2 (2 d, C-1′′, C-3), 41.3 (t, C-4′′, C-6), 48.0 (t, C-2, C-2′′), 211.5 (s, C-1, C-3′′) ppm. IR (KBr): $\tilde{\nu}$ = 2955, 2930, 2860 (C–H), 1705 (C=O) cm^{-1}. MS (EI, 80 eV, 60 °C): *m/z* (%) = 222 (9) $[M]^+$, 97 (100) $[C_6H_9O]^+$. HRMS (EI, 80 eV, 60 °C): calcd. for $C_{14}H_{22}O_2$ 222.16199; found 222.16322. $C_{14}H_{22}O_2$ (222.3): calcd. C 75.63, H 9.97; found C 75.97, H 10.02.

Conversion of 1-(2-Phenylcyclopropyl)ethanone (9) into 5-Phenylpentan-2-one (11), 5,6-Diphenyldecane-2,9-dione (10) and Styrene (12): According to the general procedure above, ketone **9** (160 mg, 1.00 mmol) afforded after column chromatography on silica gel (hexane/ethyl acetate, 6:1) **11** as a colorless oil (30 mg, 19%), **10** as a colorless solid (35 mg, 22%) and **12** as a colorless oil (10 mg, 10%). The spectroscopic data of **10** and **12** are in agreement with those reported in the literature.[22,23] **10:** M.p. 127–129 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.60 (m_c, 4 H, 4-H, 7-H), 1.86 (s, 6 H, CH_3), 2.06 (m_c, 4 H, 3-H, 8-H), 2.69 (m_c, 2 H, 5-H, 6-H), 7.17 (d, ^3J = 7.2 Hz, 4 H, Ph), 7.23 (tt, ^4J = 1.2 Hz, ^3J = 7.2 Hz, 2 H, Ph), 7.32 (t, ^3J = 7.2 Hz, 4 H, Ph) ppm. ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 28.5 (t, C-4, C-7), 29.7 (q, C-1, C-10), 41.7 (t, C-3, C-8), 51.5

(d, C-5, C-6), 126.6, 128.3, 128.6, 143.1 (3 d, s, Ph), 208.7 (s, C-2, C-9) ppm. IR (KBr): $\tilde{\nu}$ = 3080, 3055, 3025, 3000, 2955, 2885, 2870 (=CH, C–H), 1710 (C=O) cm^{-1}. MS (EI, 80 eV, 170 °C): *m*/*z* (%) = 322 (0.4) $[M]^+$, 161 (48) $[M/2]^+$, 43 (100) $[COCH_3]^+$. HRMS (EI, 80 eV, 170 °C): calcd. for $C_{22}H_{26}O_2$ 322.19327; found 322.19422.

Coupling of Cyclopropyl Phenyl Ketone (13) To Afford 4-[4-(Cyclopropylcarbonyl)phenyl]-1-phenylbutan-1-one (14): According to the general procedure above, ketone **13** (146 mg, 1.00 mmol) afforded **14** as a colorless solid[24] (119 mg, 81%) after column chromatography on silica gel (hexane/ethyl acetate, 4:1), m.p. 91–93 °C. ^1H NMR ($CDCl_3$, 500 MHz): δ = 1.00 (m_c, 2 H, cyclopropane-H), 1.21 (m_c, 2 H, cyclopropane-H), 2.10 (quint, ^3J = 7.4 Hz, 2 H, 3-H), 2.65 (m_c, 1 H, cyclopropane-H), 2.77 (t, ^3J = 7.4 Hz, 2 H, 2-H), 2.98 (t, ^3J = 7.4 Hz, 2 H, 4-H), 7.30 (d, ^3J = 8.2 Hz, 2 H, Ar), 7.43 (t, ^3J = 7.6 Hz, 2 H, Ph), 7.54 (tt, ^4J = 1.2 Hz, ^3J = 7.6 Hz, 1 H, Ph), 7.91 (d, ^3J = 8.2 Hz, 2 H, Ar), 7.94 (dd, ^4J = 1.3 Hz, ^3J = 8.2 Hz, 2 H, Ph) ppm. ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 11.4 (t, CH_2-cyclopropane), 16.9 (t, C-3), 25.2 (t, C-4), 35.1 (t, C-2), 37.4 (d, CH-cyclopropane), 127.9, 128.2, 128.5, 128.6, 133.0, 136.0, 136.8, 147.0 (5 d, 3 s, Ph), 199.7, 200.1 ppm (2 s, CO) ppm. IR (KBr): $\tilde{\nu}$ = 3080, 3050, 3020, 2930, 2885 (=CH, C–H), 1685, 1660 (C=O) cm^{-1}. MS (EI, 80 eV, >260 °C): *m*/*z* (%) = 292 (14) $[M]^+$, 251 (<1) $[M - C_3H_5]^+$, 173 (69) $[M - C_8H_7O]^+$, 145 (3) $[M - C_{10}H_{11}O]^+$, 120 (41) $[C_8H_7O]^+$, 105 (59) $[C_7H_5O]^+$, 77 (76) $[Ph]^+$, 69 (22) $[C_4H_5O]^+$, 44 (100), 41 (21) $[C_3H_5]^+$. HRMS (EI, 80 eV, >260 °C): calcd. for $C_{20}H_{20}O_2$ 292.14633; found 292.14548. $C_{20}H_{20}O_2$ (292.4) calcd. C 82.16, H 6.89; found C 81.78, H 6.81.

Coupling of (4-*tert*-Butylphenyl)cyclopropylmethanone (15) To Afford 1-(4-*tert*-Butylphenyl)butan-1-one (16), 1,5-Bis(4-*tert*-butylphenyl)-5-cyclopropyl-5-hydroxypentan-1-one (17) and 4-[5-*tert*-Butyl-2-(cyclopropylcarbonyl)phenyl]-1-(4-*tert*-butylphenyl)butan-1-one (18): According to the general procedure above, ketone **15** (606 mg, 2.99 mmol) afforded after column chromatography on silica gel (hexane/ethyl acetate, 4:1) **16** as a colorless oil (200 mg, 33%), **17** as a colorless solid (169 mg, 28%) and **18** as a colorless oil (155 mg, 26%). The spectroscopic data of **16** are in agreement with those reported in the literature.[25] **17:** M.p. 88–90 °C. ^1H NMR ($CDCl_3$, 250 MHz): δ = 0.28–0.36 (m, 2 H, 7-H_a, 8-H_a), 0.37–0.52 (m, 2 H, 7-H_b, 8-H_b), 1.01–1.20 (m, 1 H, 6-H), 1.23 (s, 9 H, *t*Bu), 1.26 (s, 9 H, *t*Bu), 1.64–2.01 (m, 5 H, OH, 3-H, 4-H), 2.89 (t, ^3J = 6.8 Hz, 2 H, 2-H), 7.30–7.44 (m, 6 H, Ar), 7.85 (d, ^3J = 8.2 Hz, 2 H, Ar) ppm. ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 0.6 (t, C-7), 1.2 (t, C-8), 18.5 (t, C-3), 21.7 (d, C-6), 30.1, 31.3, 38.4, 41.7 (2 q, 2 s, *t*Bu), 34.2 (t, C-4), 34.9 (t, C-2), 74.5 (s, C-5), 124.7, 125.1, 125.3, 127.9, 134.0, 143.2, 149.0, 156.4 (4 d, 4 s, Ar), 200.0 (s, CO) ppm. IR (KBr): $\tilde{\nu}$ = 3515 (O–H), 3085, 2960, 2905, 2865 (=CH, C–H), 1680 (C=O) cm^{-1}. MS (EI, 80 eV, 140 °C): *m*/*z* (%) = 406 (<1) $[M]^+$, 405 (<1) $[M - H]^+$, 391 (<1) $[M - CH_3]^+$, 365 (6) $[M - C_3H_5]^+$, 349 (<1) $[M - C_4H_9]^+$, 231 (10) $[M - C_{12}H_{15}O]^+$, 203 (100), 176 (20) $[C_{12}H_{16}O]^+$, 57 (43) $[C_4H_9]^+$, 41 (14) $[C_3H_5]^+$. HRMS (EI, 80 eV, 140 °C): calcd. $C_{28}H_{37}O_2$ $[M - H]^+$ 405.27936; $[M - CH_3]^+$ 391.26370; found $[M - H]^+$ 405.27866, $[M - CH_3]^+$ 391.26465. **18:** ^1H NMR ($CDCl_3$, 250 MHz): δ = 0.96–1.00, 1.04–1.24 (2 m, 1 H, 2 H, cyclopropane-H), 1.30 (s, 9 H, *t*Bu), 1.98 (s, 9 H, *t*Bu), 2.04 (q, ^3J = 7.5 Hz, 2 H, 3-H), 2.41 (sept, ^3J = 4.2 Hz, 1 H, cyclopropane-H), 2.96 (m_c, 4 H, 2-H, 4-H), 7.27–7.30 (m, 2 H, Ar), 7.45 (d, ^3J = 8.7 Hz, 2 H, Ar), 7.70 (d, ^3J = 8.0 Hz, 1 H, Ar), 7.87 (d, ^3J = 8.7 Hz, 2 H, Ar) ppm. ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 11.7 (t, CH_2-cyclopropane), 20.6 (t, C-3), 26.5 (t, C-4), 31.0 (q, *t*Bu), 33.2 (d, CH-cyclopropane), 33.2 (q, *t*Bu), 34.7, 35.0 (2 s, *t*Bu), 38.1 (t, C-2), 122.8, 125.4, 127.9, 128.6, 134.5, 136.7, 140.8, 154.2, 156.4 (5 d, 4 s, Ar), 199.8, 204.5 (2 s, CO) ppm. IR (KBr): $\tilde{\nu}$ = 3480, 2965, 2905, 2870 (=CH, C–H), 1670 (C=O) cm^{-1}. MS (EI, 80 eV, 140 °C): *m*/*z* (%) = 404 (14) $[M]^+$, 337 (4) $[M - C_4H_9]^+$, 229 (100) $[M - C_{12}H_{15}O]^+$, 176 (42) $[C_{12}H_{16}O]^+$, 161 (74) $[C_{11}H_{13}O]^+$, 69 (29) $[C_4H_5O]^+$, 57 (52) $[C_4H_9]^+$. HRMS (EI, 80 eV, 140 °C): calcd. for $C_{28}H_{36}O_2$ 404.27155; found 404.27362.

Coupling of 1-(1-Methylcyclopropyl)ethanone (19) To Afford 6-Hydroxy-3-methyl-6-(1-methylcyclopropyl)heptan-2-one (20): According to the general procedure above, ketone **19** (98 mg, 1.00 mmol) afforded **20** as a colorless oil (45 mg, 45%, ca. 1:1.5 mixture of diastereomers) after column chromatography on neutral alumina (hexane/ethyl acetate, 5:1). ^1H NMR ($CDCl_3$, 250 MHz): δ = 0.10–0.17, 0.50–0.55, 0.69–0.74 (3 m, 2 H, 1 H, 1 H, cyclopropane-H), 1.03 (s, 3 H, CH_3), 1.10 (d, ^3J = 6.4 Hz, CH_3), 1.16 (s, 3 H, CH_3), 1.44–1.55 (m, 3 H, 4-H_a, 5-H), 1.72–1.86 (m, 1 H, 4-H_b), 2.15 (s, 3 H, CH_3), 2.51 (m_c, 1 H, 3-H) ppm. The signal corresponding to the hydroxy proton was not observed. ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 8.8, 8.9, 9.9 (3 t, CH_2-cyclopropane), 16.4, 21.5 (2 q, CH_3), 22.8 (s, C-7), 25.4, 25.5 (2 q, CH_3), 26.7, 26.8 (2 t, C-4), 28.0 (q, CH_3), 37.3, 37.4 (2 t, C-5), 47.4, 47.5 (2 d, CH), 76.7 (s, C–OH), 212.8 (s, CO) ppm. IR (KBr): $\tilde{\nu}$ = 3490 (O–H), 3080, 3000, 2960, 2935, 2875 (C–H), 1705 (C=O) cm^{-1}. MS (EI, 80 eV, 30 °C): *m*/*z* (%) = 198 (<1) $[M]^+$, 183 (4) $[M - CH_3]^+$, 170 (15) $[M - C_2H_4]^+$, 143 (6) $[MH - C_4H_8]^+$, 43 (100) $[C_2H_3O]^+$. HRMS (EI, 80 eV, 30 °C): calcd. for $C_{12}H_{22}O_2$ 198.16199; found 198.16200.

Coupling of Cyclopropyl(2-thienyl)methanone (21) To Afford Cyclopropyl{5-[cyclopropyl(hydroxy)(2-thienyl)methyl]-2-thienyl}-methanone (22): According to the general procedure above, ketone **21** (152 mg, 1.00 mmol) afforded **22** as a colorless oil (58 mg, 38%) after column chromatography on silica gel (hexane/ethyl acetate, 7:3) and preparative HPLC (hexane/ethyl acetate, 21:4, 64 mL/ min, 47 bar). ^1H NMR ($CDCl_3$, 500 MHz): δ = 0.59–0.61, 0.61–0.65, 1.00, 1.21, 1.74 (2 m, 3 m_c, 1 H, 3 H, 2 H, 2 H, 1 H, cyclopropane-H), 2.43 (s, 1 H, OH), 2.49 (m_c, 1 H, cyclopropane-H), 6.96 (dd, ^3J = 5.1 Hz, 3.8 Hz, 1 H, Ar), 7.03 (d, ^3J = 4.0 Hz, 1 H, Ar), 7.06 (dd, ^3J = 2.5 Hz, ^4J = 1.2 Hz, 1 H, Ar), 7.26 (dd, ^3J = 3.8 Hz, ^4J = 1.2 Hz, 1 H, Ar), 7.67 (d, ^3J = 4.0 Hz, 1 H, Ar) ppm. ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 2.2, 2.7, 11.3, 17.8, 23.8 (3 t, 2 d, cyclopropane), 74.4 (s, C–OH), 125.1, 125.2, 125.4, 125.5, 126.6, 143.4, 150.6, 160.0 (5 d, 3 s, Ar), 193.1 (s, CO) ppm. IR (KBr): $\tilde{\nu}$ = 3440 (O–H), 3090, 3010, 2955, 2925, 2850 (=CH, C–H), 1635 (C=O) cm^{-1}. MS (EI, 80 eV, 90 °C): *m*/*z* (%) = 304 (21) $[M]^+$, 263 (59) $[M - C_3H_5]^+$, 235 (27) $[M - C_4H_5O]^+$, 111 (100), 69 (59) $[C_4H_5O]^+$, 41 (39) $[C_3H_5]^+$. HRMS (EI, 80 eV, 90 °C): calcd. for $C_{16}H_{16}O_2S_2$ 304.05917; found 304.05844.

3,8-Dimethyldecane-2,9-dione (23): Samarium (720 mg, 4.40 mmol) and 1,2-diiodoethane (1.24 g, 4.40 mmol) were suspended in THF (50 mL) under argon and stirred at room temperature until the color of the suspension turned into dark blue (approximately 2 h). The flask was then evacuated and HMPA (6.40 mL, 32.0 mmol) was added. Argon was purged for 10 min through a solution of cyclopropyl methyl ketone (**3**) (168 mg, 2.00 mmol) and methyl iodide (0.37 mL, 6.00 mmol) in THF (30 mL), this mixture was added to the deep violet solution of SmI_2/HMPA. The resulting solution was stirred at room temperature for 16 h and then quenched by addition of a satd. aq. $NaHCO_3$ solution (15 mL). The aqueous phase was extracted with diethyl ether (3 × 30 mL) and the combined organic layers were washed once with water and twice with brine, then dried with $MgSO_4$, filtered and the solvent was removed under reduced pressure to leave the crude product. Compound **23**[26] was obtained as a colorless oil (108 mg, 55%) after column chromatography on alumina (hexane/ethyl acetate, 5:1). ^1H NMR ($CDCl_3$, 500 MHz): δ = 1.06 (d, ^3J = 7.0 Hz, 6 H, 3-CH_3, 8-CH_3), 1.12–1.26 (m, 4 H, 5-H, 6-H), 1.26–1.35 (m, 2 H,

4-H_a, 7-H_a), 1.60–1.66 (m, 2 H, 4-H_b, 7-H_b), 2.12 (s, 6 H, 1-H, 10-H), 2.49 (sext, ^3J = 7.0 Hz, 2 H, 3-H, 8-H) ppm. ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 16.2 (q, 3-CH_3, 8-CH_3), 27.2 (t, C-5, C-6), 27.9 (q, C-1, C-10), 32.6 (t, C-4, C-7), 47.1 (d, C-3, C-8), 212.6 (s, C-2, C-9) ppm. IR (KBr): $\tilde{\nu}$ = 2965, 2935, 2860 (C–H), 1710, 1690 (C=O) cm^{-1}. MS (EI, 80 eV, 40 °C): *m/z* (%) = 198 (5) $[M]^+$, 180 (1) $[M - H_2O]^+$, 43 (100) $[C_2H_3O]^+$. HRMS (EI, 80 eV, 40–70 °C): calcd. for $C_{12}H_{22}O_2$ 198.16199; found 198.16223.

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