Bromine-Induced Facile Synthesis of Butenolides and Spirobutenolides from Sterically Congested Tetrasubstituted Dialkyl Alkylidene Succinates

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Abstract: Starting from sterically congested tetrasubstituted dialkyl alkylidene succinates, facile general approach to several dialkyl substituted butenolides and spirobutenolides with the generation of quaternary carbon center has been demonstrated via bromine-induced dealkylative regioselective intramolecular cyclization and dehydrobromination pathway. The mechanistic aspects involved in the formation of butenolides have been also described in brief.

Key words: alkylidene succinates, bromine, intramolecular cyclizations, butenolides, spirobutenolides

The natural and unnatural γ-butenolides are an important class of compounds that find major applications in organic, medicinal, and polymer chemistry, and a broad range of biological properties have been conferred on them.[1–5] Moreover, the two important pesticides spirodiclofen and spiromesifen used to keep a control on severe crop damaging pests (*Tetranychus urticae*, *Panonychus ulmi*, and *Bemisia tabaci*), also possess spirobutenolide skeletons (Figure 1).[2]

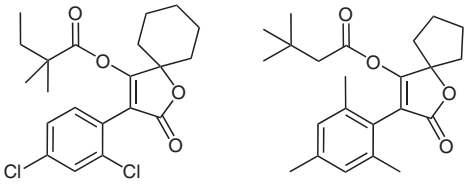
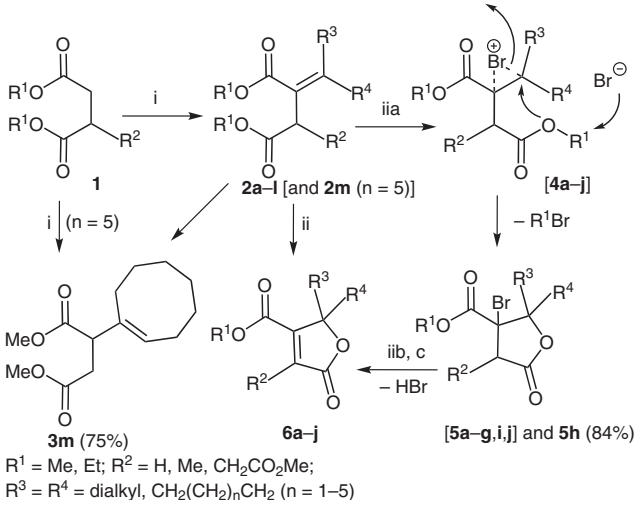


Figure 1 Pesticidal spirobutenolides of commercial interest

Basically, the diverse range of γ-butenolide skeletons has been designed by employing new carbon–oxygen bond construction reactions and metal-catalyzed carbon–carbon bond formations. A very large number of such γ-butenolides has been synthesized during the past century using several elegant synthetic strategies.[3] Methods for the construction of such type of building blocks with a quaternary carbon center are of special interest to organic chemists due to their presence in natural products.[4]

They have been synthesized by using an excellent iodide-catalyzed methyl–oxygen bond cleavage in 2-methoxyfurans, metal-catalyzed carbonylation, oxidative cyclization, palladium-catalyzed arylation, and photocyclization methodologies.[4,5] All these studies indicate that the development of new potential routes to γ-butenolides is still a challenging task of current interest. In continuation of our studies on cyclic anhydrides to bioactive natural and unnatural products,[6] we recently synthesized the tetrasubstituted dialkyl alkylidene succinates and systematically studied their bromination reactions. Our preliminary studies on halogenation of dimethyl 2-(propan-2-ylidene)succinate (**2a**) revealed the formation of methyl 2,2-dimethyl-5-oxo-2,5-dihydrofuran-3-carboxylate (**6a**) as the product, instead of the corresponding expected dihalo compound. We prepared a systematic plan to completely explore our observed fact with a perspective to develop a new general route to γ-butenolides. In this context, we herein report our results on the synthesis of target molecules (Scheme 1).



Scheme 1 Synthesis of butenolides and spirobutenolides via the bromination of tetrasubstituted C=C bonds. *Reagents and conditions*: (i) (a) *t*-BuOK, *t*-BuOH, R^2COR^3, 25 °C, 45 min, (b) MeOH or EtOH, H^+/H_2SO_4, reflux, 8 h (50–78%); (ii) (a) Br_2 (1.5 equiv), CCl_4, 25 °C, 8 h, (b) Et_3N (1.5 equiv), 25 °C, 2 h (82–88%, 44% for **6d**), (c) Et_3N (1.5 equiv), reflux, 2 h (84% for **6h** and 82% for **6i**).

The base-catalyzed Stobbe condensation of dimethyl succinate with acetone, isobutyl methyl ketone, cyclobutanone, cyclopentanone, cyclohexanone, 4-*tert*-butylcyclohexanone, cycloheptanone, α-tetralone, and benzophenone, followed by esterification of the formed intermediate monoesters,[7] respectively furnished the corresponding desired starting materials, the dimethyl alkyl-

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idene succinates **2a**, **2c–g** and **2j–l** in 50–78% yields.[8] Similarly, the condensation of diethyl succinate with acetone, condensation of dimethyl methylsuccinate with cyclohexanone and condensation of trimethyl propane-1,2,3-tricarboxylate with cyclohexanone, respectively furnished the required starting materials **2b**, **2h**, and **2i** in 52–69% yields. In our hands, the Stobbe condensation of dimethyl succinate with cyclooctanone directly furnished the product **3m**[8c] via the expected intermediate **2m**. We feel that, herein the selective exocylic to endocyclic C=C bond migration is notable, as the double bond in the intermediate **2m** does not get in conjugation with the two ester functionalities to form the corresponding dimethyl cyclooctyl fumarate.

On having all these potential starting materials **2a–l** in hand, we studied their reactions with bromine to obtain the desired butenolides. The reactions of dialkyl alkylidene succinates **2a–c** with bromine in CCl_4 at room temperature directly furnished the corresponding butenolides **6a–c** in 82–84% yields. During these studies, we noticed that the addition of triethylamine after an eight-hour reaction time provides the desired products with slight improvement in yields (86–88%) (Table 1).

Table 1 Synthesis of Butenolides **6a–j**

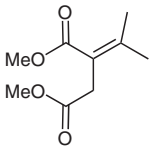
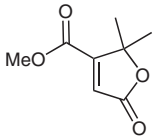
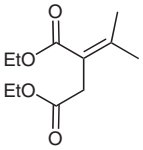
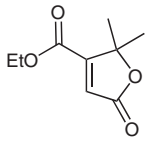
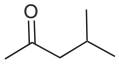
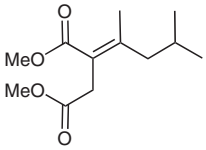
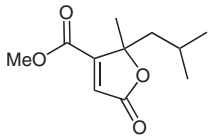
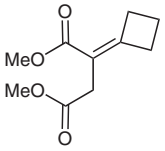
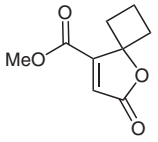
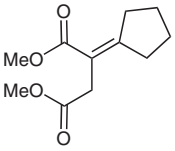
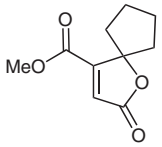
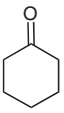
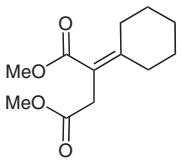
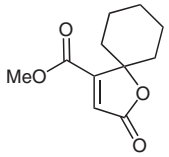
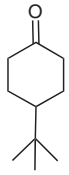
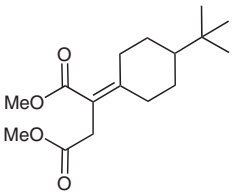
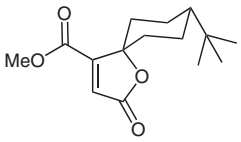
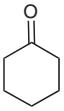
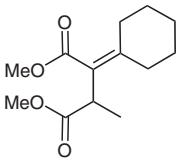
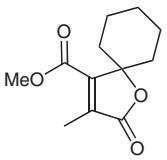
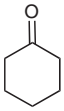
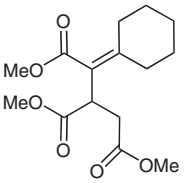
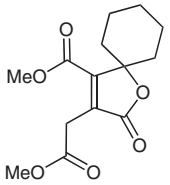
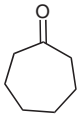
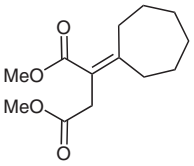
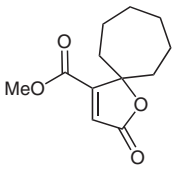
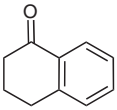
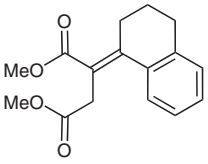
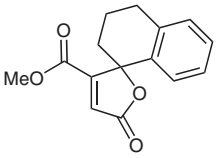
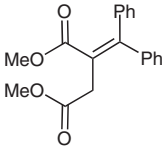
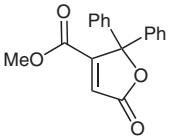
Entry	Ketones	Dialkyl alkylidines	Butenolides
1		 **2a** (69%)	 **6a** (88%)
2		 **2b** (69%)	 **6b** (87%)
3		 **2c** (62%)	 **6c** (86%)
4		 **2d** (74%)	 **6d** (44%)
5		 **2e** (52%)	 **6e** (82%)
6		 **2f** (60%)	 **6f** (85%)

Table 1 Synthesis of Butenolides **6a–j** (continued)

Entry	Ketones	Dialkyl alkylidines	Butenolides
7		 **2g** (56%)	 **6g** (84%)
8		 **2h** (53%)	 **6h**[a] (84%)
9		 **2i** (52%)	 **6i** (82%)
10		 **2j** (50%)	 **6j** (83%)
11		 **2k** (72%)	 **6k** (not obtained)
12		 **2l** (78%)	 **6l** (not obtained)

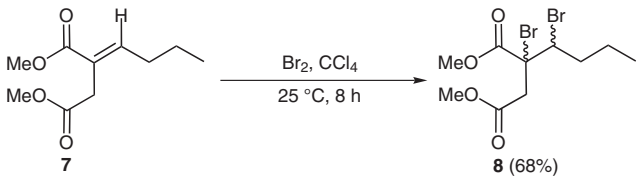
[a] Possesses antifungal and C1 esterase inhibitor activities.[9]

As expected, the substrates **2d–j**, obtained by using cyclic ketones, on sequential treatment with bromine in CCl_4 and triethylamine gave the expected spirobutenolides products **6d–j** in 82–85% yields, except for **6d**. In the case of conversion of **2d** to **6d**, though we got the expected product, the yield was only 44% while the remaining was decomposed material, probably originated by an in situ cleavage of the cyclobutane ring during the course of reaction. As expected, in the bromination reaction of **2g**, we got an inseparable, nearly 1:1 mixture of diastereomers of **6g**. The substrates **2k** and **2l**, wherein the tetrasubstituted C=C bonds are in conjugation with the aromatic ring, remained unreacted in our hands in the presence of bromine–triethylamine under the standard reaction conditions and we were unable to obtain products **6k** and **6l** (Table 1). The analytical and spectral data obtained for all the γ-butenolides were in complete agreement with the assigned structures. In the ^{1}H NMR spectra of **6a–g** and **6j**, the characteristic vinylic proton singlet appeared at δ = ~6.57.

In an attempt to study the mechanistic aspects involved in the conversion of compounds **2a–j** to **6a–j**, we noticed that the methine proton in the compound **5h** is not easily accessible to the base at room temperature for the last dehydrobromination process. Hence, we could successfully isolate the corresponding intermediate saturated bromo-

lactone **5h** in 84% yield. The isolated intermediate **5h**, in the presence of triethylamine as the base, under reflux conditions gave the desired product **6h** in quantitative yield. Based on the isolated intermediate **5h**, we surmise that during the course of the bromination reaction, the bromonium ion intermediates **4a–j**, as depicted in Scheme 1, are formed. In the proposed intermediates **4a–j**, the bulkier bromide anion is unable to approach the quaternary carbons to form the expected dibromides. Hence the lone pair on the relatively smaller oxygen atom, intramolecularly and regioselectively, attacks the bromonium bridge to form the γ-lactone. The simultaneous bromide anion-induced dealkylation takes place to cancel the positive charge on an oxygen atom to form the intermediate products **5a–j**, which on dehydrobromination yield the target compounds **6a–j**.

The corresponding substrate **7**[10] with a trisubstituted C=C bond, upon bromination, exclusively gave the corresponding dibromo compound **8** in 68% yield, while it remained unreacted with iodine (Scheme 2); these results directly support both our proposed strategy and described mechanistic pathway.



Scheme 2 Bromination of trisubstituted C=C bond

In summary, we have demonstrated a simple and efficient general approach to *gem*-dialkyl-substituted quaternary butenolides by taking advantage of bromine stimulated structural rearrangement of sterically congested tetrasubstituted dialkyl alkylidene succinates. We feel that an in situ dealkylative intramolecular cyclization process involved in the present approach along with the formation of oxygen–carbon bond, is noteworthy.

Melting points are uncorrected. The ^{1}H NMR spectra were recorded on 200 MHz, 300 MHz, and 500 MHz NMR spectrometer using TMS as an internal standard. The ^{13}C NMR spectra were recorded on 200 NMR spectrometer (50 MHz) and 500 NMR spectrometer (125 MHz). The IR spectra were recorded on an FT-IR spectrometer. Elemental analyses were obtained by using Flash EA 1112 series and Elementar Vario EL analyzer at NCL, Pune. Column chromatographic separations were carried out on silica gel (60–120 mesh). Commercially available dimethyl succinate, diethyl succinate, dimethyl methylsuccinate, trimethyl propane-1,2,3-tricaboxylate, isopropyl methyl ketone, cyclobutanone, cyclopentanone, cyclohexanone, *tert*-butylcyclohexanone, cycloheptanone, cyclooctanone, α-tetralone, benzophenone, and *t*-BuOK were used. Petroleum ether (PE) used refers to the fraction boiling in the range 60–80 °C.

Dimethyl 2-(Propan-2-ylidene)succinate (2a); Typical Procedure

To a stirred solution of *t*-BuOK (1.22 g, 10.0 mmol) in *t*-BuOH (10 mL) was added a solution of dimethyl succinate (1.46 g, 10.0 mmol) in *t*-BuOH (5 mL) in a dropwise fashion under argon with constant stirring. After stirring the reaction mixture for 10 min, a solution of acetone (696 mg, 12.0 mmol) in *t*-BuOH (5 mL) was added dropwise under argon and the mixture was stirred for 45 min at 25 °C. The mixture was concentrated in vacuo. The obtained residue was dissolved in H_2O (50 mL) and the aqueous layer was washed with EtOAc (2 × 20 mL). The aqueous layer was acidified to pH 2 using aq 2 N HCl (20 mL). The acidified aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with H_2O (25 mL), brine (25 mL), dried (Na_2SO_4), and concentrated in vacuo, and the dried residue was dissolved in MeOH (30 mL). To the above solution was added concd H_2SO_4 (1 mL) and the mixture was refluxed for 8 h with constant stirring. The mixture was allowed to reach 25 °C and concentrated in vacuo. The obtained residue was dissolved in EtOAc (50 mL) and the organic layer was washed with 5% aq $NaHCO_3$ (25 mL), brine (25 mL), and dried (Na_2SO_4). Concentration of the organic layer in vacuo followed by silica gel column chromatographic purification of the resulting residue using EtOAc–PE (1:9) as eluent afforded the pure product **2a** as a thick oil[8] (1.28 g, 69%).

IR (neat): 1728, 1642 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.86 (s, 3 H), 2.14 (s, 3 H), 3.38 (s, 2 H), 3.67 (s, 3 H), 3.71 (s, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 23.2 (2 C), 35.1, 51.4, 51.8, 120.2, 149.8, 168.2, 171.8.

Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 58.16; H, 7.71.

Diethyl 2-(Propan-2-ylidene)succinate (2b)

Compound **2b** was obtained from diethyl succinate (1.74 g, 10.0 mmol) and acetone (696 mg, 12.0 mmol) using the same procedure described above for **2a**, as a thick oil[7] (1.48 g, 69%).

IR (neat): 1738, 1719, 1642 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7 Hz, 3 H), 1.27 (t, *J* = 7 Hz, 3 H), 1.86 (s, 3 H), 2.14 (s, 3 H), 3.36 (s, 2 H), 4.13 (q, *J* = 7 Hz, 2 H), 4.18 (q, *J* = 7 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2, 23.2, 23.3, 35.5, 60.2, 60.7, 120.7, 148.9, 167.9, 171.5.

(*E*)-Dimethyl 2-(4-Methylpentan-2-ylidene)succinate (2c)

Compound **2c** was obtained from dimethyl succinate (1.46 g, 10.0 mmol) and 4-methylpentan-2-one (1.20 g, 12.0 mmol) using the same procedure described above for **2a**, as a thick oil (1.41 g, 62%).

IR ($CHCl_3$): 1743, 1720, 1630 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.90 (d, *J* = 6 Hz, 6 H), 1.75–2.00 (m, 1 H), 2.07 (d, *J* = 8 Hz, 2 H), 2.10 (s, 3 H), 3.41 (s, 2 H), 3.67 (s, 3 H), 3.72 (s, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.7, 22.5, 27.2, 35.1, 45.6, 51.4, 51.9, 121.2, 152.0, 168.4, 172.0.

Anal. Calcd for $C_{12}H_{20}O_4$: C, 63.14; H, 8.83. Found: C, 62.81; H, 8.51.

Dimethyl 2-Cyclobutylidenesuccinate (2d)

Compound **2d** was obtained from dimethyl succinate (1.46 g, 10.0 mmol) and cyclobutanone (840 mg, 12.0 mmol) using the same procedure described above for **2a**, as a thick oil (1.47 g, 74%).

IR ($CHCl_3$): 1737, 1710, 1680 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.06 (quint, *J* = 8 Hz, 2 H), 2.82 (t, *J* = 8 Hz, 2 H), 3.15 (s, 2 H), 3.15 (t, *J* = 8 Hz, 2 H), 3.69 (s, 3 H), 3.71 (s, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 16.4, 30.9, 32.9, 33.7, 51.3, 51.9, 117.3, 164.2, 167.0, 171.8.

Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.40; H, 7.30.

Dimethyl 2-Cyclopentylidenesuccinate (2e)
Compound **2e** was prepared from dimethyl succinate (1.46 g, 10.0 mmol) and cyclopentanone (1.10 g, 12.0 mmol) using the same procedure described above for **2a**, as a thick oil[8] (1.10 g, 52%).

IR ($CHCl_3$): 1736, 1693, 1643 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.60–1.82 (m, 4 H), 2.40 (t, *J* = 6 Hz, 2 H), 2.82 (t, *J* = 6 Hz, 2 H), 3.35 (s, 2 H), 3.68 (s, 3 H), 3.72 (s, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 25.5, 26.9, 34.2, 34.5, 35.8, 51.3, 51.9, 116.6, 165.3, 167.5, 172.0.

Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.35; H, 7.98.

Dimethyl 2-Cyclohexylidenesuccinate (2f)
Compound **2f** was obtained from dimethyl succinate (1.46 g, 10.0 mmol) and cyclohexanone (1.18 g, 12.0 mmol) using the same procedure described above for **2a**, as a thick oil[8] (1.36 g, 60%).

IR ($CHCl_3$): 1742, 1710, 1635 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.52–1.72 (m, 6 H), 2.18–2.28 (m, 2 H), 2.58–2.68 (m, 2 H), 3.39 (s, 2 H), 3.68 (s, 3 H), 3.73 (s, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 26.2, 27.9, 28.1, 32.3, 32.4, 34.6, 51.4, 51.8, 117.2, 155.2, 168.8, 171.8.

Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.59; H, 7.72.

Dimethyl 2-(4-*tert*-Butylcyclohexylidene)succinate (2g)
Compound **2g** was obtained from dimethyl succinate (1.46 g, 10.0 mmol) and 4-*tert*-butylcyclohexanone (1.85 g, 12.0 mmol) using the same procedure described above for **2a**, as a thick oil (1.58 g, 56%).

IR ($CHCl_3$): 1741, 1705, 1652 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 0.85 (s, 9 H), 1.05–1.35 (m, 4 H), 1.80–2.05 (m, 4 H), 2.55–2.68 (m, 1 H), 3.40 (s, 2 H), 3.68 (s, 3 H), 3.73 (s, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 27.5, 28.4, 28.7, 32.0, 32.2, 32.4, 34.7, 47.7, 51.5, 51.9, 117.0, 155.4, 168.9, 171.9.

Dimethyl 2-Cyclohexylidene-3-methylsuccinate (2h)
Compound **2h** was obtained from dimethyl 2-methylsuccinate (1.60 g, 10.0 mmol) and cyclohexanone (1.18 g, 12.0 mmol) using the same procedure described above for **2a**, as a thick oil (1.27 g, 53%).

IR ($CHCl_3$): 1743, 1726, 1632 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.32 (d, *J* = 8 Hz, 3 H), 1.50–1.75 (m, 6 H), 2.24 (t, *J* = 6 Hz, 2 H), 2.30–2.60 (m, 2 H), 3.64 (q, *J* = 8 Hz, 1 H), 3.67 (s, 3 H), 3.70 (s, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 16.4, 26.4, 28.0, 28.2, 31.6, 32.9, 39.6, 51.3, 52.0, 124.7, 150.0, 169.0, 174.5.

Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.64; H, 8.70.

Trimethyl 1-Cyclohexylidenepropane-1,2,3-tricarboxylate (2i)
Compound **2i** was obtained from trimethyl propane-1,2,3-tricarboxylate (2.18 g, 10.0 mmol) and cyclohexanone (1.18 g, 12.0 mmol) using the same procedure described above for **2a**, as a thick oil (1.55 g, 52%).

IR ($CHCl_3$): 1740, 1630 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.50–1.75 (m, 6 H), 2.24–2.35 (m, 2 H), 2.36 (dd, *J* = 17, 6 Hz, 1 H), 2.44–2.55 (m, 2 H), 3.09 (dd, *J* = 17, 8 Hz, 1 H), 3.67 (s, 3 H), 3.68 (s, 3 H), 3.69 (s, 3 H), 4.17 (dd, *J* = 9, 6 Hz, 1 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 26.3, 28.0, 28.2, 31.9, 32.9, 35.8, 41.3, 51.4, 51.8, 52.2, 122.2, 152.8, 168.3, 172.3, 172.9.

Anal. Calcd for $C_{15}H_{22}O_6$: C, 60.39; H, 7.43. Found: C, 60.25; H, 7.76.

Dimethyl 2-Cycloheptylidenesuccinate (2j)
Compound **2j** was obtained from dimethyl succinate (1.46 g, 10.0 mmol) and cycloheptanone (1.34 g, 12.0 mmol) using the same procedure described above for **2a**, as a thick oil (1.20 g, 50%).

IR ($CHCl_3$): 1741, 1717, 1652 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.40–1.80 (m, 8 H), 2.36 (t, *J* = 6 Hz, 2 H), 2.71 (t, *J* = 6 Hz, 2 H), 3.38 (s, 2 H), 3.67 (s, 3 H), 3.71 (s, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 26.2, 27.2, 28.5 (2 C), 33.7, 34.0, 34.8, 51.4, 51.9, 120.1, 158.2, 168.4, 172.0.

Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.60; H, 7.90.

(*E*)-Dimethyl 2-[3,4-Dihydronapthalen-1(2*H*)-ylidene]succinate (2k)
Compound **2k** was obtained from dimethyl succinate (1.46 g, 10.0 mmol) and α-tetralone (1.75 g, 12.0 mmol) using the same procedure described above for **2a**, as a thick oil (1.97 g, 72%).

IR ($CHCl_3$): 1740, 1707, 1619 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.85 (quint, *J* = 6 Hz, 2 H), 2.56 (t, *J* = 6 Hz, 2 H), 2.75 (t, *J* = 6 Hz, 2 H), 3.56 (s, 2 H + 3 H), 3.71 (s, 3 H), 7.05–7.25 (m, 4 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 22.2, 28.7, 29.5, 36.2, 51.7, 52.1, 120.9, 125.1, 127.8, 128.0, 128.5, 135.4, 139.8, 145.2, 171.1, 171.3.

Dimethyl 2-(Diphenylmethylene)succinate (2l)
Compound **2l** was obtained from dimethyl succinate (1.46 g, 10.0 mmol) and benzophenone (2.18 g, 12.0 mmol) using the same procedure described above for **2a**, as a solid (2.42 g, 78%); mp 82–84 °C (Lit.[8] mp 78–80 °C).

IR ($CHCl_3$): 1739, 1712, 1620 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 3.47 (s, 2 H + 3 H), 3.70 (s, 3 H), 7.05–7.20 (m, 4 H), 7.20–7.40 (m, 6 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 37.9, 51.5, 51.9, 124.5, 127.8 (2 C), 128.2, 128.3, 128.5, 128.9, 140.3, 141.7, 151.7, 169.8, 171.5.

Anal. Calcd for $C_{19}H_{18}O_4$: C, 73.53; H, 5.85. Found: C, 73.70; H, 5.52.

(*E*)-Dimethyl 2-Cyclooct-1-enylsuccinate (3m)
Compound **3m** was obtained from dimethyl succinate (1.46 g, 10.0 mmol) and cyclooctanone (1.51 g, 12.0 mmol) using the same procedure described above for **2a**, as a thick oil[8] (1.91 g, 75%).

IR ($CHCl_3$): 1739, 1654 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.45 (br s, 8 H), 2.00–2.30 (m, 4 H), 2.49 (dd, *J* = 17, 6 Hz, 1 H), 2.96 (dd, *J* = 16, 10 Hz, 1 H), 3.51 (dd, *J* = 11, 4 Hz, 1 H), 3.67 (s, 3 H), 3.69 (s, 3 H), 5.58 (t, *J* = 8 Hz, 1 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 26.0, 26.2, 26.3, 27.8, 29.0, 29.4, 35.6, 48.7, 51.8, 52.0, 128.8, 136.5, 172.5, 173.8.

Methyl 10-Bromo-9-methyl-8-oxo-7-oxaspiro[5,4]decane-10-carboxylate (5h)
Compound **5h** was obtained from **2h** (480 mg, 2.00 mmol) using the same procedure described for **6a** (see below), but in the absence of Et_3N, as a thick oil (513 mg, 84%).

IR ($CHCl_3$): 1790, 1756 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.31 (d, *J* = 6 Hz, 3 H), 1.50–1.80 (m, 8 H), 1.80–1.95 (m, 1 H), 2.04 (dd, *J* = 13, 6 Hz, 1 H), 3.25 (q, *J* = 6 Hz, 1 H), 3.81 (s, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 8.9, 22.0, 22.2, 24.7, 31.1, 34.9, 47.2, 53.6, 71.5, 86.8, 167.0, 173.4.

Methyl 2,2-Dimethyl-5-oxo-2,5-dihydrofuran-3-carboxylate (6a); Typical Procedure
To a stirred solution of **2a** (372 mg, 2.00 mmol) in CCl_4 (25 mL) was added a solution of Br_2 (480 mg, 3.00 mmol) in CCl_4 (5 mL) in a dropwise fashion and the reaction mixture was stirred for 8 h at 25 °C. Then, Et_3N (303 mg, 3.00 mmol) was added dropwise and the mixture was further stirred for 2 h at 25 °C. The mixture was concentrated in vacuo. The obtained residue was dissolved in EtOAc (50 mL), the organic layer washed with H_2O (25 mL), brine (25 mL), and dried (Na_2SO_4). Concentration of the organic layer in vacuo, followed by silica gel column chromatographic purification of the resulting residue using EtOAc–PE (1:9) as eluent afforded the pure product **6a**, as a thick oil[5a] (299 mg, 88%).

IR ($CHCl_3$): 1764, 1730, 1633 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.63 (s, 6 H), 3.88 (s, 3 H), 6.58 (s, 1 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 25.1, 52.6, 87.2, 126.1, 160.9, 161.2, 169.8.

Ethyl 2,2-Dimethyl-5-oxo-2,5-dihydrofuran-3-carboxylate (6b)
Compound **6b** was obtained from **2b** (428 mg, 2.00 mmol) using the same procedure described above for **6a**, as a thick oil (320 mg, 87%).

IR ($CHCl_3$): 1770, 1725, 1633 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.36 (t, *J* = 8 Hz, 3 H), 1.62 (s, 6 H), 4.33 (q, *J* = 8 Hz, 2 H), 6.57 (s, 1 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.0, 25.1, 62.0, 87.2, 125.9, 160.8, 161.3, 169.9.

Anal. Calcd for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.73; H, 6.49.

Methyl 2-Isobutyl-2-methyl-5-oxo-2,5-dihydrofuran-3-carboxylate (6c)
Compound **6c** was obtained from **2c** (456 mg, 2.00 mmol) using the same procedure described above for **6a**, as a thick oil (365 mg, 86%).

IR (neat): 1767, 1731, 1633 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 0.87 (d, *J* = 10 Hz, 3 H), 0.90 (d, *J* = 10 Hz, 3 H), 1.55 (sept, *J* = 8 Hz, 1 H), 1.61 (s, 3 H), 1.84 (dd, *J* = 14, 6 Hz, 1 H), 1.98 (dd, *J* = 14, 6 Hz, 1 H), 3.89 (s, 3 H), 6.62 (s, 1 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 23.7, 24.0, 24.1, 25.0, 45.5, 52.6, 89.7, 126.8, 160.3, 161.4, 170.1.

Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.33; H, 7.40.

Methyl 6-Oxo-5-oxaspiro[3,4]oct-7-ene-8-carboxylate (6d)
Compound **6d** was obtained from **2d** (198 mg, 1.00 mmol) using the same procedure described above for **6a**, as a thick oil[5a] (80 mg, 44%).

IR ($CHCl_3$): 1761, 1726, 1630 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.13 (quint, *J* = 10 Hz, 2 H), 2.55–2.65 (m, 2 H), 2.77–2.85 (m, 2 H), 3.94 (s, 3 H), 6.55 (s, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.3, 31.8 (2 C), 52.7, 89.0, 125.9, 157.5, 161.6, 169.8.

Anal. Calcd for $C_9H_{10}O_4$: C, 59.34; H, 5.53. Found: C, 59.59; H, 5.70.

Methyl 7-Oxo-6-oxaspiro[4,4]non-8-ene-9-carboxylate (6e)
Compound **6e** was obtained from **2e** (424 mg, 2.00 mmol) using the same procedure described above for **6a**, as a thick oil[5a] (322 mg, 82%).

IR ($CHCl_3$): 1767, 1730, 1630 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.75–2.10 (m, 6 H), 2.20–2.45 (m, 2 H), 3.88 (s, 3 H), 6.62 (s, 1 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 25.2, 37.0, 52.6, 97.1, 126.8, 158.2, 161.4, 170.1.

Anal. Calcd for $C_{10}H_{12}O_4$: C, 61.22; H, 6.16. Found: C, 61.27; H, 6.04.

Methyl 8-Oxo-7-oxaspiro[5,4]dec-9-ene-10-carboxylate (6f)
Compound **6f** was obtained from **2f** (452 mg, 2.00 mmol) using the same procedure described above for **6a**, as a white solid (357 mg, 85%); mp 94–96 °C.

IR ($CHCl_3$): 1761, 1732, 1628 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.20–1.45 (m, 1 H), 1.45–1.85 (m, 7 H), 2.05–2.25 (m, 2 H), 3.88 (s, 3 H), 6.60 (s, 1 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.9, 24.2, 33.5, 52.6, 89.1, 126.3, 161.0, 161.4, 170.1.

Anal. Calcd for $C_{11}H_{14}O_4$: C, 62.85; H, 6.71. Found: C, 63.03; H, 6.88.

Methyl 3-*tert*-Butyl-8-oxo-7-oxaspiro[5,4]dec-9-ene-10-carboxylate (6g)
Compound **6g** was obtained from **2g** (564 mg, 2.00 mmol) using the same procedure described above for **6a**, as a yellow solid (447 mg, 84%, 1:1 mixture of diastereomers); mp 86–88 °C.

IR ($CHCl_3$): 1767, 1731, 1629 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 0.88 (s, 9 H), 0.99 (s, 9 H), 1.00–1.90 (m, 14 H), 2.03–2.30 (m, 4 H), 3.87 (s, 6 H), 6.48 (s, 1 H), 6.59 (s, 1 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.8, 23.0, 27.4, 27.7, 32.4, 32.8, 33.0, 34.1, 43.0, 46.2, 52.6, 52.7, 89.0, 89.8, 125.4, 126.5, 161.0, 161.4, 161.8, 162.5, 170.1, 170.3.

Methyl 9-Methyl-8-oxo-7-oxaspiro[5,4]dec-9-ene-10-carboxylate (6h)
Compound **6h** was obtained from **2h** (480 mg, 2.00 mmol) using the same procedure described above for **6a**, however, after addition of Et_3N, the reaction mixture was refluxed for 2 h to obtain **6h**, as a white solid (376 mg, 84%); mp 92–94 °C (Lit.[9] mp 94 °C).

IR ($CHCl_3$): 1760, 1723, 1660 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.15–1.37 (m, 1 H), 1.38–1.55 (m, 2 H), 1.60–1.85 (m, 5 H), 2.05–2.25 (m, 2 H), 2.16 (s, 3 H), 3.88 (s, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 11.3, 22.1, 24.3, 33.7, 52.2, 87.8, 136.5, 151.8, 162.9, 172.2.

Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.33; H, 7.08.

Dimethyl 8-Oxo-7-oxaspiro[5,4]dec-9-ene-9-methylene-10-dicarboxylate (6i)

Compound **6i** was obtained from **2i** (596 mg, 2.00 mmol) using the same procedure described above for **6a**; however, after addition of Et_3N, the reaction mixture was refluxed for 2 h to obtain **6i**, as a white solid (463 mg, 82%); mp 104–106 °C.

IR ($CHCl_3$): 1762, 1748, 1728, 1664 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.15–1.40 (m, 1 H), 1.45–1.90 (m, 7 H), 2.05–2.30 (m, 2 H), 3.69 (s, 2 H), 3.71 (s, 3 H), 3.87 (s, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 22.1, 24.3, 30.6, 33.6, 52.4, 52.5, 88.4, 132.9, 154.7, 162.1, 169.0, 171.0.

Anal. Calcd for $C_{14}H_{18}O_6$: C, 59.57; H, 6.43. Found: C, 59.70; H, 6.35.

Methyl 9-Oxo-8-oxaspiro[6,4]undec-10-ene-11-carboxylate (6j)

Compound **6j** was obtained from **2j** (480 mg, 2.00 mmol) using the same procedure described above for **6a**, as a white solid (372 mg, 83%); mp 70–72 °C.

IR ($CHCl_3$): 1767, 1732, 1634 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.50–2.00 (m, 10 H), 2.10–2.33 (m, 2 H), 3.87 (s, 3 H), 6.51 (s, 1 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 22.9, 28.1, 37.3, 52.6, 92.4, 125.0, 161.6, 162.3, 170.5.

Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.43; H, 7.28.

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