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Free radical reactions for heterocycle synthesis. Part 7: 2-Bromobenzoic acids as building blocks in the construction of spirobenzolactones and spirobenzolactams

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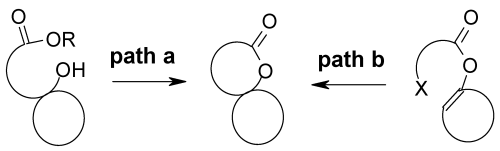
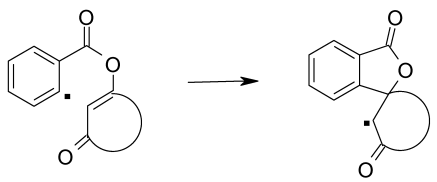
Abstract—A straightforward 2-step parallel synthesis for structurally diversified spiro compounds is developed. 2-Bromobenzoic acids are used as common building blocks to couple with a series of conjugated enoles or enamines. Sequential intramolecular free radical Michael additions lead to formation of spirobenzolactones, spirobenzolactams, spirobenzolactone-lactams, spiorbenzolactone-thiolactones, spiordilactones, and bridged-spirolactones.

1. Introduction

Spirolactones and spirolactams are frequently occurring motifs in biologically active molecules.[1] Synthesis of spirolactones, for example, can be achieved by carbon–oxygen bond formation via lactonization (Scheme 1, path a) or carbon–carbon bond formation via cyclization of esters (Scheme 1, path b).[2,3] We recently developed an intramolecular free radical conjugate addition method to synthesize nitrogen heterocycles.[4] The cyclization strategy is now extended to the construction of spiro quaternary carbon–carbon bond (Scheme 2) of spirolactone, spirolactam, and related compounds (Scheme 3).[5] This paper describes the scope and limitation of free radical spirocyclization reactions.



Scheme 1. Synthesis of spirolactone.



Scheme 2. Free radical spirocyclization.

2. Results and discussion

2.1. Synthesis of spirobenzolactones and spirobenzolactams

The synthesis of spirobenzolactones **2** proceeded through a straightforward two-step reaction sequence (Scheme 4).[5c] At the first step, 2-bromobenzoic acids were reacted with cyclic 1,3-diones using the Mukaiyama coupling agent (*N*-methyl-2-chloropridinum iodide).[6] The enol esters **1** are well-known intermediates in the preparation of the triketone inhibitor of 4-hydroxyphenylpyruvate dioxygenase (HPPD) which have important pharmaceutical[7] and agricultural[8] utilities. In this work, the enol esters were used as aryl radical precursors for spirocyclizations.[9] Tris(trimethylsilyl)silane (1.5 equiv.) and catalytic amount of 2,2′-azobis(2-methylpropisonitrile) (AIBN) in refluxing benzene promoted the radical spirocyclization of **1**. The initial radical **3** equilibrated between the *cis* and *trans* conformations by rotation of the C–O bond. The *trans*-**3** conformer underwent cyclization to afford product **2** via α-acyl stabilized radical **4** (Scheme 4). The α,β-unsaturated ketone served as a conjugate radical acceptor to facilitate the cyclization and control the regioselective 5-*exo* cyclization.[10]

A series of spirobenzolactones were prepared from readily available 1,3-cyclic diones (Table 1). Cyclizations of 5-phenyl substituted 1,3-cyclohexanediones could generate two diastereomers. Under a general reaction condition,

Keywords: free radical; spirolactone; 2-bromobenzoic acid; Michael addition; tris(trimethylsilyl)silane.

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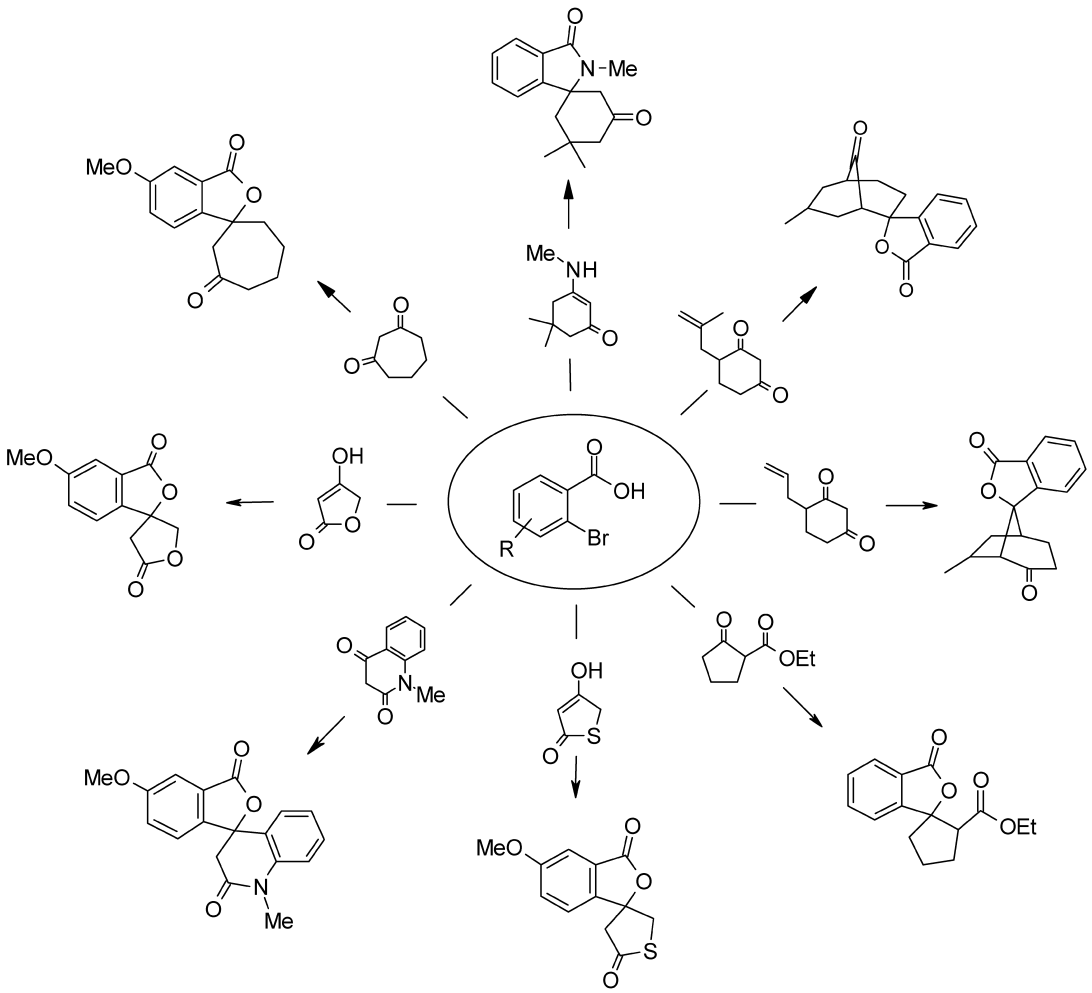
doi:10.1016/S0040-4020(03)00655-0



Scheme 3. 2-Bromobenzoic acid-based free radical reactions for spiro compounds.

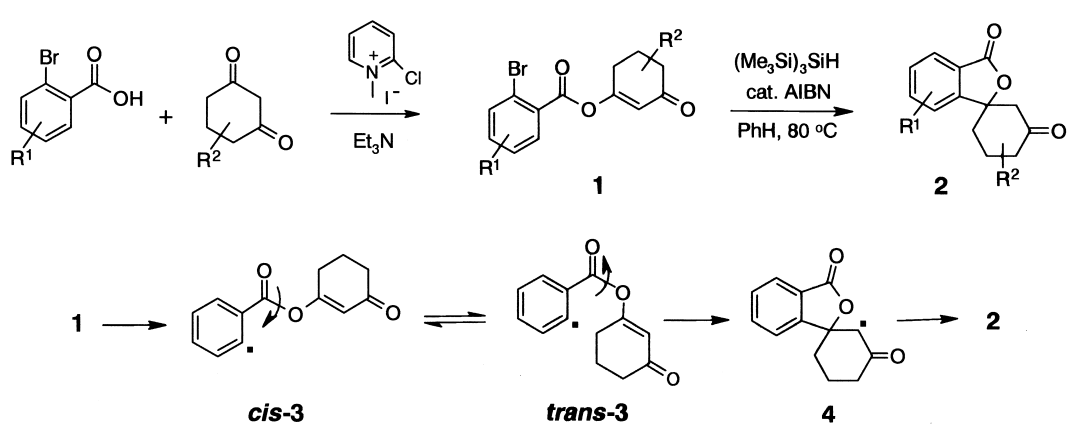
products **18** and **20** were produced as diastereomeric mixtures, while **10**, **12**, **14**, and **16** were generated in higher diaostereoselectivity. Stereostructures of **10** and **16** were determined by X-ray analyses (Fig. 1).

Scheme 5 shows the synthesis of a spirolactone ester by coupling of 2-bromobenzoic acid with a β-keto ester **23** followed by the radical cyclization of **24**. The reduction of cyclized radical **25** gave product **26** as a mixture of two diastereomers.

Spirocyclization reactions were also used to prepare spirobenzolactams **29** by coupling amines **27** with 2-bromobenzoyl chlorides followed by free radical cyclizations of **28** (Scheme 6). Details for this kind of reactions have been disclosed in a recent paper from our group.[4]

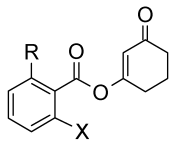
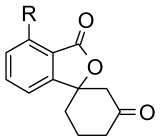
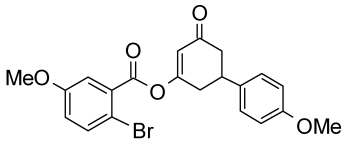
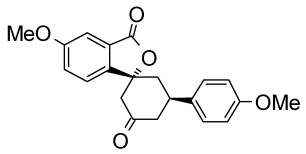
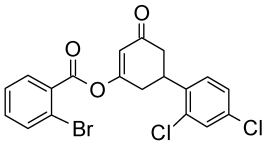
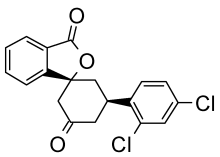
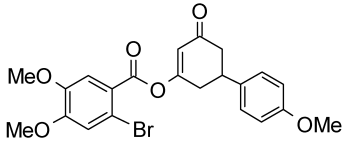
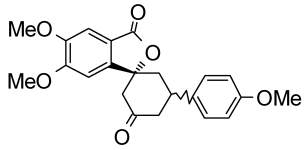
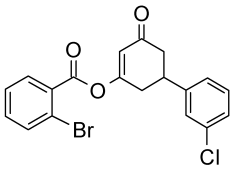
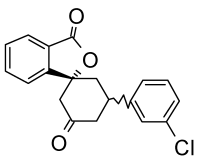
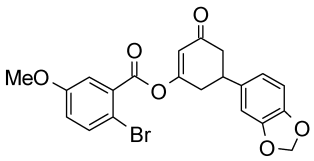
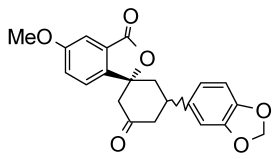
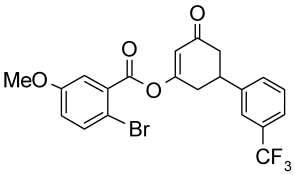
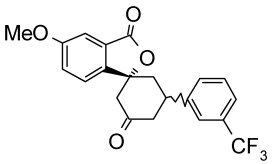
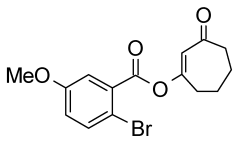
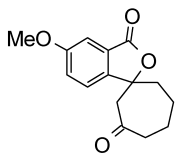
2.2. Synthesis of spirodilactones

Scheme 7 outlines the synthesis of spirodilactones by cyclization of tetronic acid derivatives.[5b] The intermediate



Scheme 4. Intramolecular aryl radical cyclizations for spirobenzolactones.

Table 1. Preparation of spirobenzolactones

Entry	Enol ester[a]	Product[b]	Entry	Enol ester	Product
1	 R=H, X=Br, **5,** 99% R=F, X=I, **7,** 89%	 R=H, **6**, 83% R=F, **8,** 68%	5	 **15,** 51%	 **16,** 42%
2	 **9,** 70%	 **10,** 68%	6	 **17,** 84%	 **18** (1:1)[c], 70%
3	 **11,** 88%	 **12** (1:5), 76%	7	 **19,** 100%	 **20** (1:2), 83%
4	 **13,** 68%	 **14** (1:6), 64%	8	 **21,** 83%	 **22,** 76%

[a]1.0 equiv. of bromobenzoic acid, 1.1 equiv. of 1,3-diketone, 1.2 equiv. of 2-chloro-1-methylpyridinium iodide, 2.7 equiv. of Et_3N, THF, rt, [b]1.5 equiv. of $(Me_3Si)_3SiH$, cat. AIBN, benzene, 80°C, [c]The diastereomer ratio was determined by H NMR.

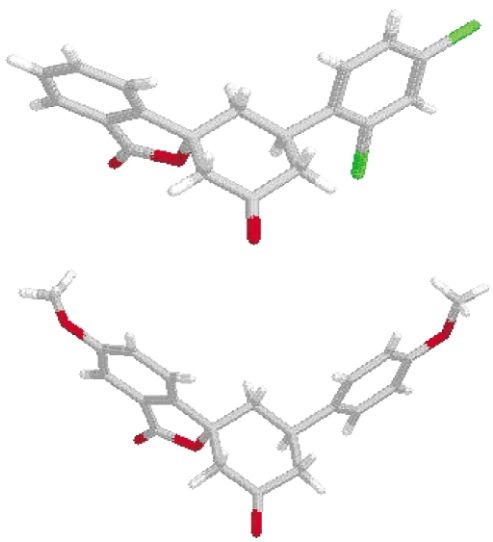
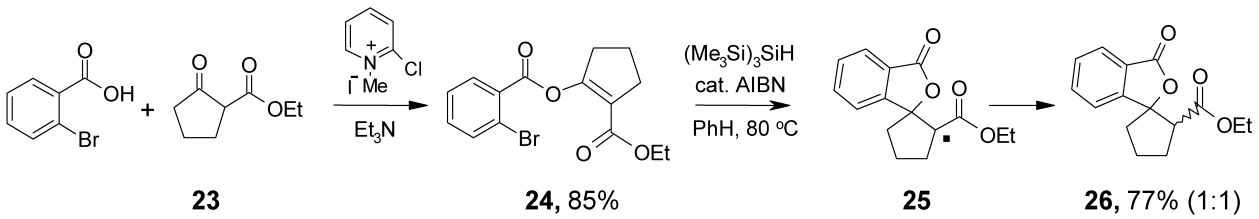


Figure 1. X-Ray structures of compounds **10** (top) and **16** (bottom).

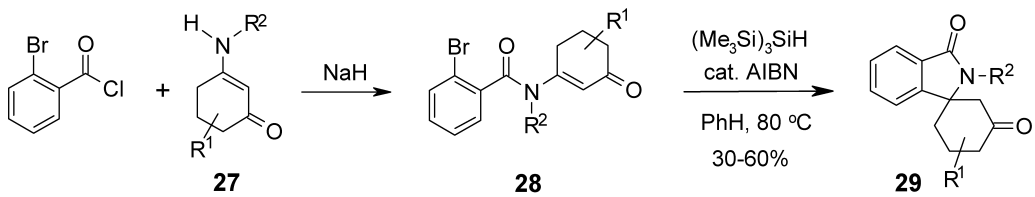
enol esters **30** were reported having antifungal activity.[11] Cyclized spirodilactones **31** possess a unique heterocyclic system that was also found in natural product altenuic acid II.[12] There are more examples of natural products containing spirotetronic acid units.[13] To the best of our knowledge, no synthetic method for spirodilactones such as **31** has been reported.[14]

The scope of spirodilactone synthesis is demonstrated by the examples listed in Table 2. Entry 1 demonstrated the preparation of spirodilactones having substituents on the benzene ring. Purifications of enol ester intermediates **32**, **34**, and **36** and corresponding cyclization products **33**, **35** and **37** were straightforward; all these compounds were simply precipitated out from the concentrated reaction mixture at room temperature. Successful extension of this method to a reaction of 1-bromo-2-naphthoic acid derivative **38** resulted tetracyclic spirodi-γ-lactone **39**. The use of 5,6-dihydro-4-hydroxy-6-methyl-2*H*-pyran-2-one instead of tetronic acid as a starting material led to formation of spiro-γ/δ-dilactone **41** as a mixture of diastereomers (entry 3). Entry 4 provides another example for the synthesis of tetracyclic spiro-γ/δ-dilactone **43**. The synthesis of dispiro-γ/δ-dilactone **45** using readily available spirodihydropyranon[15] as a starting material is shown in Scheme 8.

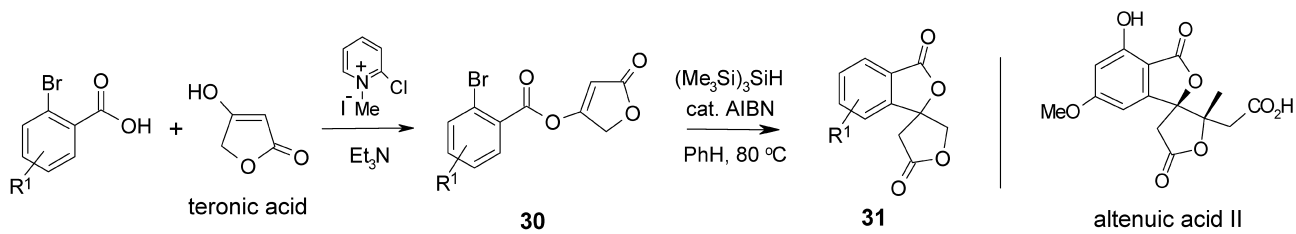
To further investigate the reaction scope, cyclization of enol ester **46** containing a phenyl group at 3-position of tetronic acid was carried out (Scheme 9). No cyclization product **49** was observed. Surprisingly, three intermolecular coupling products **50a–50c** were isolated from a complex reaction mixture. It is believed that the initial radical **47** was involved in a reversible 5-*exo* cyclization to form a highly unreactive and persistent tertiary benzylic radical **48**. This could provide a safe 'sink' for transient radical **47** to allow it to be continually re-generated in low but stable concentration so that it eventually coupled with solvent benzene, transient isopropionnitrile radical, or tris(trimethylsilyl)silyl radical to generate **50a–50c**, respectively.[16] The structure of **50a** was confirmed by X-ray analysis (Fig. 2).



Scheme 5.

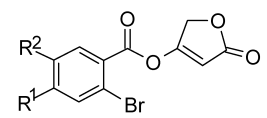
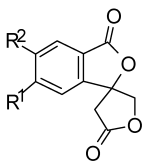
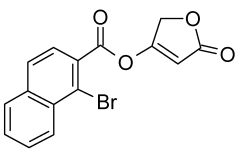
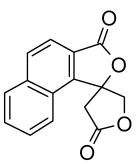
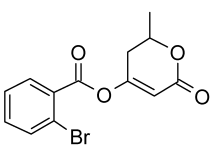
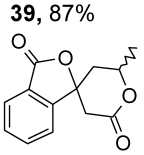
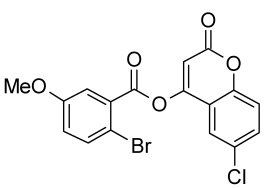
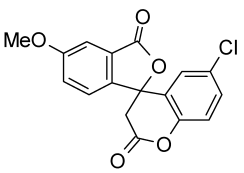


Scheme 6. Synthesis of spirolactams.



Scheme 7. Synthesis of spirodilactones.

Table 2. Preparation of spirodilactones

Entry	Enol ester[a]	Product[b]
1		
	R_1, R_2=H, **32,** 83% R_1=H, R_2=OMe, **34,** 83% R_1, R_2=OMe, **36,** 47%	R_1, R_2=H, **33,** 75% R_1=H, R_2=OMe, **35,** 50% R_1, R_2=OMe, **37**, 76%
2		
	38, 100%	**39,** 87%
3		
	40, 90%	**41** (1:1.2), 70%
4		
	42, 94%	**43**, 74%

[a] 1.0 equiv. of carboxylic acid, 1.1 equiv. of keto lactone, 1.2 equiv. of 2-chloro-1-methylpyridinium iodide, 2.7 equiv. of Et_3N, THF, rt.
[b] 1.5 equiv. of $(Me_3Si)_3SiH$, cat. of AIBN, benzene, 80°C.

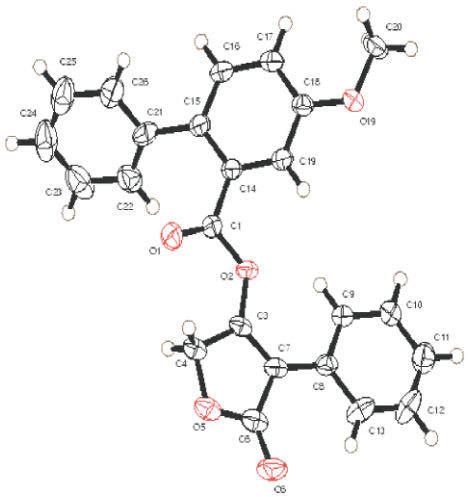
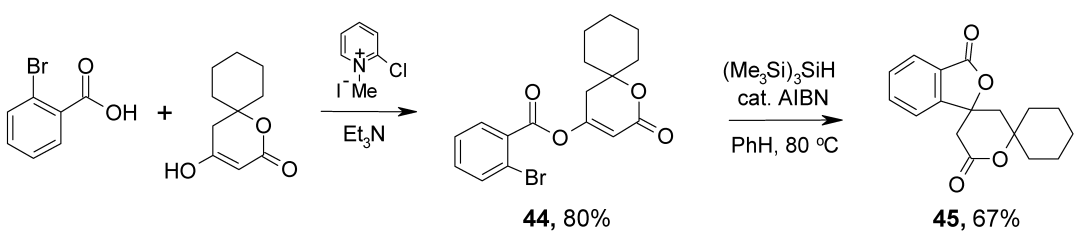


Figure 2. X-Ray structure of compound **50a**.

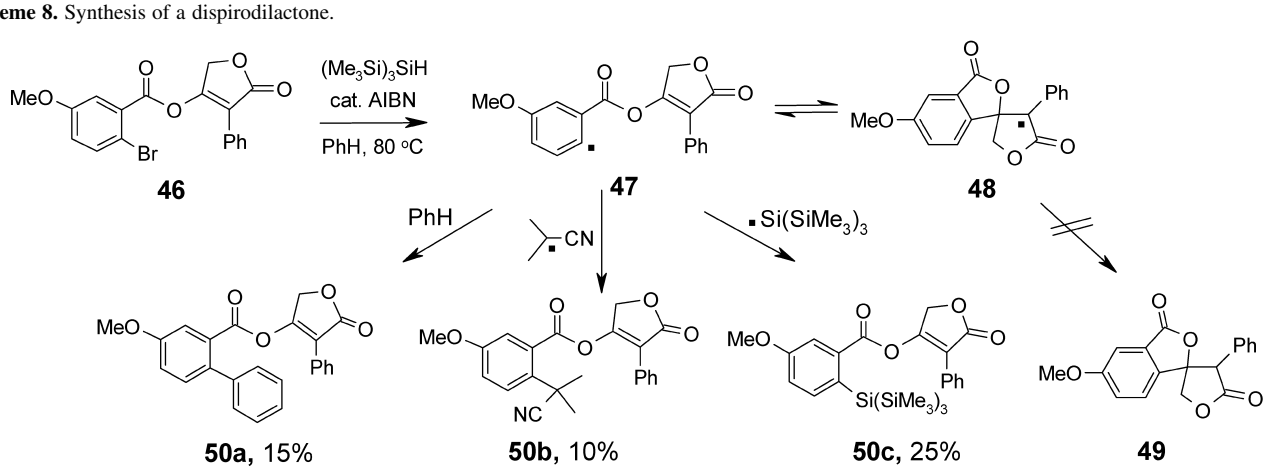
2.3. Synthesis of spirolactone-lactams and spirolactone-thiolactones

Free radical spirocyclizations have been applied in the synthesis of spirolactone-lactams using readily available lactams **51** and **54**[17] as starting materials (Scheme 10). Both products **53** and **56** contain attractive functionalized polycyclic systems. The structure of product **53** was confirmed by X-ray crystal analysis (Fig. 3).

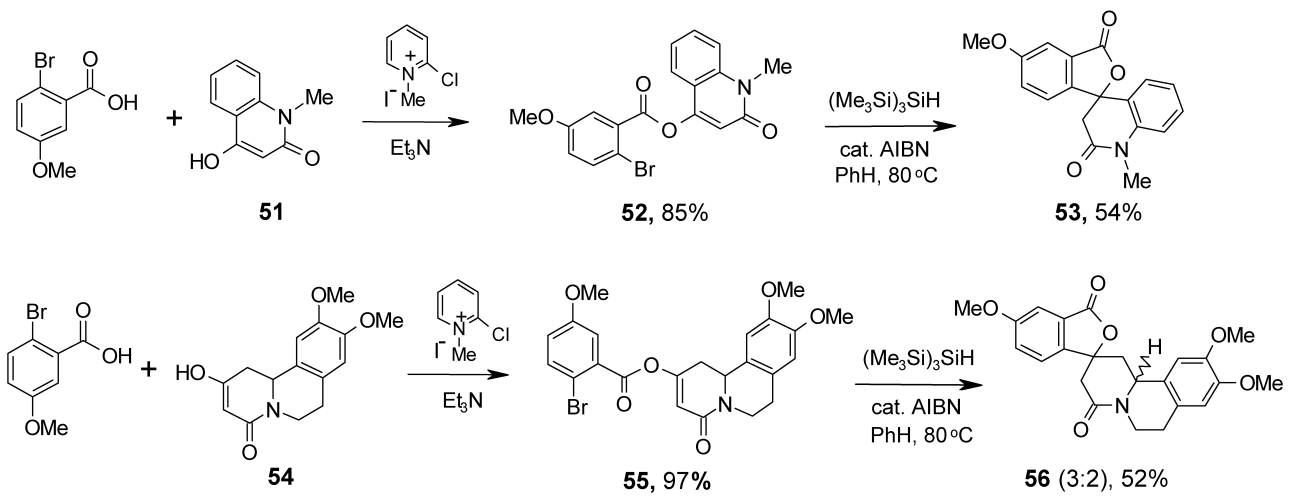
The radical spirocyclization has been further employed in the synthesis of spirolactone-thiolactone **59** using commercially available thiotetronic acid **57** as the starting material (Scheme 11).



Scheme 8. Synthesis of a dispirodilactone.



Scheme 9. Radical reaction of **46**.



Scheme 10. Synthesis of spirolactone-lactams **53** and **56**.

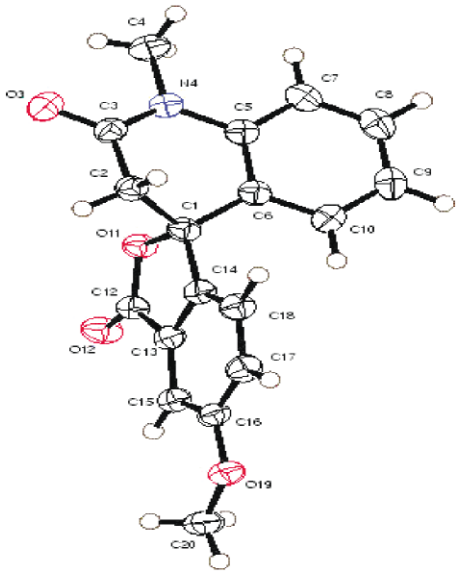


Figure 3. X-Ray structure of compound **53**.

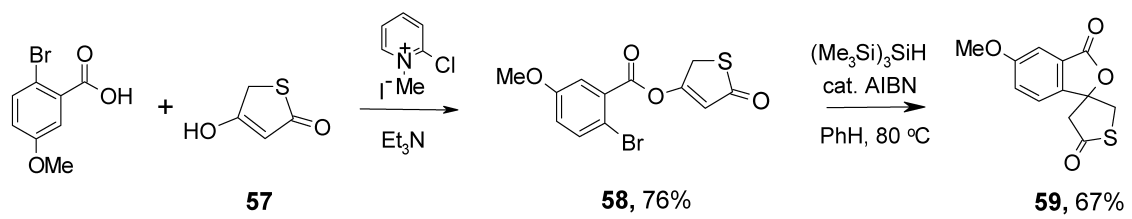
2.4. Synthesis of bridged-lactones by tandem cyclizations

Tandem, or cascade, cyclizations have a high synthetic efficiency, and are widely used in the construction of fused polycyclic compounds.[18] We designed a double cyclization sequence in the preparation of complex heterocyclic systems containing spiro and bridged rings.[5a]

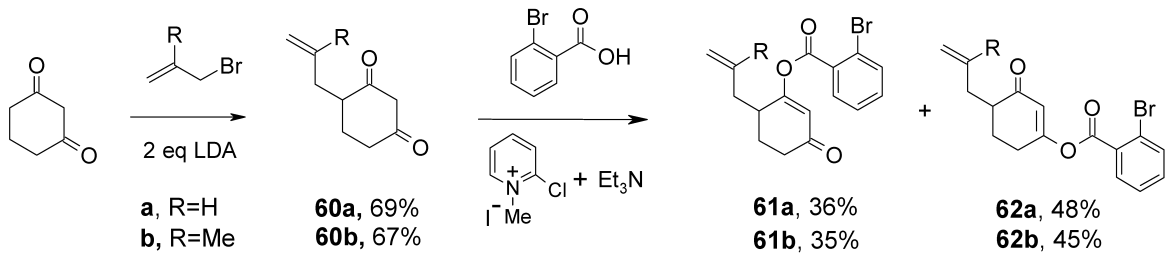
Aryl bromides with allyl groups at different positions of keto enol esters were prepared (Scheme 12). The regio-isomers of **61** and **62** were separated by flash column chromatography. When **61a** was treated with tris(timethylsilyl)silane, the initial radical underwent double cyclizations (Scheme 13): an intramolecular conjugate addition was followed by a 5-*exo* cyclization to give bridged spirolactones **64** as a mixture of two diastereomers. A small amount of monocyclization product **65** was also observed. The formation of **64** suggested that the spirocyclization (**66** to **67**) was processed through an equatorial attack of **66** to form a carbon–carbon bond *trans* to the vinyl group. The sequential 5-*exo* cyclization (**67** to **68**) gave a mixture of diastereomers **64** due to the free rotation of allylic carbon–carbon single bond.

Reactions using substrates **61b** containing a 2-methylallyl side chain afforded a dicyclization product **69**. In this case, the spirocyclization was followed by a cyclization of 6-*endo* instead of 5-*exo*. The bridged spirolactones **69** was generated as a single diastereomer (Scheme 14). The reaction of enol ester **62a** produced only a 5-*exo* monocyclization product. No dicyclization product was observed. Similar results were observed by Simpkins and co-workers in the synthesis of spiroethers.[19] Radical precursor **62b** which has a methyl group on the allyl side chain induced the second 6-*endo* cyclization (Scheme 15). In this case, adequate amount of dicyclization product **72** was generated as a single diastereomer together with the monocyclization product **73**. The structure of **72** was confirmed by X-ray structure analysis (Fig. 4).

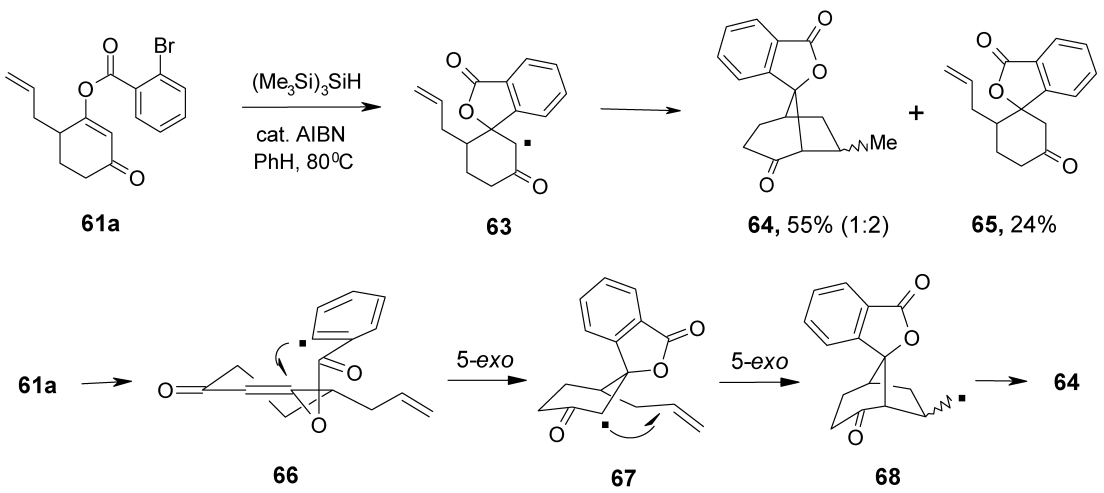
In summary, a general synthetic method to construct a variety of spiro compounds has been developed. The formation of spiro-quaternary carbon–carbon bonds by intramolecular free radical conjugate addition of



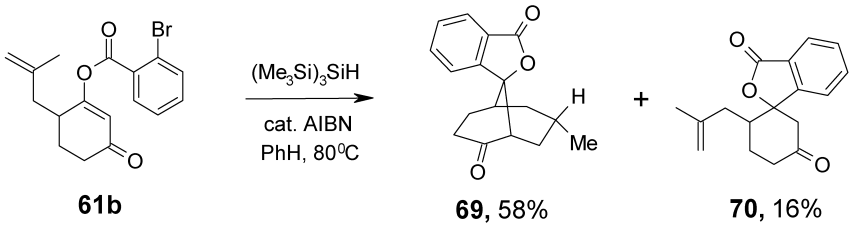
Scheme 11. Synthesis of spirolactone-thiolactone **59**.



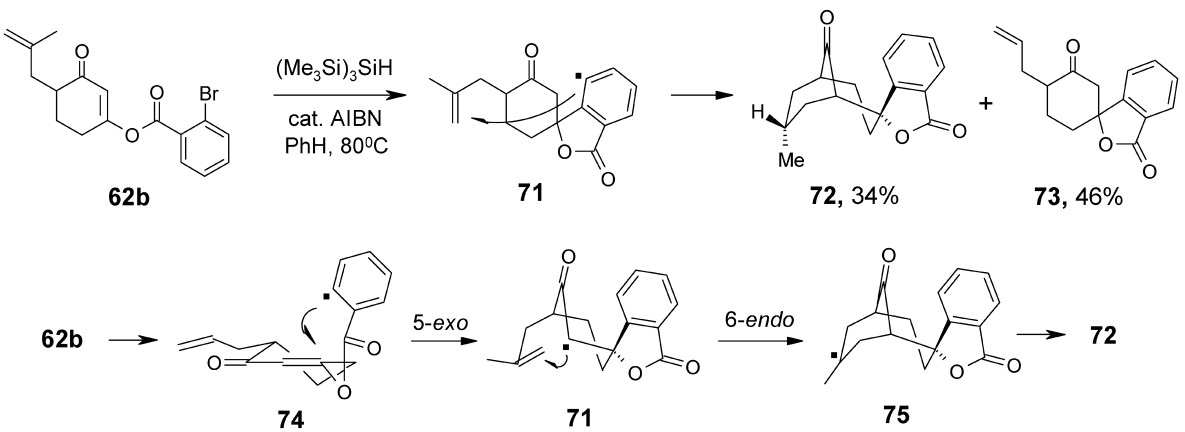
Scheme 12. Synthesis of radical precursors **61** and **62**.



Scheme 13. Synthesis of bridged-spirolactone **64**.



Scheme 14. Synthesis of bridged-spirolactone **69**.



Scheme 15. Synthesis of bridged-spirolactone **72**.

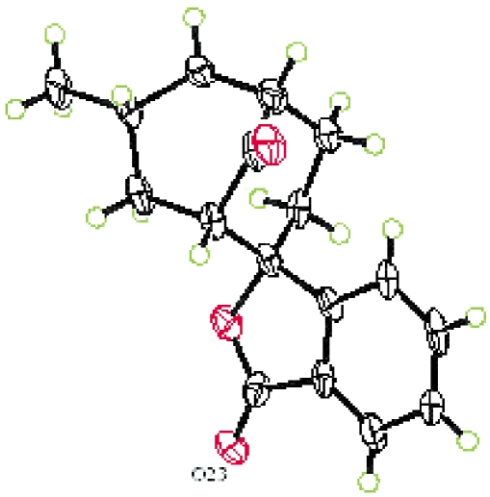


Figure 4. X-Ray structure of compound **72**.

2-bromobenzoic acid derivatives provided an easy access to some novel benzolactone and benzolactam systems.

3. Experimental

3.1. General

Bromobenzoic acids and cyclic 1,3-diketone compounds were obtained from commercial sources unless otherwise indicated. The coupling reagent *N*-methyl-2-chloropridinium iodide and radical initiator 2,2′-azobis(2-methylpropisonitrile) (AIBN) were purchased from Aldrich. Tris(trimethylsilyl)silane for radical reactions was purchased from Fluka. Anhydrous benzene obtained from Fluka was used without further purification.

3.2. General procedure for allylation of 1,3-cyclohexanedione

To a solution of 1,3-cyclohexanedione (89.3 mmol) in 200 mL of anhydrous THF and 50 mL of HMPA was added 2 M of lithium diisopropylamine (in hexane, 98.2 mL, 196.4 mmol) at −78°C. After 1 h, the reaction temperature was raised to −40°C and 2-methylallyl bromide (98.2 mmol) was added quickly. The mixture was slowly warmed up to room temperature and stirred for an additional 10 h. The concentrated reaction mixture was diluted with 5% HCl, extracted with diethyl ether. The organic layer was washed with 3% aqueous HCl and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by flash column chromatography with hex/EtOAc (50:50) to afford allylation product **60**.

3.3. General procedure for preparation of radical precursors, enol esters

A mixture of 2-bromobenzoic acid (5.0 mmol), 1,3-cyclohexanedione (5.5 mmol), 2-chloro-1-methylpyridinium iodide (5.8 mmol), and triethylamine (13.5 mmol) in 100 mL of anhydrous THF was stirred at room for 10 h. After ethyl acetate workup, the organic layer was washed with aqueous NH_4Cl and brine, dried over $MgSO_4$, and concentrated in vacuo to afford the enol ester.

3.4. General procedure for radical spirocyclization

To a refluxing solution of radical precursor (1.0 equiv.) in dry benzene (20 mL per mmol of radical precursor) was added $(CH_3Si)_3SiH$ (1.5 equiv.) and AIBN (0.05–0.1 equiv.). After 2 h, a second portion of AIBN (0.05 equiv.) was added and the reaction mixture was refluxed for an additional 5–25 h. The concentrated reaction mixture was triturated with BuCl or further purified by flash chromatography to give a cyclization product.

3.4.1. Compound 6. 0.27 g, 83% yield after chromatography as a clear oil; IR ν_{max} (neat) 2954, 1765, 1721, 1467, 1362, 1289, 1253, 1200, 1120, 1072, 931, 764, 694, 628, 600, 554 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.00–2.70 (6H), 2.84 (d, J=15.2 Hz, 1H), 7.43 (d, J=7.7 Hz, 1H), 7.57 (t, J=7.7 Hz, 1H), 7.72 (t, J=7.5 Hz, 1H), 7.92 (d, J=7.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.0, 33.8, 38.4, 49.2, 87.0, 119.8, 123.7, 124.3, 128.1, 133.3, 150.1, 167.2, 204.3; LRMS (AP+) *m/z* (rel. intensity) 217 (M^++H, 100), 176 (10), 150 (12); HRMS calcd for $C_{13}H_{12}O_3$ 216.0786, found 216.0797.

3.4.2. Compound 8. 0.27 g, 68% yield after chromatography as a white solid. Mp 133–135°C; IR ν_{max} (neat) 2954, 1769, 1723, 1626, 1483, 1362, 1249, 1122, 1023, 945, 814, 686 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.18–2.62 (m, 7H), 2.82 (d, J=15.2 Hz, 1H), 7.21 (m, 2H), 7.74 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.8, 33.6, 38.5, 49.0, 84.9, 86.6, 115.2, 115.5, 135.7, 152.8, 156.4, 159.9, 203.9; LRMS (AP+) *m/z* (rel. intensity) 235 (M^++H, 100), 217 (47), 191 (23); HRMS calcd for $C_{13}H_{11}FO_3$ 234.0692, found 234.0692.

3.4.3. Compound 10. 0.56 g, 68% yield after chromatography as white solid. Mp 177–178°C; IR ν_{max} (neat) 1760, 1724, 1475, 1286, 1262, 1066, 1047, 960, 897, 818, 764, 737, 694 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.15 (m, 1H), 2.45 (t, J=13.5 Hz, 1H), 2.65 (t, J=13.7 Hz, 2H), 2.84 (m, 1H), 2.95 (d, J=15.5 Hz, 1H), 4.15 (m, 1H), 7.24 (m, 2H), 7.41 (s, 1H), 7.51 (d, J=7.7 Hz, 1H), 7.60 (t, J=7.7 Hz, 1H), 7.78 (t, J=7.7 Hz, 1H), 7.91 (d, J=7.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.1, 39.4, 44.2, 48.6, 85.9, 119.5, 123.6, 124.7, 126.1, 126.4, 128.1, 128.5, 131.9, 132.8, 133.3, 136.6, 146.9, 167.1, 202.7; LRMS (AP+) *m/z* (rel. intensity) 361 (M^++H, 100); HRMS calcd for $C_{19}H_{14}Cl_2O_3$ 360.0320, found 360.0323.

3.4.4. Compound 12. 0.62 g, 76% yield after chromatography (two diastereomers in a ratio of 1:5). The major isomer as a white solid. Mp 206–208°C; IR ν_{max} (neat) 1754, 1723, 1466, 1260, 1062, 961, 918, 764, 692 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.12 (m, 1H), 2.42–2.75 (m, 3H), 2.85 (m, 1H), 3.00 (d, J=15.3 Hz, 1H), 3.68 (m, 1H), 7.15 (m, 1H), 7.24 (m, 3H), 7.27 (d, J=7.7 Hz, 1H), 7.61 (t, J=7.7 Hz, 1H), 7.74 (t, J=7.5 Hz, 1H), 7.95 (d, J=7.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 37.6, 41.1, 45.7, 48.5, 85.8, 119.3, 123.6 (2C), 124.8, 125.1, 125.9, 128.4, 128.7, 133.2 (2C), 142.9, 149.8, 167.0, 202.7; LRMS (AP+) *m/z* (rel. intensity) 327 (M^++H, 92), 264 (39), 223 (51), 181

(100); LRMS (AP+) *m/z* (rel. intensity) 327 (M^++H, 100), 309 (7), 278 (9); HRMS calcd for $C_{19}H_{15}ClO_3$ 362.0710, found 362.0713.

3.4.5. Compound 14. 0.80 g, 64% yield after chromatography (two diastereomers in a ratio of 1:6). The major isomer; IR ν_{max} (neat) 1763, 1722, 1498, 1330, 1288, 1164, 1122, 1076, 1027, 961, 924, 803, 749, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.13 (m, 1H), 2.40–2.72 (m, 3H), 2.84 (m, 1H), 2.98 (d, J=15.4 Hz, 1H), 3.75 (m, 1H), 3.88 (s, 3H), 7.26–7.50 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 37.9, 41.1, 45.7, 48.7, 54.3, 85.9, 106.6, 120.4, 121.6, 121.9, 122.6, 124.3, 125.0, 128.0, 128.9, 129.7, 142.0, 142.4, 159.7, 167.1, 203.1; LRMS (AP+) *m/z* (rel. intensity) 391 (M^++H, 100), 313 (19), 300 (8); HRMS calcd for $C_{21}H_{17}F_3O_4$ 390.1079, found 390.1099.

3.4.6. Compound 16. 0.28 g, 42% yield after chromatography as white solid. Mp 75–76°C; IR ν_{max} (neat) 2959, 1765, 1722, 1612, 1514, 1498, 1466, 1336, 1289, 1254, 1181, 1068, 1026, 959, 834 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.06 (m, 1H), 2.38–2.70 (m, 3H), 2.80 (m, 1H), 2.94 (d, J=15.3 Hz, 1H), 3.61 (m, 1H), 3.79 (s, 3H), 3.88 (s, 3H), 6.87 (d, J=8.7 Hz, 2H), 7.19 (d, J=8.7 Hz, 2H), 7.27 (m, 1H), 7.34 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 37.2, 41.8, 46.3, 48.8, 53.8, 45.4, 86.1, 106.5, 112.7 (2C), 120.3, 121.9, 125.1, 126.1 (2C), 133.2, 142.7, 157.1, 159.6, 167.2, 203.8; LRMS (AP+) *m/z* (rel. intensity) 353 (M^++H, 95), 309 (16), 263 (10), 234 (17), 222 (100), 208 (57), 171 (14); HRMS calcd for $C_{21}H_{20}F_3O_5$ 352.1311, found 352.1317.

3.4.7. Compound 18. 0.54 g, 70% yield after chromatography as a mixture of two diastereomers (1:1); IR ν_{max} (neat) 1744, 1718, 1604, 1514, 1300, 1251, 1222, 1099, 1012, 934, 840 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.00–2.80 (m), 2.93 (d, J=15.0 Hz), 3.10 (d, J=14.5 Hz), 3.32 (m, $1H_a$), 3.63 (m, 1H), 3.79 (s, 3H), 3.94 (s, 3H), 3.98 (s, 3H), 4.01 (s, 3H), 6.73 (s), 6.87 (m), 7.18 (t, J=6.2 Hz), 7.28 (m), 7.36 (s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 35.5, 37.1, 41.7, 45.9, 46.2, 48.7, 53.8, 54.8, 55.0, 83.9, 85.3, 100.6, 101.7, 104.9, 105.1, 112.7, 112.8, 115.6, 115.8, 126.0, 126.1, 126.8, 132.5, 133.2, 144.7, 144.8, 149.4, 153.3, 153.6, 157.1, 157.2, 167.3, 203.6, 204.9; LRMS (AP+) *m/z* (rel. intensity) 383 (M^++H, 100); HRMS calcd for $C_{22}H_{22}O_6$ 382.1416, found 382.1410.

3.4.8. Compounds 20a and 20b. Diastereomers **20a** and **20b** were separated by chromatography. Diastereomer **20a**, 0.15 g, 26% yield as a yellow semisolid; IR ν_{max} (neat) 1765, 1722, 1492, 1442, 1285, 1037, 934, 742 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.21 (m, 1H), 2.58–2.77 (m, 4H), 3.15 (d, J=13.9 Hz, 1H), 3.25 (m, 1H), 3.87 (s, 3H), 5.94 (s, 2H), 6.73 (m, 3H), 7.25 (m, 2H), 7.38 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 35.9, 41.8, 46.1, 49.0, 54.3, 48.3, 99.7, 105.4, 106.9, 107.0, 118.2, 121.1, 121.2, 125.5, 134.4, 142.6, 145.2, 146.6, 159.6, 167.0, 204.3; LRMS (AP+) *m/z* (rel. intensity) 367 (M^++H, 100), 346 (13), 273 (18), 208 (17). Diastereomer **20b**, 0.30 g, 51% yield as an reddish oil; IR ν_{max} (neat) 1764, 1722, 1492, 1442, 1336, 1287, 1037, 930, 748 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.06 (m, 1H), 2.35–2.62 (m, 3H), 2.79 (m, 1H), 2.99 (d, J=15.2 Hz, 1H), 3.53 (m, 1H), 3.88 (s, 3H), 5.93 (s, 2H), 6.72 (m, 3H), 7.32 (m, 2H), 7.39 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 37.7, 41.8, 46.4, 48.7, 55.3, 85.9, 99.6, 105.4, 106.5, 107.0, 118.2, 120.2, 121.9, 125.1, 135.0, 142.6, 145.1, 146.5, 159.6, 167.1, 203.4; LRMS (AP+) *m/z* (rel. intensity) 367 (M^++H, 100); HRMS calcd for $C_{21}H_{18}O_6$ 366.1103, found 366.1133.

3.4.9. Compound 22. 0.75 g, 76% yield after chromatography as a white solid. Mp 126–127°C; IR ν_{max} (neat) 2937, 1767, 1702, 1624, 1497, 1435, 1334, 1291, 1263, 1179, 1112, 1076, 1029, 1015, 990, 953, 928, 885, 840, 786, 750, 574 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.79 (m, 1H), 1.90–2.20 (m, 5H), 2.60–2.96 (m, 3H), 3.18 (d, J=15.4 Hz, 1H), 3.87 (s, 3H), 7.20–7.38 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.9, 23.7, 39.5, 42.5, 51.4, 54.3, 83.4, 106.3, 120.0, 121.7, 123.9, 145.8, 159.2, 167.7, 206.8; LRMS (AP+) *m/z* (rel. intensity) 261 (M^++H, 100); 243 (62); HRMS calcd for $C_{15}H_{16}O_4$ 260.1049, found 260.1049.

3.4.10. Compound 26. 0.20 g, 77% yield after chromatography as a mixture of two diastereomers **26a** and **26b** (1:1); IR ν_{max} (neat) 2979, 1769, 1733, 1466, 1372, 1348, 1286, 1197, 1063, 957, 758, 693 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.84 (t, J=7.2 Hz, 3H), 2.10 (m, 2H), 2.27 (m, 4H), 3.32 (m, 1H), 3.80 (m, 2H), 7.39 (d, J=7.6 Hz, 1H), 7.52 (t, J=7.6 Hz, 1H), 7.62 (t, J=7.5 Hz, 1H), 7.86 (d, J=7.5 Hz, 1H); LRMS (AP−) *m/z* (rel. intensity) 259 (M^+−H, 100), 197 (47), 180 (63); HRMS calcd for $C_{15}H_{16}O_4$ 260.1049, found 260.1077.

3.4.11. Compound 33. 0.76 g, 75% yield after BuCl trituration as a yellow solid. Mp 207–208°C; IR ν_{max} (neat) 1771, 1230, 1024, 762 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.06 (d, J=18.2 Hz, 1H), 3.14 (d, J=18.2 Hz, 1H), 4.60 (s, 2H), 7.57 (d, J=7.7 Hz, 1H), 7.67 (t, J=7.7 Hz, 1H), 7.81 (t, J=7.5 Hz, 1H), 7.93 (d, J=7.5 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 38.6, 74.5, 82.8, 119.7, 124.9, 127.5, 129.0, 129.3, 133.7, 142.2, 165.3; LRMS (AP+) *m/z* (rel. intensity) 205 (M^++H, 100), 195 (70), 157 (27), 150 (33); HRMS calcd for $C_{11}H_8O_4$ 204.0423, found 204.0453.

3.4.12. Compound 35. 0.63 g, 50% yield after BuCl trituration as a white solid. Mp 170–171°C; IR ν_{max} (neat) 1774, 1020, 749 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.01 (d, J=18.2 Hz, 1H), 3.08 (d, J=18.2 Hz, 1H), 3.90 (s, 3H), 4.56 (s, 2H), 7.30–7.46 (3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 38.9, 54.6, 74.1, 86.9, 106.3, 121.7, 122.6, 126.0, 136.2, 160.0, 166.1, 172.6; LRMS (AP+) *m/z* (rel. intensity) 235 (M^++H, 100), 211 (27), 191 (7); HRMS calcd for $C_{12}H_{10}O_5$ 234.0528, found 234.0528.

3.4.13. Compound 37. 0.76 g, 76% yield after BuCl trituration as a white solid. Mp 72–74°C; IR ν_{max} (neat) 1789, 1764, 1604, 1502, 1474, 1377, 1331, 1281, 1228, 1154, 1100, 1025, 913, 743 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.03 (d, J=18.2 Hz, 1H), 3.12 (d, J=18.2 Hz, 1H), 3.97 (s, 3H), 4.02 (s, 3H), 4.58 (s, 2H), 6.92 (s, 1H), 7.30 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 38.9, 54.7, 54.8, 74.2, 86.1, 103.6, 104.5, 116.0, 138.7, 149.6, 153.5, 166.4, 172.7; LRMS (AP+) *m/z* (rel. intensity) 265 (M^++H, 100), 247 (11), 205 (6); HRMS calcd for $C_{13}H_{12}O_6$ 264.0634, found 264.0644.

3.4.14. Compound 39. 0.31 g, 87% yield after BuCl

trituration as white solid. Mp 220°C (decomposed); IR ν_{max} (neat) 1767, 913, 744 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.19 (d, J=18.8 Hz, 1H), 3.53 (d, J=18.8 Hz, 1H), 4.73 (d, 1H), 5.00 (d, J=10.8 Hz, 1H), 7.77–7.90 (3H), 7.90 (d, J=8.4 Hz, 1H), 8.10 (d, J=8.4 Hz, 1H), 8.13 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 38.9, 73.4, 87.6, 118.5, 123.1, 123.3, 124.5, 127.2, 127.9, 128.3, 130.7, 134.7, 141.9, 166.5, 172.4; LRMS (AP+) m/z (rel. intensity) 255 (M^++H, 100), 237 (26), 195 (26), 155 (19); HRMS calcd for $C_{15}H_{10}O_4$ 254.0579, found 254.0577.

3.4.15. Compound 41. 0.67 g, 70% yield after BuCl trituration as a mixture of two diastereomers (a/b=1:1.2). Mp 172–173°C; IR ν_{max} (neat) 1769, 1467, 1387, 1288, 1256, 1083, 962, 913, 725, 964 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.49 (d, J=6.4 Hz, $3H_a$), 1.55 (d, J=6.4 Hz, $3H_b$), 2.00–2.20 (m, 1H), 2.33 (m, 1H), 2.96 (m, 2H), 4.70 (m, $1H_b$), 5.00 (m, 1Ha), 7.42 (m, 1H), 7.62 (t, J=7.5 Hz, 1H), 7.75 (m, 1H), 7.93 (d, J=7.5 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 18.9, 19.8, 38.7, 38.9 (2C), 70.9, 72.4, 82.2, 82.8, 120.7, 120.8, 123.1, 123.3, 123.7, 123.8, 128.5, 128.6, 133.6, 133.7, 149.5, 150.3, 166.7 (2C), 167.8; LRMS (AP+) m/z (rel. intensity) 233 (M^++H, 100), 215 (33), 189 (42), 171 (13), 145 (38); HRMS calcd for $C_{13}H_{12}O_4$ 232.0736, found 232.0776.

3.4.16. Compound 43. 0.58 g, 74% yield after BuCl trituration as a yellow solid. Mp 250–252°C; IR ν_{max} (neat) 1776, 1480, 1335, 1286, 1200, 1091, 913, 743 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.26 (s, 2H), 3.93 (s, 3H), 6.83 (s, 1H), 7.18 (d, J=8.7 Hz, 1H), 7.28–7.53 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 39.3, 54.5, 80.2, 106.9, 117.7, 121.9, 122.5, 124.1, 125.8, 128.9, 130.2, 138.5, 148.6, 160.4, 161.8, 166.1; LRMS (AP+) m/z (rel. intensity) 331 (M^++H, 100), 297 (9); HRMS calcd for $C_{17}H_{11}ClO_5$ 330.0295, found 330.0311.

3.4.17. Compound 45. 0.58 g, 67% yield after BuCl trituration as yellow solid. Mp 154–157°C; IR ν_{max} (neat) 2938, 1766, 1727, 1374, 1286, 913, 742, 695 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.20–2.40 (12H), 2.90 (d, J=18.0 Hz, 1H), 3.03 (d, J=18.0 Hz, 1H), 7.44 (d, J=7.7 Hz, 1H), 7.63 (t, J=7.7 Hz, 1H), 7.76 (t, J=7.5 Hz, 1H), 7.93 (d, J=7.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.1, 20.2, 23.3, 35.7, 38.4, 38.5, 41.7, 81.4, 81.9, 119.6, 123.6, 124.6, 128.6, 133.5, 149.9, 165.8, 166.8; LRMS (AP+) m/z (rel. intensity) 287 (M^++H, 87), 269 (100), 251 (66), 223 (13), 198 (7), 147 (22); HRMS calcd for $C_{17}H_{18}O_4$ 274.1205, found 286.1209.

3.4.18. Compound 50a. 0.12 g, 15% yield after chromatography as a white solid. Mp 132–133°C; IR ν_{max} (neat) 3058, 3027, 2935, 2359, 1757, 1683, 1607, 1483, 1366, 1271, 1199, 1037 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.87 (s, 3H), 5.45 (s, 2H), 7.10–7.55 (m, 9H), 7.63 (br s, 1H), 7.75 (d, J=7.7 Hz, 1H), 7.90 (d, J=7.5 Hz, 2H); LRMS (AP+) m/z (rel. intensity) 387 (M^++H, 17), 311 (40), 211 (100), 177 (39); HRMS calcd for $C_{24}H_{18}O_5$ 386.1154, found 386.1154.

3.4.19. Compound 50b. 0.076 g, 10% yield after chromatography; IR ν_{max} (neat) 3304, 1740, 1667, 1603, 1527, 1301, 1061, 1032 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.55 (s, $2CH_3$), 3.89 (s, 3H), 5.05 (s, 2H), 7.00–7.15 (2H), 7.20–7.40 (5H), 7.45 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.4 (2C), 45.3, 54.0, 70.6, 112.6, 114.9, 119.0, 121.8, 124.9, 126.7 (2C), 126.9, 127.5 (2C), 128.0, 129.6, 134.0, 147.5, 148.7, 165.8, 171.7; LRMS (AP+) m/z (rel. intensity) 377 (M^+, 100), 350 (64), 293 (30), 386.

3.4.20. Compound 50c. 0.28 g, 25% yield after chromatography; IR ν_{max} (neat) 2959, 1752, 1605, 1245, 1055, 1025, 841 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.20 (s, $9CH_3$), 3.85 (s, 3H), 4.98 (s, 2H), 6.99–7.35 (m, 7H), 7.58 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 2.11 ($9CH_3$), 23.4, 39.3, 42.0, 55.7, 72.3, 117.9, 120.1, 121.4, 126.1, 128.3 (2C), 128.8 (2C), 129.5, 130.8, 160.1, 160.2, 170.2, 173.5; LRMS (AP+) m/z (rel. intensity) 557 (M^++H, 66), 383 (8), 352 (15), 311 ($M^+-Si(SiMe_3)_3$, 100), 265 (26).

3.4.21. Compound 53. 0.096 g, 54% yield after chromatography as a white solid. Mp>250°C; IR ν_{max} (neat) 1749, 1676, 1603, 1495, 1466, 1364, 1332, 1274, 1100, 1021, 986, 918, 764 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.10 (d, J=16.5 Hz, 1H), 3.20 (d, J=16.5 Hz, 1H), 3.49 (s, 3H), 3.91 (s, 3H), 6.82 (d, J=7.5 Hz, 1H), 6.97 (t, J=7.5 Hz, 1H), 7.18 (d, J=7.5 Hz, 1H), 7.26–7.50 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.1, 41.9, 54.4, 82.4, 106.5, 114.0, 121.6, 121.8, 122.0, 122.6, 124.4, 126.3, 129.4, 139.1, 140.2, 159.9, 164.2, 167.1; LRMS (AP+) m/z (rel. intensity) 310 (M^++H, 100); HRMS calcd for $C_{18}H_{15}NO_4$ 309.1001, found 309.1010.

3.4.22. Compound 56. 0.37 g, 52% yield after chromatography as a mixture of two diastereomers (1:1.5); IR ν_{max} (neat) 1765, 1644, 1516, 1496, 1464, 1362, 1335, 1285, 1257, 1223, 1095, 914, 731 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.20–3.15 (7H), 3.80 (s, 3H), 3.87 (s, 3H), 3.90 (s, 3H), 4.89–5.20 (m, 2H), 6.57 (d, J=10.7 Hz, 1H), 6.66 (s, 1H), 7.26–7.40 (3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.7, 27.0, 38.5, 39.1, 39.5, 40.4, 40.8, 51.6, 51.8, 54.4, 54.5, 80.7, 81.3, 106.0, 106.4, 106.5, 106.9, 110.1, 120.4, 121.1, 121.7, 122.0, 125.2, 125.3, 125.5, 125.7, 125.8, 125.9, 141.6, 142.2, 146.4, 146.5, 146.7, 159.8, 163.9, 164.1, 167.1, 167.4; LRMS (AP+) m/z (rel. intensity) 410 (M^++H, 100), 408 (50), 390 (18), 364 (21); HRMS calcd for $C_{23}H_{23}NO_6$ 409.1525, found 409.1523.

3.4.23. Compound 59. 0.36 g, 67% yield after BuCl trituration as a yellow solid. Mp 181–183°C; IR ν_{max} (neat) 1765, 1710, 1497, 1286, 1286, 1984, 913, 744 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.99 (d, J=15.3 Hz, 1H), 3.13 (d, J=15.3 Hz, 1H), 3.63 (d, J=12.4 Hz, 1H), 3.90 (s, 3H), 3.90 (d, J=12.4 Hz, 1H), 7.30–7.40 (2H), 7.48 (d, J=7.5 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 41.0, 49.6, 54.6, 87.9, 106.4, 121.5, 122.3, 125.9, 138.7, 159.7, 166.3, 202.4; LRMS (AP+) m/z (rel. intensity) 251 (M^++H, 100), 233 (40), 207 (32), 193 (27), 175 (16), 152 (47); HRMS calcd for $C_{12}H_{10}O_4S$ 250.0300, found 250.0318.

3.4.24. Compound 64. 0.020 g, 55% yield after chromatography as a mixture of two diastereomers (a/b=1:2); IR ν_{max} (neat) 2956, 1766, 1713, 1466, 1278, 1121, 1025, 994, 975, 759, 695 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.09 (d, J=7.3 Hz, $3H_a$), 1.38 (d, J=7.3 Hz, $3H_b$), 1.80–2.80 (9H), 7.10 (d, J=7.7 Hz, 1H), 7.50–7.64 (m, 2H), 7.95 (m, 1H);

LRMS (AP+) *m/z* (rel. intensity) 257 (M^++H, 100), 239 (25); HRMS calcd for $C_{16}H_{16}O_3$ 256.1099, found 256.1079.

3.4.25. Compound 69. 0.025 g, 58% yield after chromatography as a clear oil; IR ν_{max} (neat) 1767, 1713, 1260, 750 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.02 (d, J=6.0 Hz, 3H), 1.70–2.60 (7H), 3.03 (m, 1H), 3.58 (br d, 1H), 7.24–7.50 (m, 3H), 7.92 (d, J=7.5 Hz, 1H); LRMS (AP+) *m/z* (rel. intensity) 271 (M^++H, 100), 253 (40), 197 (9), 159 (7); HRMS calcd for $C_{17}H_{18}O_3$ 270.1256, found 270.1256.

3.4.26. Compound 72. 0.045 g, 34% yield after chromatography as a clear oil; IR ν_{max} (neat) 1766, 1723, 1465, 1289, 1262, 1122, 1021, 768, 732, 692, 554 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.01 (d, J=5.3 Hz, 3H), 1.50–2.40 (m, 8H), 2.60 (m, 1H), 2.78 (m, 1H), 2.97 (m, 1H), 7.22 (d, J=7.5 Hz, 1H), 7.50–7.62 (m, 2H), 7.90 (d, J=7.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.4, 25.0 (2C), 25.4, 34.6, 37.6, 41.4, 52.5, 88.2, 120.7, 123.7, 124.6, 128.0, 132.6, 150.2, 167.3, 214.6; LRMS (AP+) *m/z* (rel. intensity) 271 (M^++H, 100), 251 (60); HRMS calcd for $C_{17}H_{18}O_3$ 270.1256, found 270.1251.

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References

1. (a) Dervon, T. K.; Scott, A. I. *Handbook of Naturally Occurring Compounds*; Academic: New York, 1972; Vol. II. (b) Collins, I. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1377. (c) Hibino, S.; Choshi, T. *Nat. Prod. Rep.* **2002**, *19*, 148.
2. General reviews, see: (a) Ogliaruso, M. A.; Wolfe, J. F. In *Synthesis of Lactones and Lactams*. Patai, S., Pappoport, Z., Eds.; Wiley: Chichester, 1993. (b) Taylor, S. K. *Tetrahedron* **2000**, *56*, 1149. (c) Sannigrahi, M. *Tetrahedron* **1999**, *55*, 9007. (d) Laduwahetty, T. *Contemp. Org. Synth.* **1995**, *2*, 133.
3. Free radical spirocyclizations, see: (a) Sridar, V.; Babu, G. *Synth. Commun.* **1997**, *27*, 323. (b) Back, T. G.; Gladstone, P. L.; Masood, P. *J. Org. Chem.* **1996**, *61*, 3806. (c) Back, T. G.; Gladstone, P. L. *Synlett* **1993**, 699. (d) Harrison, T.; Pattenden, G. *Tetrahedron Lett.* **1988**, *29*, 3869.
4. Zhang, W.; Pugh, G. *Tetrahedron* **2003**, *59*, 3009.
5. Preliminary communications: (a) Zhang, W.; Pugh, G. *Tetrahedron Lett.* **2001**, *42*, 5617. (b) Zhang, W. *Tetrahedron Lett.* **2000**, *41*, 2523. (c) Zhang, W.; Pugh, G. *Tetrahedron Lett.* **1999**, *40*, 7595.
6. Mukaiyama, T. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 707.
7. (a) Wu, C.-S.; Huang, J.-L.; Sun, Y.-S.; Yang, D.-Y. *J. Med. Chem.* **2002**, *45*, 2222. (b) Lin, Y.-L.; Wu, C.-S.; Lin, S.-W.; Huang, J.-L.; Sun, Y.-S.; Yang, D.-Y. *Bioorg. Med. Chem.* **2002**, *10*, 685. (c) Meazza, G.; Scheffler, B. E.; Tellez, M. R.; Rimando, A. M.; Romagni, J. G.; Duke, S. O.; Nanayakkara, D.; Khan, I. A.; Abourashed, E. A.; Dayan, F. E. *Phytochemistry* **2002**, *60*, 281.
8. Lee, D. L.; Knudsen, C. G.; Michaely, W. J.; Chin, H.-L.; Nguyen, N. H.; Carter, C. G.; Cromartie, T. H.; Lake, B. H.; Shribbs, J. M.; Fraser, T. *Pestic. Sci.* **1998**, *54*, 377.
9. For a review on aryl radical cyclizations, see: Banik, B. K. *Curr. Org. Chem.* **1999**, *3*, 469.
10. Zhang, W. *Tetrahedron* **2001**, *57*, 7237.
11. Kennosuke, S.; Hiroichi, M.; Jun, A. *Yakugaku Zasshi* **1968**, *88*, 919.
12. Williams, D. *Tetrahedron Lett.* **1973**, 639.
13. Isolation: (a) Kusumi, T.; Ichikawa, A.; Kakisawa, H.; Tsunakawa, M.; Konishi, M.; Oki, T. *J. Am. Chem. Soc.* **1991**, *113*, 8947. Synthesis: (b) Roush, W. R.; Barda, D. A.; Limberakis, C.; Kunz, R. K. *Tetrahedron* **2002**, *58*, 6433.
14. For synthesis of related spirodilactones, see: (a) Naito, S.; Escobar, M.; Kym, P. R.; Liras, S.; Martin, S. F. *J. Org. Chem.* **2002**, *67*, 4200. (b) Liddell, J. R.; Whiteley, C. G. *S. Afr. J. Chem.* **1991**, *44*, 35. (c) Jaroszewski, J. W.; Ettlinger, M. G. *J. Org. Chem.* **1989**, *54*, 1506.
15. Peterson, J. R.; Winter, T. J.; Miller, C. P. *Synth. Commun.* **1988**, *18*, 949.
16. Quiclet-Sire, B.; Zard, S. Z. *Pure Appl. Chem.* **1997**, *69*, 645.
17. Rohloff, J. C.; Dyson, N. H.; Gardner, J. O.; Alfredson, T. V.; Sparacino, M. L.; Robinson, III, J. *J. Org. Chem.* **1993**, *58*, 1935.
18. (a) Jasperse, C. P.; Curran, D. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237. (b) Malacria, M. *Chem. Rev.* **1996**, *96*, 289. (c) Parsons, P. J.; Penkett, C. S.; Shell, A. J. *Chem. Rev.* **1996**, *96*, 195. (d) Curran, D. P. *Comprehensive Organic Synthesis*, Trost, B. M., Fleming, I., Eds.; Pregamon: Oxford, 1991; Vol. 4, p 779.
19. (a) Middleton, D. S.; Simpkins, N. S.; Terrett, N. K. *Tetrahedron* **1990**, *46*, 545. (b) Middleton, D. S.; Simpkins, N. S.; Terrett, N. K. *Tetrahedron Lett.* **1988**, *29*, 1315.