Tetrahedron Letters 51 (2010) 4003–4006

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

γ-Lactonizations of 2*H*-chromenes via cyclopropanation

Sean Stokes, Ben Spears, Cameron Laseter, Bobby Barker, Keith T. Mead *

Department of Chemistry, Mississippi State University, Mississippi State, MS 39762, United States

ARTICLE INFO

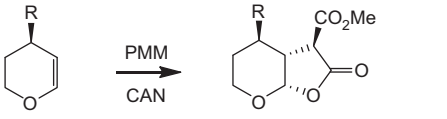
Article history:
Received 20 April 2010
Revised 11 May 2010
Accepted 13 May 2010
Available online 21 May 2010

Keywords:
γ-Lactones
Cyclopropanation
α-Diazocarbonyls
2*H*-Chromenes

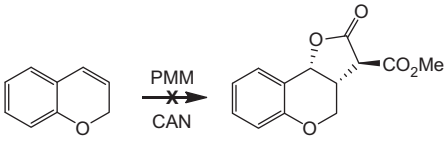
ABSTRACT

A two-step synthesis of tetrahydro-2*H*-furochromenones from 2*H*-chromenes is reported. The reaction of a series of *tert*-butyl 2-diazoacetate derivatives with 2*H*-chromenes, catalyzed by $Rh_2(OAc)_4$, generated cyclopropane intermediates that rearranged to γ-lactones on treatment with $Sn(OTf)_2$.

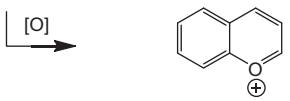
Oxidative γ-lactonizations of alkenes with potassium methyl malonate (PMM), first introduced by Fristad et al.,[1] have found widespread application in synthesis as a simple and efficient route to α-carbomethoxy γ-lactones.[2–6] These one-pot reactions are believed to involve, in addition to the alkene, an oxidatively generated PMM radical, and in many cases they occur with a high degree of regio- and stereoselectivity. Our group, for example, has used this method to lactonize substituted dihydropyrans (Eq. 1) and used the fused ring products as templates for the stereocontrolled synthesis of *C*-alkyl and *C*-aryl pyranosides.[4–6]



(1)



(2)



(3)

PMM = MeO_2C CO_2K

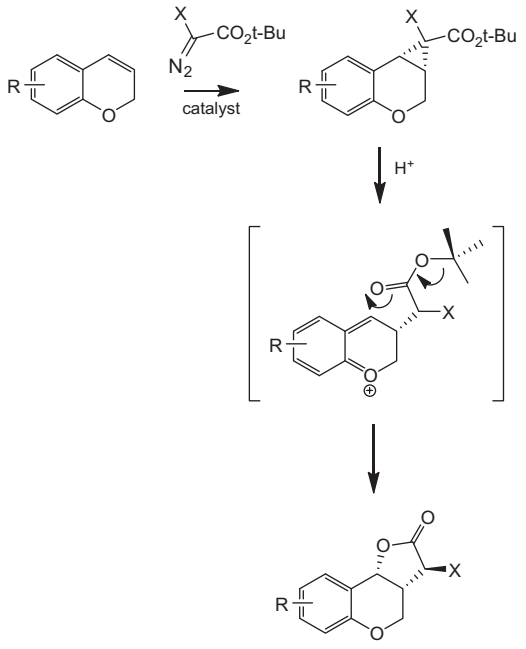
With an interest in extending the scope of these reactions, as well as preparing novel flavan ring structures, we recently tried to apply oxidative γ-lactonization to 2*H*-chromenes (Eq. 2), reasoning that stabilization of both benzylic radical and carbocation intermediates would provide single isomer products analogous to dihydropyrans.[7] However, all attempts failed, presumably because of competing oxidation of the 2*H*-chromene to the corresponding chromenylium ion (Eq. 3), as suggested by the immediate purple color formed on contact with CAN.

Inspired by the groups of Theodorakis and co-workers[8] and Davies and Hu[9] who have independently reported formations of γ-lactones from cyclopropyl esters, we considered a two-step approach involving cyclopropane intermediates that avoids the use of strongly oxidizing conditions (Scheme 1). Prior to the onset of this study, we were aware of only one other example of a cyclopropanation of a 2*H*-chromene with a diazo ester.[10] Cyclopropanations of alkenes with α-diazocarbonyls initiated by a variety of catalysts are well documented[11] and applied to 2*H*-chromenes, we reasoned that subsequent acid-induced cyclopropane ring cleavage should occur regioselectively to generate an oxy-stabilized benzyl carbocation. By using substituted *tert*-butyl diazoacetates we hoped to maximize the rate of rearrangement and achieve selective γ-lactone formation even in the presence of other potential donors (X). Moreover, several alpha-substituted *tert*-butyl acetates, from which these diazoacetates could be made, are commercially available. Based on our previous work preparing fused ring bicyclic lactones from dihydropyrans, a single diastereomeric lactone was predicted with the substituent X *exo* to the fused ring system.

To test the feasibility of the cyclopropanation step, a variety of methoxy-substituted 2*H*-chromenes were reacted with three different diazo esters (Table 1). Our first reaction involved compound **1a** (entry 1) with diazoester **2a** in the presence of catalytic $Rh_2(OAc)_4$, which gave the cyclopropane derivative **3a** as a mixture of diastereomers, along with a minor product identified as the insertion adduct **4a**. The 2*H*-chromenes **1b** and **1c** gave similar

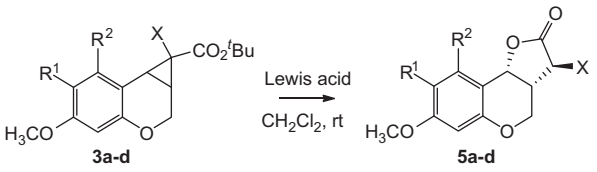
* Corresponding author. Tel.: +1 662 325 3584; fax: +1 662 325 1618.
E-mail address: kmead@ra.msstate.edu (K.T. Mead).

0040-4039/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2010.05.059



Scheme 1.

Table 2
Ring expansions of cyclopropane products



Entry	R^1	R^2	X	Substrate	Lewis acid	Product	Yield (%)
1	H	H	CO_2CH_3	**3a**	$BF_3{\cdot}OEt_2$[a]	**5a**	45
2	H	H	CO_2CH_3	**3a**	$Sn(OTf)_2$[b]	**5a**	72
3	H	OCH_3	CO_2CH_3	**3b**	$Sn(OTf)_2$[b]	**5b**	57
4	OCH_3	H	CO_2CH_3	**3c**	$BF_3{\cdot}OEt_2$[a]	**5c**	65
5	OCH_3	H	CO_2CH_3	**3c**	$Sn(OTf)_2$[b]	**5c**	71
6	OCH_3	H	CO_2CH_3	**3c**	$Cu(OTf)_2$[b]	**5c**	27
7	OCH_3	H	CO_2CH_3	**3c**	$Sn(OTf)_3$[b]	**5c**	24
8	OCH_3	H	CN	**3d**	$Sn(OTf)_2$[b]	**5d**	63
9	OCH_3	H	CN	**3d**	$BF_3{\cdot}OEt_2$[a]	**5d**	40
10	OCH_3	H	CN	**3d**	$Cu(OTf)_2$[b]	**5d**	29
11	OCH_3	H	CN	**3d**	$Sn(OTf)_2$[b]	**5d**	31

[a] 0.3 equiv.
[b] 0.5 equiv.

results with diazoesters **2a** and **2b** (entries 2–4). Compounds **3b** and **3c** were also formed as a mixture of diastereomers, but the cyano-substituted cyclopropane **3d** formed as a single isomer. Use of $AgSbF_6$ or $Cu(OTf)_2$ instead of $Rh_2(OAc)_4$ resulted in no cyclopropane product formation. Best yields were obtained by the addition of an excess (2 equiv) of the diazo compound via a syringe pump to a stirred solution of the 2*H*-chromene and catalyst (2 mol %) over 5 h followed by overnight stirring.[12] Notably, the extent of insertion relative to cyclopropanation decreased with the dimethoxy-substituted derivatives **1b** and **1c** (compare entries 2–4 with entry 1). Unfortunately, all attempts to react diazophosphoryl derivative **2c** were unsuccessful.[13]

Next we studied Lewis acid-induced rearrangements of these cyclopropane substrates (Table 2). Beginning with the monomethoxy-substituted compound **3a** (entry 1), we found that $BF_3{\cdot}OEt_2$ provided a very clean reaction, as monitored by tlc, but gave a disappointingly low yield of the product **5a**. On the other hand, stronger Lewis acids such as $TiCl_4$ and $SnCl_4$ caused immediate decomposition, even at −78 °C. However, we were delighted to find better results with $Sn(OTf)_2$ at room temperature (entry 2). Indeed, this Lewis acid proved to be the reagent of choice for other substrates (see entries 3, 5, and 8).[14] Both $Cu(OTf)_2$ and $Sc(OTf)_3$ proved to be disappointing, while protic acids such as TFA and *p*-

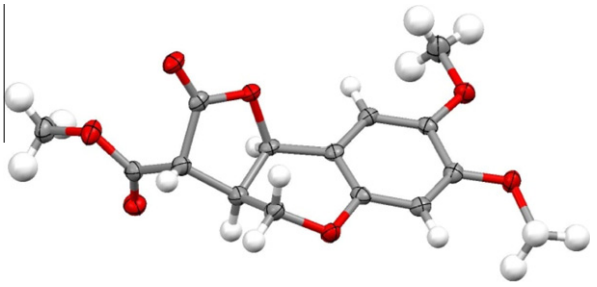
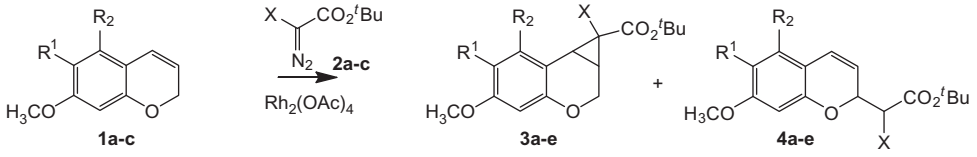


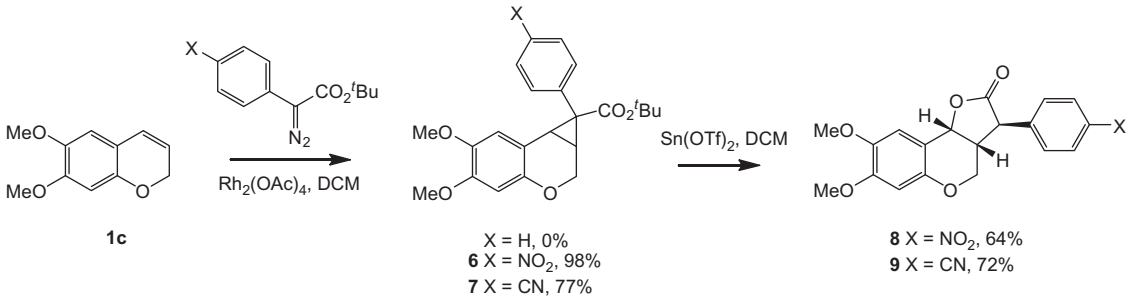
Figure 1. X-ray structure of compound **5c**.

Table 1
Cyclopropanations of 2*H*-chromenes[a]



Entry	R^1	R^2	Chromene	X	Product	Yield (%)	Product	Yield (%)
1	H	H	**1a**	CO_2CH_3 (**2a**)	**3a**	62	**4a**	12
2	H	OCH_3	**1b**	CO_2CH_3 (**2a**)	**3b**	78	**4b**	5
3	OCH_3	H	**1c**	CO_2CH_3 (**2a**)	**3c**	83	**4c**	7
4	OCH_3	H	**1c**	CN (**2b**)	**3d**	74	**4d**	4
5	OCH_3	H	**1c**	$PO(OEt)_2$ (**2c**)	**3e**	0	**4e**	0

[a] Reaction conditions: 2*H*-chromene **1** (1 equiv), diazoester **2** (2 equiv), $Rh_2(OAc)_4$ (2 mol %), CH_2Cl_2, 25 °C.



Scheme 2.

TsOH (not shown) gave complex mixtures of products and were not analyzed further. All products **5a–d** formed as single isomers (see Fig. 1).

A single-crystal X-ray structure of compound **5c** confirmed the assigned stereochemistry of the lactone products, showing the substituent X, in this case methyl ester, to be *exo* to the fused ring system.[15]

A number of routes to α-aryl γ-lactones have been reported.[16] One commonly used method involves the α-arylation of an α-activated γ-lactone using toxic lead- and mercury-based reagents.[16c–e] To see if we could prepare these derivatives using our two-step protocol, 2*H*-chromene **1c** was reacted with three different α-aryl-α-diazo *tert*-butyl acetates to form cyclopropane intermediates (Scheme 2). Not surprisingly, our results indicated a direct relationship between the yield of cyclopropane product and the electron deficiency of the aryl ring on the diazo reagent and suggested a need for the presence of an electron-withdrawing group for the reaction to proceed. Notably, there was no evidence of an insertion product in either of the successful cyclopropanations. Moreover, both cyclopropane products **6** and **7** rearranged to γ-lactones **8** and **9**, respectively, on treatment with $Sn(OTf)_2$.

A useful method for effecting successful γ-lactonizations of 2*H*-chromenes has been described, which avoids the use of strongly oxidizing conditions. We hope to use these intermediates as templates for targeting novel flavan ring structures.

References and notes

1. Fristad, W. E.; Peterson, J. R.; Ernst, A. B. *J. Org. Chem.* **1985**, *50*, 3143–3148.
2. del Rosario-Chow, M.; Ungwitayatorn, J.; Currie, B. L. *Tetrahedron Lett.* **1991**, *32*, 1011–1014.
3. (a) D'Annibale, A.; Trogolo, C. *Tetrahedron Lett.* **1994**, *35*, 2083–2086; (b) Allegretti, M.; D'Annibale, A.; Trogolo, C. *Tetrahedron* **1993**, *49*, 10705–10714.
4. Cakir, S. P.; Mead, K. T.; Smith, L. *Tetrahedron Lett.* **2003**, *44*, 6355–6358.
5. Cakir, S. P.; Mead, K. T. *J. Org. Chem.* **2004**, *69*, 2203–2205.
6. Cakir, S. P.; Mead, K. *Heterocycl. Commun.* **2005**, *11*, 471–474.
7. For previous routes to related 6,6,5-tricyclic γ-lactones, see: (a) Bentley, J.; Nilsson, P. A.; Parsons, A. F. *J. Chem. Soc., Perkin Trans. 1* **2002**, *12*, 1461–1469; (b) Kablaoui, N. M.; Hicks, F. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 4424–4431; (c) Szczepanik, M.; Obara, R.; Szumny, A.; Gabrys, B.; Halarewicz-Pacan, A.; Nawrot, J.; Wawrzenczyk, C. *J. Agric. Food. Chem.* **2005**, *53*, 5905–5910.
8. Kim, C.; Brady, T.; Kim, S. H.; Theodorakis, E. A. *Synth. Commun.* **2004**, *34*, 1951–1965.
9. Davies, H. M. L.; Hu, B. *J. Org. Chem.* **1992**, *57*, 4309–4312.
10. Blanchard, L. A.; Schneider, J. A. *J. Org. Chem.* **1986**, *51*, 1372–1374.
11. For a review, see: Davies, H. M. L.; Antoulinakis, E. G. *Org. React.* **2001**, *57*, 1.
12. *General procedure for formation of the cyclopropanes: 1-tert-butyl 1-methyl 5-methoxy-1a,2-dihydrocyclopropa[c]chromene-1,1(7bH)-dicarboxylate* (**3a**). In a 5-mL round-bottomed flask, 7-methoxy-2*H*-chromene (200 mg, 1.2 mmol) was dissolved in 2 mL of dry DCM. Once dissolution was achieved, $Rh_2(OAc)_4$ (11 mg, 0.024 mmol) was added and the reaction vessel was purged with argon. This mixture was stirred for 5 min and then 1-*tert*-butyl 3-methyl 2-diazomalonate (480 mg, 2.4 mmol) dissolved in 1 mL of dry DCM was added via a syringe pump over 5 h. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography using mixtures of hexane and ethyl acetate as the eluting solvents. Yellow oil (253 mg, 63%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.21 (d, *J* = 8.4 Hz, 1H), 6.54 (dd, *J* = 8.4 and 2.6 Hz, 1H), 6.34 (d, *J* = 2.5 Hz, 1H), 4.52 (dd, *J* = 11.3 and 0.9 Hz, 1H), 3.98 (dd, *J* = 11.3 and 2.1 Hz, 1H), 3.75 (s, 3H), 3.59 (s, 3H), 2.76 (d, *J* = 9.5 Hz, 1H), 2.41 (ddd, *J* = 9.5, 2.1 and 0.9 Hz, 1H), 1.47 (s, 9H); ^{13}C NMR (300 mHz): δ 169.8, 158.4, 155.5, 129.7, 119.5, 105.7, 100.3, 82.4, 68.7, 55.8, 52.2, 37.2, 29.8, 28.7, 28.3. *1-tert-Butyl 1-methyl 5,7-dimethoxy-1a,2-dihydrocyclopropa[c]chromene-1,1(7bH)-dicarboxylate* (**3b**). Yellow oil (296 mg, 78%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.15 (s, 1H), 5.90 (s, 1H), 4.12 (dd, 10.1 and 1.3 Hz, 1H), 3.97 (dd, 10.1 and 0.8 Hz, 1H), 3.82 (s, 3H), 3.81 (s, 3H), 3.79 (s, 3H), 2.50 (d, 9.0 Hz, 1H), 2.36 (dd, 9.0, 1.3 and 0.8 Hz), 1.35 (s, 9H); ^{13}C NMR (300 mHz): δ 170.0, 160.8, 157.9, 156.5, 104.4, 92.6, 91.8, 82.4, 68.6, 56.1, 55.8, 52.2, 37.5, 30.1, 28.5, 22.4. *1-tert-Butyl 1-methyl 5,6-dimethoxy-1a,2-dihydrocyclopropa[c]chromene-1,1(7bH)-dicarboxylate* (**3c**). Yellow oil (315 mg, 83%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.85 (s, 1H), 6.41 (s, 1H), 4.05 (dd, *J* = 10.9 and 1.0 Hz, 1H), 3.93 (dd, *J* = 10.9 and 2.5 Hz, 1H), 3.83 (s, 3H), 3.80 (s, 3H), 3.76 (s, 3H), 2.70 (d, *J* = 9.2 Hz, 1H), 2.42 (ddd, *J* = 9.2, 2.5, and 1.0 Hz, 1H), 1.50 (s, 9H); ^{13}C NMR (300 mHz): δ 168.2, 147.8, 141.2, 120.5, 107.5, 100.2, 82.5, 68.4, 56.1, 52.5, 36.8, 29.5, 28.9, 28.2. *tert-Butyl 1-cyano-5,6-dimethoxy-1,1a,2,7b-tetrahydrocyclopropa[c]chromene-1-carboxylate* (**3d**). White solid (248 mg, 74% before recrystallized; 190 mg, 55% after recrystallization with hexane and ethyl acetate); mp: 147–149 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.79 (s, 1H), 6.47 (s, 1H), 4.48 (dd, *J* = 12.2 and 2.0 Hz, 1H), 4.33 (dd, *J* = 12.2 and 3.6 Hz, 1H), 3.87 (s, 3H), 3.83 (s, 3H), 3.00 (d, *J* = 9.5 Hz, 1H), 2.61 (ddd, *J* = 9.5,3.6, and 2.0 Hz, 1H), 1.54 (s, 9H); ^{13}C NMR (300 mHz): δ 165.0, 150.1, 147.1, 144.1, 115.0, 112.3, 107.2, 101.6, 84.5, 60.6, 56.4, 55.9, 30.7, 29.8, 27.9, 27.7. *tert-Butyl 5,6-dimethoxy-1-(4-nitrophenyl)-1,1a,2,7b-tetrahydrocyclopropa[c]chromene-1-carboxylate* (**6**). Yellow oil (436 mg, 98%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99 (d, *J* = 8.7 Hz, 2H), 7.10 (d, *J* = 8.7 Hz, 2H), 6.89 (s, 1H), 5.98 (s, 1H), 4.39 (d, *J* = 11.7 Hz, 1H), 4.05 (dd, *J* = 11.8 and 2.2 Hz, 1H), 3.93 (s, 3H), 3.70 (s, 3H), 2.96 (d, *J* = 9.7 Hz, 1H), 2.64 (dd, *J* = 9.7 and 1.4 Hz, 1H), 1.35 (s, 9H); ^{13}C NMR (300 mHz): δ 164.8, 147.8, 147.6, 145.6, 145.1, 141.2, 129.0, 123.7, 120.5, 107.5, 100.2, 82.7, 68.9, 55.9, 36.8, 36.6, 36.2, 28.7. *tert-Butyl 1-(4-cyanophenyl)-5,6-dimethoxy-1,1a,2,7b-tetrahydrocyclopropa[c]chromene-1-carboxylate* (**7**). Yellow oil (326 mg, 77%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.22 (d, *J* = 9.0 Hz, 2H), 7.65 (d, *J* = 9.0 Hz, 2H), 6.90 (s, 1H), 5.99 (s, 1H), 4.39 (d, *J* = 11.1 Hz, 1H), 4.06 (d, *J* = 11.1 Hz, 1H), 3.94 (s, 3H), 3.69 (s, 3H), 2.96 (d, *J* = 8.7 Hz, 1H), 2.64 (dd, *J* = 8.7 and 1.0 Hz, 1H), 1.36 (s, 9H); ^{13}C NMR (300 mHz): δ 164.5, 147.8, 147.6, 143.8, 141.2, 132.0, 128.8, 120.5, 118.6, 109.8, 107.5, 100.2, 82.5, 68.7, 56.2, 36.9, 36.5, 36.1, 28.3.
13. For examples of cyclopropanations of alkenes with α-trifluoromethyldiazophosphonate, see: Titanyuk, I. D.; Beletskaya, I. P.; Peregudov, A. S.; Osipov, S. N. *J. Fluorine Chem.* **2007**, *128*, 723–728.
14. *General procedure for the preparation of the lactones: methyl 7-methoxy-2-oxo-3,3a,4,9b-tetrahydro-2H-furo[3,2-c]chromene-3-carboxylate* (**5a**). In a 5-mL round-bottomed flask, a solution of compound **3a** (50 mg, 0.15 mmol) in 3 mL of dry DCM was cooled to 0 °C and tin(II) triflate (31 mg, 0.075 mmol) was added. The reaction vessel was purged with argon and stirred overnight, slowly allowing the solution to warm to room temperature. The reaction was quenched with a few drops of water and then dried over $MgSO_4$. The solvent was removed under reduced pressure and then the crude product was purified using flash column chromatography using mixtures of hexane and ethyl acetate as the eluting solvents. Off-white solid (30 mg, 72%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.28 (d, *J* = 8.6 Hz, 1H), 6.62 (dd, *J* = 8.6 and 2.4 Hz, 1H), 6.41 (d, *J* = 2.4 Hz, 1H), 5.68 (d, *J* = 7.3 Hz, 1H), 4.21 (dd, *J* = 11.8 and 3.4 Hz, 1H), 4.01 (dd, *J* = 11.8 and 6.2 Hz, 1H), 3.86 (s, 3H), 3.79 (s, 3H), 3.61 (d, *J* = 7.4 Hz, 1H), 3.43–3.35 (m, 1H); ^{13}C NMR (300 mHz): δ 171.0, 169.9, 158.1, 155.8, 128.7, 120.0, 108.6, 99.7, 81.1, 68.5, 55.8, 51.9, 49.5, 32.6. *Methyl 7,9-dimethoxy-2-oxo-3,3a,4,9b-tetrahydro-2H-furo[3,2-c]chromene-3-carboxylate* (**5b**). Off-white solid (24 mg, 57%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.17 (s, 1H), 5.98 (s, 1H), 5.62 (d, *J* = 7.0 Hz, 1H), 4.19 (dd, *J* = 11.3 and 3.8 Hz, 1H), 3.99 (dd, *J* = 11.3 and 6.0 Hz, 1H), 3.88 (s, 3H), 3.85 (s, 3H), 3.83 (s, 3H), 3.63 (d, *J* = 7.5 Hz, 1H), 3.47–3.38 (m, 1H); ^{13}C NMR (300 mHz): δ 172.6, 165.3, 158.1, 146.2, 142.6, 111.78, 109.9, 100.3, 78.4, 65.1, 55.4, 55.0, 53.2, 48.6, 39.7. *Methyl 7,8-dimethoxy-2-oxo-3,3a,4,9b-tetrahydro-2H-furo[3,2-c]chromene-3-carboxylate* (**5c**). White solid (30 mg, 71%); mp: 149–150 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.79 (s, 1H), 6.42 (s, 1H), 5.67 (d, *J* = 7.4 Hz, 1H), 4.18 (dd, *J* = 11.8 and 3.3 Hz, 1H), 4.01 (dd, *J* = 11.8 and 5.9 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.85 (s, 3H), 3.64 (d, *J* = 7.8 Hz, 1H), 3.43–3.35 (m, 1H); ^{13}C NMR (300 mHz): δ 170.6, 167.3, 151.1, 149.2, 144.7, 111.7, 109.2, 100.7, 73.8, 64.2, 56.3, 56.0, 53.4, 47.6, 38.2. *7,8-Dimethoxy-2-oxo-3,3a,4,9b-tetrahydro-2H-furo[3,2-c]chromene-3-carbonitrile*

(**5d**). Off-white solid (27 mg, 63%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.82 (s, 1H), 6.40 (s, 1H), 5.57 (d, J = 7.2 Hz, 1H), 4.20 (dd, J = 11.2 and 3.0 Hz, 1H), 4.00 (dd, J = 11.2 and 6.1 Hz, 1H), 3.84 (s, 3H), 3.83 (s, 3H), 3.59 (d, J = 7.6 Hz, 1H), 3.45–3.37 (m, 1H); ^{13}C NMR (300 mHz): δ 165.3, 148.1, 147.5, 143.4, 120.5, 116.8, 113.9, 99.7, 81.3, 68.5, 56.2, 55.9, 35.8, 32.6. *7,8-Dimethoxy-3-(4-nitrophenyl)-3,3a,4,9b-tetrahydro-2H-furo[3,2-c]chromen-2-one* (**8**). Off-white solid (28 mg, 64%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (d, J = 8.6 Hz, 2H), 7.56 (d, J = 8.7 Hz, 2H), 6.88 (s, 1H), 6.42 (s, 1H), 5.46 (d, J = 4.7 Hz, 1H), 4.21 (dd, J = 12.3 and 2.5 Hz, 1H), 4.10 (dd, J = 12.3 and 2.4 Hz, 1H), 3.88 (s, 3H), 3.85 (s, 3H), 3.60 (d, J = 7.4 Hz, 1H), 3.33–3.23 (m, 1H); ^{13}C NMR (300 mHz): δ 174.2, 148.2, 147.3, 144.8, 143.4, 143.0, 129.5, 123.1, 120.4, 111.7, 100.5, 82.7, 67.8, 56.5, 56.3, 53.5, 38.9. *4-(7,8-Dimethoxy-2-oxo-3,3a,4,9b-tetrahydro-2H-furo[3,2-c]chromen-3-yl)benzonitrile* (**9**). Off-white solid (31 mg, 72%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.89 (d, J = 8.2 Hz, 2H), 7.47 (d, J = 8.3 Hz, 2H), 6.87 (s, 1H), 6.44 (s, 1H), 5.49 (d, J = 4.3 Hz, 1H), 4.24 (dd, J = 12.1 and 2.1 Hz, 1H), 4.15 (dd, J = 12.1 and 2.0 Hz, 1H), 3.89 (s, 3H), 3.86 (s, 3H), 3.63 (d, J = 7.2 Hz, 1H), 3.39–3.27 (m, 1H); ^{13}C NMR (300 mHz): δ 174.4, 148.1, 147.8, 143.8, 141.7, 131.7, 129.8, 121.6, 119.7, 112.2, 108.5, 100.7, 82.3, 69.9, 56.7, 56.3, 53.4, 40.5.

15. Crystal data for **5c**: $C_{15}H_{16}O_7$, M_w = 308.28, crystal size: 0.06 × 0.16 × 0.19 mm, crystal system: orthorhombic, space group: P b c a, a = 15.7986(15) Å, b = 7.2968(7) Å, c = 23.947(2) Å, $\alpha = \beta = \gamma = 90°$, U = 2760.6(5) Å^3, Z = 8, T = 100(2) K, reflections collected 23670, 2144 independent (R_{int} = 0.0681), R_1 = 0.0405, wR_2 = 0.1115. The crystallographic data were deposited with the Cambridge Crystallographic Data Centre (deposition number CCDC 774002). The data can be obtained free of charge from www.ccdc.cam.ac.uk.
16. (a) Spielvogel, D. J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 3500–3501; (b) Fox, J. M.; Huang, X.; Chieffi, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 1360–1370; (c) Sakaguchi, K.; Kitamura, T.; Shiomi, Y.; Koden, M.; Kuratate, T. *Chem. Lett.* **1991**, 1383–1386; (d) Pinhey, J. T.; Rowe, B. A. *Aust. J. Chem.* **1980**, *33*, 113–120; (e) Deng, H.; Konopelski, J. P. *Org. Lett.* **2001**, *3*, 3001–3004; (f) Gong, J.; Lin, G.; Li, C.-c.; Yang, Z. *Org. Lett.* **2009**, *11*, 4770–4773.