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Halonium-initiated double oxa-cyclization cascade as a synthetic strategy for halogenated furo[3,2-*c*]pyran-4-ones†

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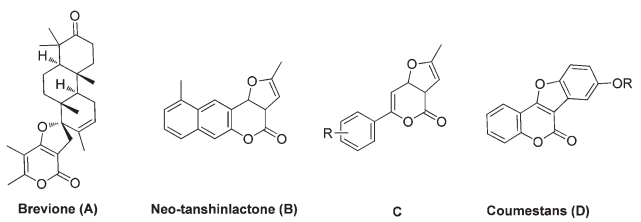
The reaction of 1-alkenoylcyclopropane carboxylic acids with NBS or NIS was investigated, which provides an efficient route to biologically important 7-halogenated furo[3,2-*c*]pyran-4-ones in a one-pot transformation. The major pathway for the formation of the *O*–*O* heterocycles was proposed as a halo-oxa-cyclization, HBr elimination, cyclopropane ring-opening and recyclization (intramolecular oxa-cyclization), and bromination cascade. The double-oxa-cyclization represents a novel synthetic strategy towards functionalized furo[3,2-*c*]pyranones.

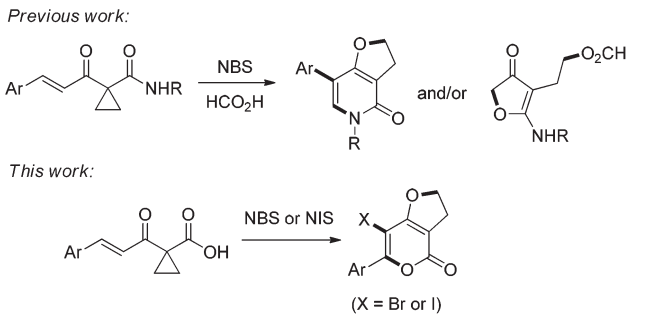
Introduction

Furo[3,2-*c*]pyran-4-ones constitute the core structure of many naturally occurring and unnatural compounds, which display important pharmaceutical and biological properties (Scheme 1).[1] For example, Brevione (**A**) may inhibit etiolated wheat coleoptile growth.[1a] Neo-tanshinlactone (**B**) and its derivative **C** have been reported as potent and highly selective anti-breast cancer agents.[1b] Coumestans (**D**) have the potential for estrogenic activity in human health.[1c] As such, a considerable effort has been devoted towards the development of new methods for the construction of this type of *O*–*O*-bicycle. General methods mainly rely upon annulation onto the existing furan or pyran scaffold.[2] However, examples of direct assembly of both pyran and furan rings from acyclic substrates *via* tandem double cyclization are less reported.



Scheme 1 Biologically significant molecules containing a furo[3,2-*c*]pyranone skeleton.

Cascade reactions are becoming more and more important in organic synthesis due to the intriguing step- and atom-efficient creation of molecular complexity in a one-pot reaction.[3] During the course of our study on the synthetic potential of doubly-EWG activated cyclopropanes[4] toward various carbo- and heterocycles,[5] we recently developed an electrophilic haloaza-cyclization-initiated cascade of readily available 1-alkenoylcyclopropanecarboxamides with an NBS–carboxylic acid combination, giving efficient access to structurally interesting and biologically significant dihydrofuropyridinones and 3(2*H*)-furanones (Scheme 2, top).[5d] In connection with this work and our continued interest in halogen-mediated organic reactions,[6] we have started to explore the electrophilic cyclization by the utilization of 1-alkenoylcyclopropane carboxylic acids in the presence of a halonium-producing reagent (Scheme 2, bottom). Consequently, a strategically novel route to halogenated furo[3,2-*c*]pyran-4-ones was realized. Such a type of *O*–*O*-bicycle was fundamentally formed *via* a process of tandem halo-



Scheme 2 Halonium-initiated electrophilic cascades.

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oxa-cyclization, HBr elimination, cyclopropane ring-opening and recyclization, and bromination cascade.

Results and discussion

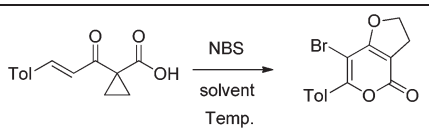
Initially, the model reaction of 1-alkenoylcyclopropane carboxylic acid (**1a**) with NBS was examined to optimize the reaction conditions (Table 1). In this case, no additional acid catalyst was required. Solvents and reaction temperature were then screened. No target molecule was detected in the mixture of **1a** and NBS (2.2 equiv.) in toluene at 80 °C (entry 1). When THF was used as the solvent, the reaction took place and 7-bromo-6-(*p*-tolyl)-2*H*-furo[3,2-*c*]pyran-4(3*H*)-one (**2a**) was obtained in 18% isolated yield (entry 2). Other solvents like DMF, DCE and nitromethane gave improved yields (entries 3–5), and MeCN was proved to be the most efficient, affording **2a** in 85% yield (entry 6). Contrary to our previous observation, no aryl migration product was obtained.[5d]

With the optimal conditions established above (Table 1, entry 6), a range of reactions were carried out with various substrates **1** in the presence of NBS (2.2 equiv.) (Table 2). The scope of the substitutes on the α,β-unsaturated enone moieties of substrates **1** was investigated. The substituent Ar comprised of electron-rich aryls (*i.e.*, 4-methylphenyl, 2-methylphenyl, 2-methoxyphenyl, 3,4-methylenedioxyphenyl), phenyl, halogen-substituted phenyl (2-Cl and 4-Cl), electron-poor aryl (*e.g.* 4-nitrophenyl), 1-naphthyl, heteroaryl (*i.e.*, 2-thienyl) and β-phenylvinyl. Products **2a–i** and **2k** were obtained in fair to high yields (31–87%, entries 1–10 and 12). The reaction for the substrate **1j** with a 2-furyl group gave a mixture of brominated and unbrominated products, which are difficult to isolate (entry 11). The structure of **2e** was confirmed unambiguously by X-ray single crystal diffraction (Fig. 1).

It is noteworthy that in the reaction of 1-(3-(4-(dimethylamino)phenyl)acryloyl)cyclopropanecarboxylic acid **1m** with NBS (2.2 equiv.) in MeCN at 50 °C for 12 h, 6-(3-bromo-4-(dimethylamino)phenyl)-2*H*-furo[3,2-*c*]pyran-4(3*H*)-one **3** was obtained in 77% yield, and the bromination did not take place at the 7-position of the furo[3,2-*c*]pyran-4-one skeleton, but at the *ortho*-position of the dimethylamino substituent on the phenyl group (Scheme 3, eqn (1)). When 3.3 equiv. of NBS was introduced to the reaction system, as expected, dibrominated furo-[3,2-*c*]pyran-4-one **2m** was separated in 58% yield (eqn (2)).

In the following work, other *N*-halosuccinimides such as NIS and NCS were subjected to the reaction sequence. It was

Table 1 Optimization of the reaction conditions[a]

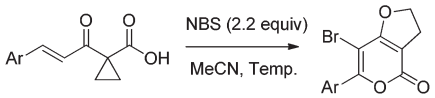


1a **2a**

Entry	Solvent	Temp.	Time (h)	Yield[b] (%)
1	Toluene	80	24	n.d.
2	THF	Reflux	24	18
3	DMF	80	12	66
4	DCE	80	24	69
5	$MeNO_2$	80	24	80
6	**MeCN**	**Reflux**	**24**	**85**

[a] Reactions were carried out with **1a** (1.0 mmol), and NBS (2.2 equiv.) in solvent (4.0 mL). [b] Isolated yield.

Table 2 Bromonium-initiated cascade reactions leading to 7-bromonated dihydrofuro[3,2-*c*]pyran-4-ones **2**[a]



1 **2**

Entry	1	Ar	Temp. (°C)	Time (h)	2	Yield[b] (%)
1	**1a**	4-MeC_6H_4	Reflux	24	**2a**	85
2	**1b**	2-MeC_6H_4	Reflux	12	**2b**	83
3	**1c**	2-$MeOC_6H_4$	Reflux	24	**2c**	79
4	**1d**	3,4-$OCH_2OC_6H_3$	Reflux	24	**2d**	65[c]
5	**1e**	C_6H_5	Reflux	24	**2e**	78
6	**1f**	4-ClC_6H_4	Reflux	24	**2f**	75
7	**1g**	2-ClC_6H_4	Reflux	24	**2g**	45
8	**1h**	4-$NO_2C_6H_4$	85	24	**2h**	31[c]
9	**1i**	$C_{10}H_7$	Reflux	24	**2i**	70
10	**1j**	2-Thienyl	Reflux	24	**2j**	84
11	**1k**	2-Furyl	50	24	**2k**	70[d]
12	**1l**	$C_6H_5CH{=}CH$	Reflux	12	**2l**	74

[a] Reactions were carried out with **1a** (1.0 mmol) and NBS (2.2 equiv.) in MeCN (4.0 mL). [b] Isolated yield. [c] DMF (4.0 mL) was used as the solvent due to the poor solubility of the substrate in MeCN. [d] A mixture of brominated and unbrominated products.

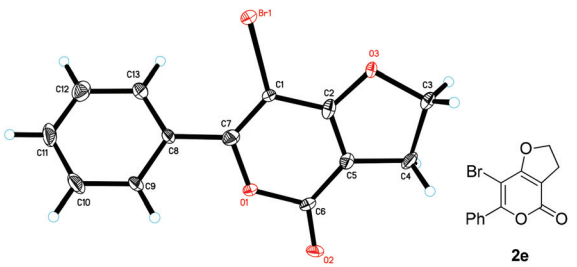
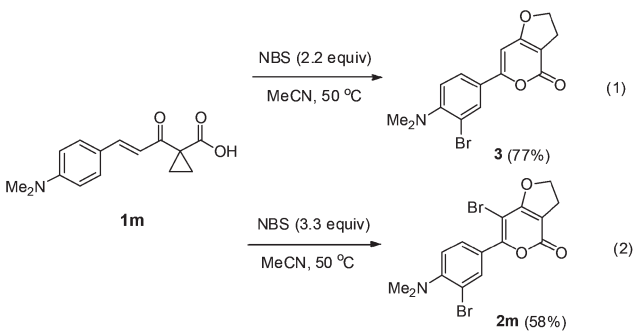
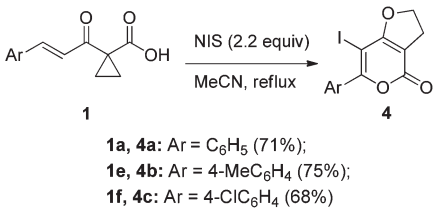


Fig. 1 X-ray crystal structure of **2e**.



Scheme 3 Reaction of **1m** with NBS.

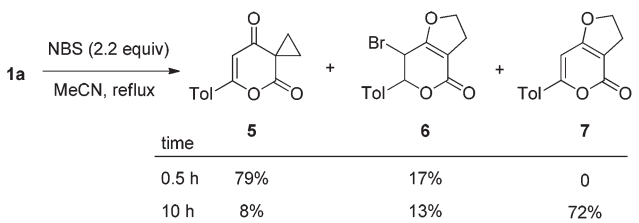


Scheme 4 Reactions of **1** with NIS.

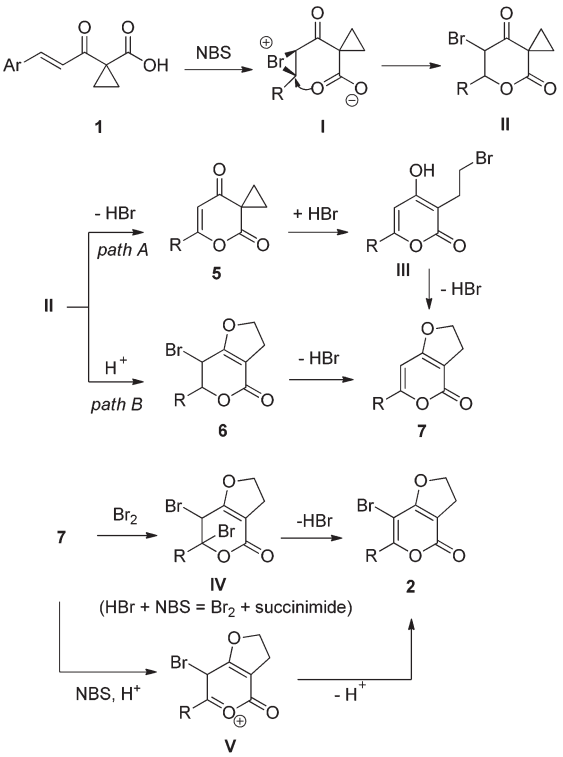
found that NIS showed comparable reactivity to NBS, while NCS was inefficient. The reaction of NIS with selected substrates **1a**, **1e** and **1f** afforded the iodinated furopyranones **4a–c** in 68–75% yields (Scheme 4). The halogen functionalities (*e.g.* Br and I) may allow one to introduce an alkyl or aromatic substituent *via* a transition metal catalyzed cross-coupling reaction.[7]

To gain insight into the mechanism of the double oxa-cyclization based on 1-alkenoylcyclopropane carboxylic acid substrates, the reaction of **1a** with NBS (2.2 equiv.) was quenched with water after the reaction had proceeded for 0.5 h and 10 h (Scheme 5). For the former, after workup and purification by column chromatography of the resulting mixture, 6-(*p*-tolyl)-5-oxaspiro[2.5]oct-6-ene-4,8-dione **5** and 7-iodo-6-(*p*-tolyl)-2*H*-furo[3,2-*c*]pyran-4(3*H*)-one **6** were successfully isolated in 79% and 17% yields, respectively. For the latter, only 8% of **5** and 13% of **6** were obtained in the reaction system, and 6-(*p*-tolyl)-2*H*-furo[3,2-*c*]pyran-4(3*H*)-one **7** was separated in 72% yield. It was found that, with the prolonged reaction time, the spiro compound **5** gradually transformed into the fused compound **7** in the process.

On the basis of all the results described above, a possible mechanism for the cascade transformation of substrates **1** into **2** is depicted in Scheme 6. Initially, the bromonium ion intermediate **I** is formed *via* electrophilic activation of the alkene. Then, intramolecular oxa-cyclization (in a 6-*endo-tet* fashion) takes place, giving the spiro-pyranone intermediate **II**. There are two possible pathways for the conversion of **II** into **7**. Path A involves a sequential HBr elimination, ring-opening of cyclopropane and recyclization (**II**→**5**→**III**→**7**). In path B, ring-opening of cyclopropane and recyclization take place first, followed by HBr elimination (**II**→**6**→**7**). Since the content of intermediate **6** during the transformation is rather low (Scheme 5), path A is proposed to be the main pathway. The intermediate **7** further reacts with Br_2 (generated *in situ* by the reaction of NBS and HBr) or NBS (in the presence of acid catalyst) to afford the final product **2**.



Scheme 5 Control experiment.



Scheme 6 Possible mechanism for the formation 2,3-dihydrofuro[3,2-*c*]pyranones **2**.

Conclusion

In summary, we have developed a strategically novel double oxa-cyclization approach for the synthesis of 7-halogenated furo[3,2-*c*]pyran-4-ones *via* a halonium-initiated cascade process. The major pathway for the formation of the *O–O* heterocycle involves a process of halo-oxa-cyclization, HBr elimination, cyclopropane ring-opening and recyclization, and bromination cascade (2 carbon–oxygen bonds and 1 carbon–halogen bond were constructed successively). The reaction features readily available starting materials, mild conditions, high efficiency, and high chemo- and regioselectivity. Further work on halogen-mediated organic reactions is ongoing.

Experimental

General methods

All reagents were purchased from commercial sources and used without treatment, unless otherwise indicated. The products were purified by column chromatography over silica gel. ^{1}H NMR and ^{13}C NMR spectra were recorded at 25 °C on a Varian 500 MHz and 125 MHz, respectively, with TMS as the internal standard. IR spectra (KBr) were recorded on a Magna-560 FTIR spectrophotometer in the range of 400–4000 cm^{-1}.

Elemental analyses were measured on an E-2400 analyzer (Perkin-Elmer). Mass spectra were recorded on an Agilent 1100 LCMsD mass spectrometer.

General procedure for the preparation of 2. Synthesis of 2a

To a solution of 1-alkenoylcyclopropane carboxylic acid **1a** (230 mg, 1.0 mmol) in MeCN (4 mL) NBS (392 mg, 2.2 mmol) was added. The mixture was stirred at reflux for 24 h. Then the reaction mixture was cooled to room temperature and poured into water and then extracted with CH_2Cl_2 (3 × 5 mL). The combined organic phase was washed with water (3 × 10 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (silica gel, ethyl acetate–petroleum ether = 1 : 6) to give **2a** (260 mg, 85%) as a white solid.

Physical data of compounds isolated

7-Bromo-6-(*p*-tolyl)-2*H*-furo[3,2-*c*]pyran-4(3*H*)-one (2a). Yield: 85% (260 mg, 0.85 mmol); white solid; m.p. 165–167 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 2.42 (s, 3H), 3.25 (t, J = 9.5 Hz, 2H), 4.86 (t, J = 9.5 Hz, 2H), 7.26 (d, J = 7.5 Hz, 2H), 7.73 (d, J = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz, ppm) δ 21.5, 27.1, 74.3, 89.4, 101.0, 128.4, 128.9, 129.1, 141.4, 160.3, 160.4, 169.3; IR (KBr, cm^{-1}): ν = 1742, 1612, 1553, 1509, 963, 733; MS calcd m/z 306.0, found 307.2 $[(M + 1)]^+$. Anal. calcd for $C_{14}H_{11}BrO_3$: C, 54.75; H, 3.61; found: C, 54.92; H, 3.59.

7-Bromo-6-(*o*-tolyl)-2*H*-furo[3,2-*c*]pyran-4(3*H*)-one (2b). Yield: 83% (254 mg, 0.83 mmol); white solid; m.p. 125–127 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 2.32 (s, 3H), 3.26 (t, J = 9.5 Hz, 2H), 4.87 (t, J = 9.5 Hz, 2H), 7.25–7.40 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 19.4, 27.2, 74.4, 92.0, 101.4, 125.6, 129.3, 130.4, 130.5, 131.4, 136.9, 160.4, 162.1, 168.7; IR (KBr, cm^{-1}): ν = 1727, 1617, 1559, 1489, 1086, 961, 735; MS calcd m/z 306.0, found 307.1 $[(M + 1)]^+$. Anal. calcd for $C_{14}H_{11}BrO_3$: C, 54.75; H, 3.61; found: C, 55.02; H, 3.68.

7-Bromo-6-(2-methoxyphenyl)-2*H*-furo[3,2-*c*]pyran-4(3*H*)-one (2c). Yield: 79% (254 mg, 0.79 mmol); white solid; m.p. 152–154 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 3.25 (t, J = 9.5 Hz, 2H), 3.85 (s, 3H), 4.85 (t, J = 9.5 Hz, 2H), 6.98 (t, J = 1.1 Hz, 1H), 7.03 (t, J = 4.0 Hz, 1H), 7.34–7.36 (m, 1H), 7.44–7.48 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 27.2, 55.6, 74.3, 92.7, 101.3, 111.3, 120.3, 120.8, 130.6, 132.2, 157.0, 159.8, 160.7, 168.8; IR (KBr, cm^{-1}): ν = 1713, 1618, 1555, 1492, 957, 751; MS calcd m/z 322.0, found 323.2 $[(M + 1)]^+$. Anal. calcd for $C_{14}H_{11}BrO_4$: C, 52.04; H, 3.43; found: C, 52.27; H, 3.46.

6-(Benzo[*d*][1,3]dioxol-5-yl)-7-bromo-2*H*-furo[3,2-*c*]pyran-4(3*H*)-one (2d). Yield: 65% (218 mg, 0.65 mmol); yellow solid; m.p. 176–178 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 3.24 (t, J = 9.5 Hz, 2H), 4.84 (t, J = 9.5 Hz, 2H), 6.05 (s, 2H), 6.87 (d, J = 8.0 Hz, 1H), 7.31 (d, J = 2.0 Hz, 1H), 7.39–7.41 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 27.1, 74.3, 89.1, 100.9, 101.7, 108.0, 109.3, 109.7, 124.5, 124.9, 147.5, 149.8, 159.7, 160.1, 169.3; IR (KBr, cm^{-1}): ν = 1725, 1554, 1501, 1249, 1039, 734; MS calcd m/z 336.0, found 337.0 $[(M + 1)]^+$. Anal. calcd for $C_{14}H_9BrO_5$: C, 49.88; H, 2.69; found: C, 50.11; H, 2.61.

7-Bromo-6-phenyl-2*H*-furo[3,2-*c*]pyran-4(3*H*)-one (2e). Yield: 78% (228 mg, 0.78 mmol); white solid; m.p. 138–140 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 3.26 (t, J = 9.5 Hz, 2H), 4.87 (t, J = 9.5 Hz, 2H), 7.47–7.50 (m, 3H), 7.81–7.83 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 27.1, 74.3, 89.9, 101.3, 128.2, 129.1, 130.9, 131.3, 160.1, 160.2, 169.2; IR (KBr, cm^{-1}): ν = 1731, 1615, 1548, 1493, 962, 694; MS calcd m/z 292.0, found 293.3 $[(M + 1)]^+$. Anal. calcd for $C_{13}H_9BrO_3$: C, 53.27; H, 3.09; found: C, 53.45; H, 3.07.

X-ray crystallographic analysis of compound 2e

A colorless block crystal having approximate dimensions of 0.80 × 0.50 × 0.30 mm was mounted on a glass fiber. All measurements were made on a CCD area detector with graphite-monochromated Mo Kα radiation. The structure was solved by Patterson methods (SHELXL-97) and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined using the riding model. The final cycle of full-matrix least-squares refinement on F was based on 13 527 observed reflections ($I > 0.00\sigma(I)$) and 8387 variable parameters and converged (largest parameter shift was 0.001 times its esd) with unweighted and weighted agreement factors of R = 0.079 and R_w = 0.226. Crystal data for **2e**: $C_{13}H_9BrO_3$, M_r = 293.10, triclinic, space group $P\bar{1}$, a = 9.2625(10) Å, b = 16.6193(18) Å, c = 23.112(3) Å, α = 102.761(2)°, β = 100.394(2)°, γ = 90.159(2)°, V = 3409.6(7) Å^3, Z = 12, D_c = 1.713 g cm^{-3}, $F(000)$ = 1752.0, μ(Mo Kα) = 0.95 cm^{-3}.

7-Bromo-6-(4-chlorophenyl)-2*H*-furo[3,2-*c*]pyran-4(3*H*)-one (2f). Yield: 75% (244 mg, 0.75 mmol); white solid; m.p. 177–179 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 3.26 (t, J = 9.5 Hz, 2H), 4.87 (t, J = 9.5 Hz, 2H), 7.43–7.45 (m, 2H), 7.78 (d, J = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 27.2, 74.4, 90.1, 101.5, 128.6, 129.7, 130.5, 137.1, 159.0, 159.9, 169.0; IR (KBr, cm^{-1}): ν = 1743, 1615, 1549, 1488, 1094, 964, 722, 701; MS calcd m/z 325.9, found 326.9 $[(M + 1)]^+$. Anal. calcd for $C_{13}H_8BrClO_3$: C, 47.67; H, 2.46; found: C, 47.92; H, 2.49.

7-Bromo-6-(2-chlorophenyl)-2*H*-furo[3,2-*c*]pyran-4(3*H*)-one (2g). Yield: 45% (147 mg, 0.45 mmol); brown solid; m.p. 141–143 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 3.27 (t, J = 9.5 Hz, 2H), 4.88 (t, J = 9.5 Hz, 2H), 7.35–7.50 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 27.2, 74.5, 93.1, 102.1, 126.7, 130.0, 130.8, 131.0, 131.8, 133.4, 159.1, 160.1, 168.4; IR (KBr, cm^{-1}): ν = 1722, 1620, 1558, 1475, 1054, 954, 736; MS calcd m/z 325.9, found 327.0 $[(M + 1)]^+$. Anal. calcd for $C_{13}H_8BrClO_3$: C, 47.67; H, 2.46; found: C, 47.81; H, 2.41.

7-Bromo-6-(4-nitrophenyl)-2*H*-furo[3,2-*c*]pyran-4(3*H*)-one (2h). Yield: 31% (104 mg, 0.31 mmol); yellow solid; m.p. 187–189 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 3.28 (t, J = 9.5 Hz, 2H), 4.89 (t, J = 9.5 Hz, 2H), 8.03 (d, J = 8.5 Hz, 2H), 8.32 (t, J = 8.5 Hz, 2H); MS calcd m/z 337.0, found 338.0 $[(M + 1)]^+$. Anal. calcd for $C_{13}H_8BrNO_5$: C, 46.18; H, 2.38; N, 4.14; found: C, 46.32; H, 2.35; N, 4.19.

7-Bromo-6-(naphthalen-1-yl)-2*H*-furo[3,2-*c*]pyran-4(3*H*)-one (2i). Yield: 70% (239 mg, 0.70 mmol); yellow solid;

m.p. 179–181 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 3.31 (t, J = 9.5 Hz, 2H), 4.91 (t, J = 9.5 Hz, 2H), 7.52–7.56 (m, 3H), 7.61 (d, J = 7.0 Hz, 1H), 7.72–7.74 (m, 1H), 7.91–7.93 (m, 1H), 7.99 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 27.2, 74.5, 93.0, 101.7, 124.7, 124.8, 126.5, 127.2, 128.3, 128.6, 129.1, 130.3, 131.1, 133.4, 160.4, 161.1, 168.7; IR (KBr, cm^{-1}): ν = 1728, 1615, 1554, 1431, 959, 781; MS calcd m/z 342.0, found 343.0 [(M + 1)]$^+$. Anal. calcd for $C_{17}H_{11}BrO_3$: C, 59.50; H, 3.23; found: C, 59.77; H, 3.28.

7-Bromo-6-(thiophen-2-yl)-2*H*-furo[3,2-*c*]pyran-4(3*H*)-one (2j). Yield: 84% (250 mg, 0.84 mmol); yellow solid; m.p. 159–161 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 3.24 (t, J = 9.3 Hz, 2H), 4.84 (t, J = 9.5 Hz, 2H), 7.17–7.19 (m, 1H), 7.60–7.61 (m, 1H), 8.09–8.10 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 27.1, 74.3, 87.6, 100.4, 127.6, 131.0, 131.9, 133.3, 154.4, 159.2, 169.2; IR (KBr, cm^{-1}): ν = 1727, 1612, 1540, 1498, 1325, 1048, 965, 728; MS calcd m/z 297.9, found 298.9 [(M + 1)]$^+$. Anal. calcd for $C_{11}H_7BrO_3S$: C, 44.17; H, 2.36; found: C, 44.46; H, 2.39.

(*E*)-7-Bromo-6-styryl-2*H*-furo[3,2-*c*]pyran-4(3*H*)-one (2l). Yield: 74% (235 mg, 0.74 mmol); yellow solid; m.p. 201–203 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 3.23 (t, J = 9.5 Hz, 2H), 4.82 (t, J = 9.5 Hz, 2H), 7.14 (d, J = 16.0 Hz, 1H), 7.37–7.42 (m, 3H), 7.57 (d, J = 8.5 Hz, 2H), 7.63 (d, J = 16.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 27.3, 74.3, 90.9, 101.6, 116.3, 127.8, 129.0, 129.9, 135.1, 138.8, 157.6, 159.7, 168.7; IR (KBr, cm^{-1}): ν = 1709, 1629, 1531, 1431, 959, 696; MS calcd m/z 318.0, found 319.0 [(M + 1)]$^+$. Anal. calcd for $C_{15}H_{11}BrO_3$: C, 56.45; H, 3.47; found: C, 56.71; H, 3.40.

7-Bromo-6-(3-bromo-4-(dimethylamino)phenyl)-2*H*-furo[3,2-*c*]-pyran-4(3*H*)-one (2m). Yield: 58% (241 mg, 0.58 mmol); yellow solid; m.p. 145–147 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 2.90 (s, 6H), 3.24 (t, J = 9.5 Hz, 2H), 4.85 (t, J = 9.5 Hz, 2H), 7.06 (d, J = 8.5 Hz, 1H), 7.78–7.80 (m, 1H), 8.08 (d, J = 2.0 Hz); ^{13}C NMR, ($CDCl_3$, 125 MHz, ppm): δ 27.2, 43.6, 74.3, 89.2, 101.0, 116.8, 119.1, 125.6, 129.1, 134.9, 154.0, 158.6, 160.0, 169.2; IR (KBr, cm^{-1}): ν = 1716, 1609, 1593, 1495, 1329, 1139, 968, 736; MS calcd m/z 412.9, found 414.0 [(M + 1)]$^+$. Anal. calcd for $C_{15}H_{13}Br_2NO_3$: C, 43.40; H, 3.16; N, 3.37; found: C, 43.62; H, 3.21; N, 3.30.

6-(3-Bromo-4-(dimethylamino)phenyl)-2*H*-furo[3,2-*c*]pyran-4(3*H*)-one (3). Yield: 77% (258 mg, 0.77 mmol); yellow solid; m.p. 168–170 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 2.89 (s, 6H), 3.11 (t, J = 9.3 Hz, 2H), 4.76 (t, J = 9.5 Hz, 2H), 6.46 (s, 1H), 7.06 (d, J = 8.5 Hz, 1H), 7.68–7.72 (m, 1H), 8.02 (d, J = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 25.9, 43.6, 74.0, 92.0, 100.4, 117.8, 119.9, 125.6, 125.9, 131.5, 154.0, 161.3, 161.6, 172.0; IR (KBr, cm^{-1}): ν = 1703, 1594, 1562, 1129, 820; MS calcd m/z 335.0, found 336.0 [(M + 1)]$^+$. Anal. calcd for $C_{15}H_{14}BrNO_3$: C, 53.59; H, 4.20; N, 4.17; found: C, 53.81; H, 4.23; N, 4.21.

7-Iodo-6-phenyl-2*H*-furo[3,2-*c*]pyran-4(3*H*)-one (4a). Yield: 71% (241 mg, 0.71 mmol); white solid; m.p. 139–141 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 3.28 (t, J = 9.5 Hz, 2H), 4.83 (t, J = 9.5 Hz, 2H), 7.45–7.48 (m, 3H), 7.73–7.75 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 27.5, 59.3, 73.6, 100.1, 128.1, 129.5, 130.9, 133.2, 160.7, 163.1, 171.1; IR (KBr, cm^{-1}): ν = 1691, 1605, 1538, 1491, 966, 699; HRMS (ESI-TOF): calcd for $C_{13}H_9IO_3$ 362.9596 (M + Na$^+$), found 362.9565.

7-Iodo-6-(*p*-tolyl)-2*H*-furo[3,2-*c*]pyran-4(3*H*)-one (4b). Yield: 75% (265 mg, 0.75 mmol); white solid; m.p. 139–141 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 2.42 (s, 3H), 3.28 (t, J = 9.5 Hz, 2H), 4.82 (t, J = 9.5 Hz 2H), 7.25 (s, 2H), 7.65 (d, J = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 21.5, 27.4, 58.8, 73.6, 99.8, 128.8, 129.4, 130.3, 141.3, 160.9, 163.3, 171.2; IR (KBr, cm^{-1}): ν = 1738, 1608, 1566, 1505, 960, 732; MS calcd m/z 354.0, found 355.0 [(M + 1)]$^+$. Anal. calcd for $C_{14}H_{11}IO_3$: C, 47.48; H, 3.13; found: C, 47.67; H, 3.16.

6-(4-Chlorophenyl)-7-iodo-2*H*-furo[3,2-*c*]pyran-4(3*H*)-one (4c). Yield: 68% (254 mg, 0.68 mmol); white solid; m.p. 235–237 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 3.28 (t, J = 9.5 Hz, 2H), 4.83 (t, J = 9.3 Hz, 2H), 7.44 (d, J = 8.5 Hz, 2H), 7.70 (d, J = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz, ppm): δ 27.5, 59.6, 73.7, 100.3, 128.5, 130.9, 131.5, 137.1, 160.5, 161.8, 170.9; IR (KBr, cm^{-1}): ν = 1740, 1610, 1544, 1487, 1093, 722, 496; MS calcd m/z 373.9, found 383.9 [(M + 1)]$^+$. Anal. calcd for $C_{13}H_8ClIO_3$: C, 41.69; H, 2.15; found: C, 41.83; H, 2.12.

6-(*p*-Tolyl)-5-oxaspiro[2.5]oct-6-ene-4,8-dione (5). White solid; m.p. 76–78 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 1.99–2.06 (m, 2H), 2.12–2.16 (m, 1H), 2.29–2.33 (m, 1H), 2.41 (s, 3H), 5.55 (s, 1H), 7.24 (s, 2H), 7.51 (d, J = 8.0 Hz, 2H); MS calcd m/z 228.1, found 229.1 [(M + 1)]$^+$. Anal. calcd for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30; found: C, 73.86; H, 5.41.

7-Bromo-6-(*p*-tolyl)-6,7-dihydro-2*H*-furo[3,2-*c*]pyran-4(3*H*)-one (6). White solid; m.p. 110–112 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 2.36 (s, 3H), 2.36–3.05 (m, 2H), 4.67–4.76 (m, 2H), 4.87–4.89 (m, 1H), 5.63 (d, J = 5.5 Hz, 1H), 7.20 (d, J = 8.0 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H). MS calcd m/z 308.0, found 309.0 [(M + 1)]$^+$. Anal. calcd for $C_{14}H_{13}BrO_3$: C, 54.39; H, 4.24; found: C, 54.55; H, 4.29.

6-(*p*-Tolyl)-2*H*-furo[3,2-*c*]pyran-4(3*H*)-one (7). White solid; m.p. 145–147 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, ppm): δ 2.40 (s, 3H), 3.11 (t, J = 9.3 Hz, 2H), 4.76 (t, J = 9.5 Hz, 2H), 6.53 (s, 1H), 7.26 (d, J = 8.0 Hz, 2H), 7.72 (d, J = 8.5 Hz, 2H); MS calcd m/z 228.1, found 229.2 [(M + 1)]$^+$. Anal. calcd for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30; found: C, 73.95; H, 5.38.

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