Oxidative Cyclization of 3-Cinnamoyltropolones with I_2/DMSO/H_2SO_4 System

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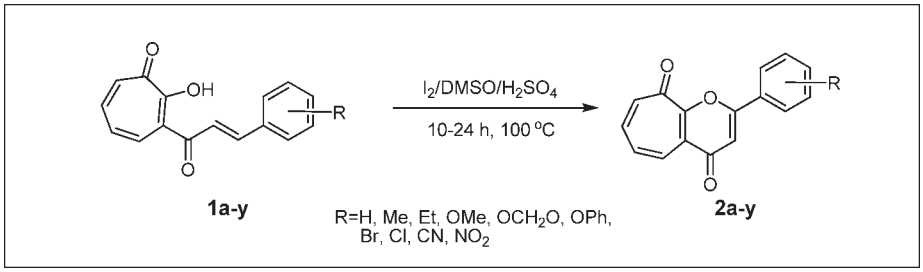
Received December 1, 2008
DOI 10.1002/jhet.150
Published online 27 October 2009 in Wiley InterScience (www.interscience.wiley.com).



In this study, a facile and general method synthesizing flavone-like 2-aryl-4,9-dihydrocyclohepta[*b*]-pyran-4,9-diones (**2a–y**) from 3-cinnamoyltropolones (**1a–y**) *via* oxidative cyclization reaction by using I_2/DMSO/H_2SO_4 system is described. The method was found to be successfully applicable to a wide range of 3-cinnamoyltropolone derivatives and characterized by generality, compatibility, and easy work-up procedures.

J. Heterocyclic Chem., **46**, 1107 (2009).

INTRODUCTION

Heterocycle-fused troponoids are a type of compounds with physiological activities such as anticancer [1], germicide, antiphlogistic [2], antihypertension [3], and antidiabetic [4]. They are included in many natural products such as alkaloids and antibiotics. For example, a new antimalarial tropolone, named cordytropolone, was discovered in a culture broth of *Cordyceps* [5]. Heterocycle-fused troponoids can be synthesized in many ways, among which one was to oxidize the side chain of tropolone for cyclization. For instance, it was reported that flavone-like heterocycle-fused troponoid compounds, 2-aryl-4,9-dihydrocyclohepta[*b*]pyran-4,9-diones, were obtained by oxidative cyclization of 3-cinnamoyltropolones using selenium dioxide [6] or 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) [7] as oxidative reagents. We have ever reported that reactions of unsubstituted 3-cinnamoyltropolone or 3-cinnamoyl-5-phenylazo-substituted tropolone with excess bromine can also give heterocycle-fused flavone-like compounds [8]. Although these practical syntheses have been described so far, these methods, however, are limited to unsubstituted or specifically substituted 3-cinnamoyltropolones and lack generality, compatibility, easy work-up procedures, regiochemical control, and high yields. Another approach reported by Wang *et al*. [9] to 2-aryl-4,9-dihydrocyclohepta[*b*]pyran-4,9-diones was based on the reactions of 3-acetyltropolone with methoxyl- and/or hydroxy-substituted benzaldehydes in the presence of triethyl orthoformate and with perchloric acid as the oxidant. However, Wang's procedure is also limited to methoxy- and/or hydroxy-substituted benzaldehyde derivatives and is not applicable to a large number of starting materials. In view of the aforementioned drawbacks, we deemed it desirable to develop a simpler, more efficient, and broadly applicable synthetic approach with a wide range of substrates to overcome the previously mentioned disadvantages. Recently, a method has been reported for the synthesis of flavone compounds from 2′-hydroxychalcone via oxidative cyclization reaction using I_2/DMSO/H_2SO_4 system [10,11]. The reactions were completed in a few hours at 100°C in DMSO, and a catalytic amount of I_2 and concentrated H_2SO_4 to give flavone compounds in good yields. In connection with our studies, we envisioned that the system could also be applied to 3-cinnamoyltropolones, from which flavone-like compounds 2-aryl-4,9-dihydrocyclohepta[*b*]pyran-4,9-diones may be synthesized through oxidative cyclization reaction. Indeed, this was found to be the case and, to the best of our knowledge, it is the first example of the application of the I_2/DMSO/H_2SO_4 system in the oxidative cyclization reaction of 3-cinnamoyltropolones.

RESULTS AND DISCUSSION

Scheme 1 outlines the synthetic sequence used in our laboratories for the preparation of heterocycle-fused flavone-like compounds **2a–y**. The starting materials of our study were readily prepared from 3-acetyltropolone and various benzaldehyde derivatives by aldol condensation [6].

To check the feasibility of this approach using I_2/DMSO/H_2SO_4 system and show a comparable result, we initially chose the representative unsubstituted 3-cinnamoyltropolone (**1a**) and methoxy-substituted 3-cinnamoyltropolones **1d–f** and **1q–t** to perform the initial experiments because their oxidative cyclization reactions have been previously reported by using different oxidative reagents [6–9,12]. As reported earlier, using hydrogen peroxide in the presence of alkali substrates, **1a**, **1d–f**, and **1q–t**, could not be converted into flavone-like compounds [12]. In [6], only **1a** and **1d–f** could be converted to corresponding flavone-like products **2a** and **2d–f** while using SeO_2 as oxidative cyclization reagent. Moreover, this method has some drawbacks, such as the use of toxic reagent, tedious work-up procedures, and narrow scope of the substrates. When under the action of elemental bromine [8], only substrate **1a** could react to give flavone-like products, but the bromination reaction of the aromatic ring of **1a** also occurred at the same time under this condition. In the oxidation cyclization of 3-cinnamoyltropolones with DDQ [7], only unsubstituted and 3-methoxy-substituted 3-cinnamoyltropolones (**1a**, **1e**) gave the flavone-like compounds **2a** and **2e**, while the other methoxy-substituted ones, such as **1d**, **1f**, and **1q–t**, are often limited and gave aurone-like products. However, in our experiment, upon treatment with I_2/DMSO/H_2SO_4 system at 100°C for 10 h, these substrates were all smoothly converted to their corresponding flavone-like compounds (**2a**, **2d–f**, and **2q–t**), which are acceptable to good yields. Thus, I_2/DMSO/H_2SO_4 system offered a general method for the oxidative cyclization reaction of a wide variety of 3-cinnamoyltropolone substrates. The compounds **2a**, **2d–f**, **2q**, and **2t** are known compounds and their structures were unambiguously confirmed by the physical and spectroscopic data, which were in good agreement with the reported values. Through an effort to optimize the reaction conditions, such as the reaction temperature and the amount of the I_2/DMSO/H_2SO_4 system, we found that the best results were achieved when the reactions were conducted at a temperature of 100°C with a ratio of 1 mmol 3-cinnamoyltropolone to 8 mL DMSO, 10 mg I_2, and 3–4 drops of concentrated H_2SO_4. We also found that the addition of increased amounts of I_2 or H_2SO_4 lowered the purity and yield of products.

To establish the generality and applicability of this method, a wide variety of 3-cinnamoyltropolones containing electron-donating (such as alkyl or alkoxyl group) and electron-withdrawing (such as cyano, nitro, or halide groups) substituents were subjected to the same set of experiments to furnish the corresponding flavone-like compounds. The results summarized in Table 1 indicated the scope and generality of the oxidation cyclization reaction with respect to various 3-cinnamoyltropolones.

Scheme 1

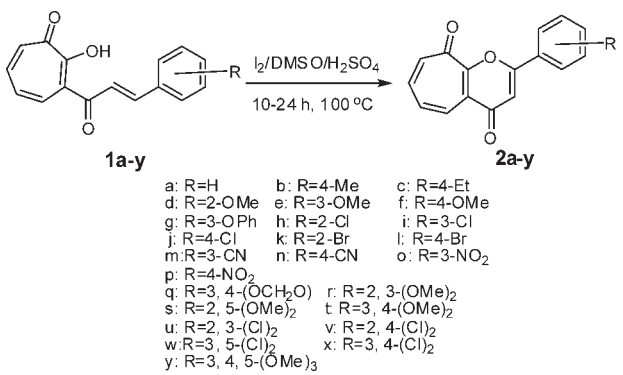


Table 1

Yields and melting points of compounds 2.

Substrate	R	Product	Yield (%)	mp (°C)
1a	H	**2a**	52 ([6]: 70)	202–204 ([6]: 201–202)
1b	4-Me	**2b**	59	190–192
1c	4-Et	**2c**	60	197–199
1d	2-OMe	**2d**	41 ([6]: 56)	216–218 ([6]: 218–220)
1e	3-OMe	**2e**	55 ([6]: 50)	211–213 ([6]: 212–214)
1f	4-OMe	**2f**	70 ([6]: 46)	238–240 ([6]: 231–233)
1g	3-OPh	**2g**	65	198–201
1h	2-Cl	**2h**	58	212–213
1i	3-Cl	**2i**	34	200–202
1j	4-Cl	**2j**	66	288–299
1k	2-Br	**2k**	52	222–223
1l	4-Br	**2l**	61	252–254
1m	3-CN	**2m**	80	296–298
1n	4-CN	**2n**	46	301–302
1o	3-NO_2	**2o**	75	298–300
1p	4-NO_2	**2p**	71	304–305
1q	3,4-(OCH_2O)	**2q**	92 ([9]: 74)	281–283 ([9]: 278–279)
1r	2,3-$(OMe)_2$	**2r**	63	192–194
1s	2,5-$(OMe)_2$	**2s**	33	186–188
1t	3,4-$(OMe)_2$	**2t**	81 ([9]: 64)	268–270 ([9]: 264–265)
1u	2,3-$(Cl)_2$	**2u**	53	218–220
1v	2,4-$(Cl)_2$	**2v**	44	226–227
1w	3,5-$(Cl)_2$	**2w**	53	272–274
1x	3,4-$(Cl)_2$	**2x**	59	260–261
1y	3,4,5-$(OMe)_3$	**2y**	63	249–251

From Table 1, we could see that this method was found to be effective for both electron-donating and electron-withdrawing substituents to afford flavone-like products in moderate to good yields. For example, 3-cinnamoyltropolones, **1c**, **1f**, and **1q**, bearing electron-donating groups on the benzene ring were reacted to give the corresponding products: 2-(4-ethylphenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (**2c**), 2-(4-methoxyphenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (**2f**), and 2-(1,3-benzodioxol-5-yl)-4,9-dihydrocyclohepta[*b*]-pyran-4,9-dione (**2q**) in 60%, 70%, and 92% yields, respectively. On the other hand, 3-cinnamoyltropolones, **1m**, **1o,** and **1x**, bearing electron-withdrawing groups gave the following products: 2-(3-cyanophenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (**2m**), 2-(3-nitrophenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (**2o**), and 2-(3,4-dichlorophenyl)-4,9-dihydrocyclohepta[*b*]-pyran-4,9-dione (**2x**) in 80%, 75%, and 59% yields, respectively. Thus, we concluded that the electronic nature of the substituents on 3-cinnamoyltropolones has no significant effect on this reaction. Among them, the compounds **2b–c**, **2g–p**, **2r–s,** and **2u–y** have never been reported, and their structures were confirmed by IR, ^{1}H NMR, ^{13}C NMR, and MS. These results showed that our protocol could tolerate a variety of functional groups on the benzene ring. However, we found that when the benzene ring of 3-cinnamoyltropolones was replaced with the pyridine ring, the reaction became complex under the same conditions and a prolonged reaction time of more than 48 h provided only a trace amount of oxidation cyclization products.

The ease of isolation of compounds **2a–y** was notable; after aqueous work-up, flavone-like compounds **2a–y** were isolated as the main products and their structures were analyzed. When the compounds were developed on thin-layer chromatography (TLC; silica gel: GF254, developing agent: ethyl acetate), there was only one main spot with no tailing. The compounds had the negative coloring test with iron (III) chloride in methanol solution. The IR spectrum exhibited an absence of hydroxyl group, which appeared in 3-cinnamoyltropolones, and the presence of two typical carbonyl absorptions for the tropone and pyran moiety at about 1640 and 1600 cm^{-1}, respectively. The ^{1}H NMR spectrum showed the absence of a hydroxy OH signal and the presence of one signal attributable to the proton of the pyran ring in addition to the signals of other groups. In ^{13}C NMR spectra, all the synthesized compounds showed peaks in the 180–183 and 169–172 ppm range for two carbonyl carbons of tropone and pyran (detailed spectral data are given in the ''Experimental'' section). In addition, the structure assigned for this reaction product was fully supported by their mass spectrum as well as their elemental analysis. All these facts show that the hydroxyl group in the tropolone ring had taken part in the reaction.

We believe that this method is the simplest route for the preparation of a wide range of flavone-like compounds, requiring only simple, cheap reagent, and mild conditions.

EXPERIMENTAL

Melting points (uncorrected) were determined using WRS-1B melting points apparatus. The ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded with a Varian Inova 400 NMR spectrometer at 400 MHz. The reported chemical shifts were against TMS. The mass spectra were determined using an MSD VL ESI1 spectrometer. Elemental analysis was performed using an Elementar Vario EL-III element analyzer. The progress of reactions was monitored by TLC on silica gel GF254 using ethyl acetate as eluent.

General procedure for the reaction of 3-cinnamoyltropolones 1a–y with I_2/DMSO/H_2SO_4 system. To a solution of 3-cinnamoyltropolones (1 mmol) in 8 mL DMSO, 3–4 drops of concentrated H_2SO_4 were added. The mixture obtained was stirred for 10 min at 100°C, and then I_2 (10 mg) was added to the mixture and continued to stir at the same temperature. After 10–24 h, the completion of reaction was monitored by TLC, the mixture was cooled to room temperature, and the precipitate formed was filtered, washed with water, and dried to yield crude 2-aryl-4,9-dihydrocyclohepta[*b*]pyran-4,9-diones, which was purified by recrystallization to give pure 2-aryl-4,9-dihydrocyclohepta[*b*]pyran-4,9-diones **2a–y** in 33–92% yield.

2-Phenyl-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2a). This compound was obtained as yellow needles (1,4-dioxane); IR (potassium bromide): ν 3058 (CH), 1660 (tropone CO), 1600 (pyran CO), 1520, 1510, 1390, 1190, 1120, 900, 820, 770, 690 cm^{-1}; ^{1}H NMR (CF_3COOD, 400 MHz): δ 8.13−9.06 ppm (m, 10H, ArH, PhH, C=CH); ^{13}C NMR (CF_3COOD, 100 MHz): δ 182.78, 182.65, 171.54, 163.09, 144.53, 138.70, 135.84, 131.83, 130.72, 129.78, 128.69, 119.91, 117.10, 114.28, 111.47, 109.29; ms: *m/z* 251 $(M+1)^+$. Anal. Calcd for $C_{16}H_{10}O_3$: C, 76.79; H, 4.03. Found: C, 76.82; H, 3.99.

2-(4-Methylphenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2b). This compound was obtained as yellowish gray needles (1,4-dioxane); IR (potassium bromide): ν 3066 (CH), 2970 (CH), 1640 (tropone CO), 1590 (pyran CO), 1510, 1470, 1420, 1380, 1350, 1300, 1185, 1120, 1040, 890, 820, 710 cm^{-1}; ^{1}H NMR (CF_3COOD, 400 MHz): δ 7.93−8.92 (m, 9H, ArH, PhH, C=CH), 2.97 ppm (s, 3H, CH_3); ^{13}C NMR (CF_3COOD, 100 MHz): δ 182.43, 182.00, 172.43, 162.58, 161.13, 144.39, 144.4, 138.80, 135.28, 131.65, 129.07, 126.71, 119.95, 117.14, 114.32, 111.50, 108.25, 21.39 ppm; ms: *m/z* 265 $(M+1)^+$. Anal. Calcd for $C_{17}H_{12}O_3$: C, 77.26; H, 4.58. Found: C, 77.37; H, 4.53.

2-(4-Ethylphenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2c). This compound was obtained as yellow needles (ethanol); IR (potassium bromide): ν 3070 (CH), 2985 (CH), 1640 (tropone CO), 1590 (pyran CO), 1520, 1505, 1420, 1375, 1220, 1110, 960, 840, 820, 700 cm^{-1}; ^{1}H NMR (CF_3COOD, 400 MHz): δ 7.29–8.33 (m, 9H, ArH, PhH, C=CH), 2.60–2.67 (q, 2H, CH_2, J = 7.6 Hz, 14.8 Hz), 1.38 ppm (t, 3H, CH_3, J = 6.2 Hz); ^{13}C NMR (CF_3COOD, 100 MHz): δ

182.66, 182.22, 172.31, 162.82, 156.63, 146.73, 144.54, 138.94, 135.35, 133.74, 132.21, 131.59, 129.29, 127.08, 120.09, 117.27, 114.45, 111.64, 108.55, 30.08, 14.72, and 14.54 ppm; ms: *m/z* 279 $(M+1)^+$. Anal. Calcd for $C_{18}H_{14}O_3$: C, 77.68; H, 5.07. Found: C, 77.74; H, 4.99.

2-(2-Methoxyphenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2d). This compound was obtained as yellow needles (1,4-dioxane); IR (potassium bromide): ν 3060 (CH), 2920 (CH), 1630 (tropone CO), 1610 (pyran CO), 1590, 1515, 1490, 1450, 1380, 1295, 1250, 1190, 1015, 750 cm^{-1}; ^1H NMR (CF_3COOD, 400 MHz): δ 7.51–8.73 (m, 9H, ArH, PhH, C=CH), 4.40 ppm (s, 3H, OCH_3); ^{13}C NMR (CF_3COOD, 100 MHz): δ 182.20, 181.97, 171.10, 162.21, 144.50, 138.89, 135.55, 132.04, 130.65, 127.79, 123.16, 120.07, 117.25, 114.44, 113.69, 113.07, 111.62, 56.53 ppm; ms: *m/z* 281 $(M+1)^+$. Anal. Calcd for $C_{17}H_{12}O_4$: C, 72.85; H, 4.32. Found: C, 72.91; H, 4.28.

2-(3-Methoxyphenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2e). This compound was obtained as yellow needles (1,4-dioxane); IR (potassium bromide): ν 3060 (CH), 2960 (CH), 1650 (tropone CO), 1590 (pyran CO), 1520, 1495, 1475, 1440, 1385, 1350, 1290, 1180, 1115, 870, 790, 700 cm^{-1}; ^1H NMR (CF_3COOD, 400 MHz): δ 7.86–9.03 (m, 9H, ArH, PhH, C=CH), 4.57 ppm (s, 3H, OCH_3); ^{13}C NMR (CF_3COOD, 100 MHz): δ 182.98, 182.92, 170.35, 162.72, 144.66, 138.81, 135.24, 132.27, 129.76, 122.38, 121.44, 120.03, 117.22, 114.50, 111.58, 109.99, 56.72 ppm; ms: *m/z* 281 $(M+1)^+$. Anal. Calcd for $C_{17}H_{12}O_4$: C, 72.85; H, 4.32. Found: C, 72.81; H, 4.35.

2-(4-Methoxyphenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2f). This compound was obtained as golden needles (1,4-dioxane); IR (potassium bromide): ν 3040 (CH), 2920 (CH), 1640 (tropone CO), 1600 (pyran CO), 1510, 1250, 1380, 1270, 1190, 1110, 1020, 830, 810, 690 cm^{-1}; ^1H NMR (CF_3COOD, 400 MHz): δ 7.60–8.82 (m, 9H, ArH, PhH, C=CH), 4.47 ppm (s, 3H, OCH_3); ^{13}C NMR (CF_3COOD, 100 MHz): δ 180.44, 178.99, 171.42, 165.85, 161.52, 142.64, 137.39, 133.93, 130.63, 128.84, 126.43, 120.35, 118.34, 116.02, 115.52, 112.70, 109.89, 105.33, 54.84 ppm; ms: *m/z* 281 $(M+1)^+$. Anal. Calcd for $C_{17}H_{12}O_4$: C, 72.85; H, 4.32. Found: C, 72.87; H, 4.29.

2-(3-Phenoxyphenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2g). This compound was obtained as yellow needles (1,4-dioxane); IR (potassium bromide): ν 3050 (CH), 1640 (tropone CO), 1605 (pyran CO), 1585, 1520, 1480, 1440, 1380, 1350, 1270, 1230, 1210, 1175, 1110, 870, 700 cm^{-1}; ^1H NMR (CF_3COOD, 400 MHz): δ 7.00–8.44 ppm (m, 14H, ArH, PhH, C=CH); ^{13}C NMR (CF_3COOD, 100 MHz): δ 183.23, 170.17, 163.54, 156.92, 144.79, 138.85, 135.25, 132.37, 131.90, 131.40, 130.04, 126.34, 125.04, 123.37, 121.14, 120.13, 117.77, 114.50, 111.68, 110.15 ppm; ms: *m/z* 343 $(M+1)^+$. Anal. Calcd for $C_{22}H_{14}O_4$: C, 77.18; H, 4.12. Found: C, 77.04; H, 4.32.

2-(2-Chlorophenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2h). This compound was obtained as pale yellow needles (1,4-dioxane); IR (potassium bromide): ν 3058 (CH), 1655 (tropone CO), 1600 (pyran CO), 1511, 1472, 1430, 1370, 1339, 1170, 1010, 1028, 815, 760, 700 cm^{-1}; ^1H NMR (CF_3COOD, 400 MHz): δ 7.78–9.02 ppm (m, 9H, ArH, PhH, C=CH); ^{13}C NMR (CF_3COOD, 100 MHz): δ 183.12, 182.94, 169.31, 163.66, 145.06, 138.72, 135.22, 132.19, 130.10, 128.58, 119.89, 117.57, 115.75, 114.26, 111.44 ppm; ms: *m/z* 285 $(M+1)^+$. Anal. Calcd for $C_{16}H_9ClO_3$: C, 67.50; H, 3.19. Found: C, 67.64; H, 3.10.

2-(3-Chlorophenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2i). This compound was obtained as yellow solids (1,4-dioxane); IR (potassium bromide): ν 3060 (CH), 1650 (tropone CO), 1600 (pyran CO), 1520, 1470, 1410, 1365, 1305, 1180, 1110, 880, 700; ^1H NMR (CF_3COOD, 400 MHz): δ 7.46–8.54 ppm (m, 9H, ArH, PhH, C=CH); ^{13}C NMR (CF_3COOD, 100 MHz): δ 182.46, 168.34, 162.45, 143.91, 138.14, 136.90, 134.55, 131.57, 129.33, 127.73, 125.90, 119.31, 116.49, 113.68, 110.86, 109.63 ppm; ms: *m/z* 285 $(M+1)^+$. Anal. Calcd for $C_{16}H_9ClO_3$: C, 67.50; H, 3.19. Found: C, 67.47; H, 3.16.

2-(4-Chlorophenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2j). This compound was obtained as yellow needles (1,4-dioxane); IR (potassium bromide): ν 3060 (CH), 1650 (tropone CO), 1614 (pyran CO), 1512, 1490, 1410, 1370, 1340, 1286, 1175, 1091, 890, 832, 810, 700 cm^{-1}; ^1H NMR (CF_3COOD, 400 MHz): δ 7.83–8.84 ppm (m, 9H, ArH, PhH, C=CH); ^{13}C NMR (CF_3COOD, 400 MHz): δ 182.80, 169.48, 162.63, 144.42, 142.77, 138.70, 135.05, 131.93, 131.07, 129.72, 128.36, 119.91, 117.09, 114.28, 111.46, 109.46 ppm; ms: *m/z* 285 $(M+1)^+$. Anal. Calcd for $C_{16}H_9ClO_3$: C, 67.50; H, 3.19. Found: C, 67.57; H, 3.12.

2-(2-Bromophenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2k). This compound was obtained as pale yellow needles (1,4-dioxane); IR (potassium bromide): ν 3040 (CH), 1660 (tropone CO), 1600 (pyran CO), 1520, 1470, 1375, 1350, 1170, 1110, 1020, 820, 770, 700 cm^{-1}; ^1H NMR (CF_3COOD, 400 MHz): δ 7.81–9.13 ppm (m, 9H, ArH, PhH, C=CH); ^{13}C NMR (CF_3COOD, 100 MHz): δ 183.07, 182.92, 170.49, 163.51, 145.10, 138.71, 135.33, 134.67, 132.64, 131.91, 130.16, 129.04, 122.52, 119.87, 117.05, 115.74, 114.24, 114.42 ppm; ms: *m/z* 331 $(M+2)^+$. Anal. Calcd for $C_{16}H_9BrO_3$: C, 58.38; H, 2.76. Found: C, 58.45; H, 2.82.

2-(4-Bromophenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2l). This compound was obtained as yellow needles (1,4-dioxane); IR (potassium bromide): ν 3050 (CH), 1650 (tropone CO), 1590 (pyran CO), 1510, 1485, 1410, 1370, 1180, 1110, 1075, 1010, 890, 830, 700 cm^{-1}; ^1H NMR (CF_3COOD, 400 MHz): δ 7.77–8.77 ppm (m, 9H, ArH, PhH, C=CH); ^{13}C NMR (CF_3COOD, 100 MHz): δ 182.78, 169.47, 163.48, 144.38, 138.67, 135.01, 134.11, 131.91, 130.96, 129.65, 128.78, 119.87, 117.06, 114.24, 111.42, 109.46 ppm; ms: *m/z* 331 $(M+2)^+$. Anal. Calcd for $C_{16}H_9BrO_3$: C, 58.38; H, 2.76. Found: C, 58.28; H, 2.78.

2-(3-Cyanophenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2m). This compound was obtained as yellow needles (1,4-dioxane); IR (potassium bromide): ν 3055 (CH), 2220 (CN), 1640 (tropone CO), 1600 (pyran CO), 1511, 1425, 1370, 1300, 1185, 1110, 850, 820, 700 cm^{-1}; ^1H NMR (CF_3COOD, 400 MHz): δ 7.00–8.37 ppm (m, 9H, ArH, PhH, C=CH); ^{13}C NMR (CF_3COOD, 100 MHz): δ 182.94, 171.96, 162.83, 155.82, 151.00, 144.74, 138.25, 136.39, 131.65, 129.52, 119.41, 116.59, 113.77, 110.96 ppm; ms: *m/z* 276 $(M+1)^+$. Anal. Calcd for $C_{17}H_9NO_3$: C, 74.18; H, 3.30. Found: C, 74.25; H, 3.28.

2-(4-Cyanophenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2n). This compound was obtained as yellow needles (1,4-dioxane); IR (potassium bromide): ν 3060 (CH), 2220 (CN), 1651 (tropone CO), 1590 (pyran CO), 1510, 1420, 1380,

1295, 1160, 1110, 870, 810, 705 cm^{-1}; ^1H NMR (CF_3COOD, 400 MHz): δ 8.13–9.09 ppm (m, 9H, ArH, PhH, C=CH); ^{13}C NMR (CF_3COOD, 100 MHz): δ 183.18, 167.07, 163.59, 144.49, 138.82, 135.58, 135.13, 134.55, 132.03, 130.14, 129.07, 119.95, 117.13, 116.25, 114.31, 111.50 ppm; ms: *m/z* 276 $(M+1)^+$. Anal. Calcd for $C_{17}H_9NO_3$: C, 74.18; H, 3.30. Found: C, 74.04; H, 3.39.

2-(3-Nitrophenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2o). This compound was obtained as yellow needles (*N*,*N*-dimethylformamide); IR (potassium bromide): ν 3090 (CH), 1645 (tropone CO), 1600 (pyran CO), 1540, 1530, 1500, 1390, 1355, 1180, 1110, 915, 820, 750, 710 cm^{-1}; ^1H NMR (CF_3COOD, 400 MHz): δ 8.10–9.50 ppm (m, 9H, ArH, PhH, C=CH); ^{13}C NMR (CF_3COOD, 100 MHz): δ 183.15, 166.86, 163.53, 149.87, 144.64, 138.91, 135.28, 134.62, 132.60, 132.19, 130.20, 128.94, 123.54, 120.03, 117.21, 114.40, 111.58, 111.37 ppm; ms: *m/z* 296 $(M+1)^+$. Anal. Calcd for $C_{16}H_9NO_5$: C, 65.09; H, 3.07. Found: C, 65.12; H, 3.11.

2-(4-Nitrophenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2p). This compound was obtained as deep yellow needles (1,4-dioxane); IR (potassium bromide): ν 3060 (CH), 1650 (tropone CO), 1605 (pyran CO), 1515, 1425, 1370, 1350, 1175, 1110, 1040, 850, 810, 755, 695 cm^{-1}; ^1H NMR (CF_3COOD, 400 MHz): δ 7.84–8.73 ppm (m, 9H, ArH, PhH, C=CH); ^{13}C NMR (CF_3COOD, 100 MHz): δ 182.94, 166.49, 162.90, 151.34, 144.32, 138.67, 136.62, 135.01, 131.81, 129.92, 125.48, 119.83, 117.01. 114.19, 111.81, 111.37 ppm; ms: *m/z* 296 $(M+1)^+$. Anal. Calcd for $C_{16}H_9NO_5$: C, 65.09; H, 3.07. Found: C, 65.16; H, 3.13.

2-(1,3-Benzodioxol-5-yl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2q). This compound was obtained as yellow needles (1,4-dioxane); IR (potassium bromide): ν 3055 (CH), 2990 (CH), 1640 (tropone CO), 1595 (pyran CO), 1510, 1460, 1394, 1340, 1260, 1190, 1120, 1030, 920, 860, 850, 816, 700 cm^{-1}; ^1H NMR (CF_3COOD, 400 MHz): δ 7.45–8.85 (m, 8H, ArH, PhH, C=CH), 6.56 ppm (s, 2H, OCH_2O); ^{13}C NMR (CF_3COOD, 100 MHz): δ 182.09, 180.95, 172.2, 163.15, 156.18, 150.74, 144.28, 138.91, 135.46, 130.70, 128.31, 127.17, 123.34, 119.93, 117.11, 114.29, 111.48, 110.82, 108.38, 107.40, 104.13 ppm; ms: *m/z* 295 $(M+1)^+$. Anal. Calcd for $C_{17}H_{10}O_5$: C, 69.39; H, 3.43. Found: C, 69.33; H, 3.36.

2-(2,3-Dimethoxyphenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2r). This compound was obtained as yellow needles (1,4-dioxane); IR (potassium bromide): ν 3060 (CH), 2965 (CH), 1644 (tropone CO), 1609 (pyran CO), 1511, 1470, 1428, 1379, 1310, 1010, 910, 850, 760, 710 cm^{-1}; ^1H NMR (CF_3COOD, 400 MHz): δ 7.45–8.65 (m, 8H, ArH, PhH, C=CH), 4.18 (s, 3H, OCH_3), 4.11 ppm (s, 3H, OCH_3); ^{13}C NMR (CF_3COOD, 100 MHz): δ 182.57, 167.99, 162.45, 153.73, 148.37, 144.21, 138.10, 134.61, 131.61, 126.79, 124.29, 122.54, 119.34, 118.75, 116.53, 114.02, 113.71, 110.90, 62.07, 56.06 ppm; ms: *m/z* 311 $(M+1)^+$. Anal. Calcd for $C_{18}H_{14}O_5$: C, 69.67; H, 4.55. Found: C, 69.63; H, 4.57.

2-(2,5-Dimethoxyphenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2s). This compound was obtained as orange needles (1,4-dioxane); IR (potassium bromide): ν 3055 (CH), 2930 (CH), 1620 (tropone CO), 1590 (pyran CO), 1510, 1468, 1429, 1370, 1330, 1170, 1140, 1070, 910, 820, 700 cm^{-1}; ^1H NMR (CF_3COOD, 400 MHz): δ 7.26–8.56 (m, 8H, ArH, PhH, C=CH), 4.15 (s, 3H, OCH_3), 4.09 ppm (s, 3H, OCH_3); ^{13}C NMR (CF_3COOD, 100 MHz): δ 182.46, 168.87, 162.93, 157.4, 153.80, 144.43, 138.60, 135.16, 131.12, 128.29, 125.04, 119.82, 118.64, 117.00, 116.32, 114.99, 114.19, 113.69, 111.38, 57.48, 56.66 ppm; ms: *m/z* 311 $(M+1)^+$. Anal. Calcd for $C_{18}H_{14}O_5$: C, 69.67; H, 4.55. Found: C, 69.78; H, 4.61.

2-(3,4-Dimethoxyphenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2t). This compound was obtained as yellow needles (1,4-dioxane); IR (potassium bromide): ν 3070 (CH), 2940 (CH), 1635 (tropone CO), 1600 (pyran CO), 1510, 1465, 1430, 1380, 1330, 1265, 1150, 1020, 850, 805, 770, 700 cm^{-1}; ^1H NMR (CF_3COOD, 400 MHz): δ 7.05–8.29 (m, 8H, ArH, PhH, C=CH), 3.95 (s, 3H, OCH_3), 3.92 ppm (s, 3H, OCH_3); ^{13}C NMR (CF_3COOD, 100 MHz): δ 182.55, 181.56, 171.44, 163.26, 156.21, 151.73, 150.24, 144.45, 138.98, 135.37, 131.29, 129.26, 125.48, 122.75, 120.09, 117.27, 116.02, 114.45, 113.13, 112.22, 111.64, 110.37, 107.92, 67.78, 56.78, and 56.71 ppm; ms: *m/z* 311 $(M+1)^+$. Anal. Calcd for $C_{18}H_{14}O_5$: C, 69.67; H, 4.55. Found: C, 69.65; H, 4.57.

2-(2,3-Dichlorophenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2u). This compound was obtained as pale yellow solids (1,4-dioxane); IR (potassium bromide): ν 3065 (CH), 1660 (tropone CO), 1600 (pyran CO), 1515, 1410, 1370, 1340, 1170, 1110, 900, 870, 795 cm^{-1}; ^1H NMR (CF_3COOD, 400 MHz): δ 7.67–8.98 ppm (m, 8H, ArH, PhH, C—CH); ^{13}C NMR (CF_3COOD, 100 MHz): δ 183.75, 183.65, 169.13, 163.91, 145.77, 139.56, 137.12, 136.06, 133.23, 130.93, 129.88, 120.69, 117.87, 116.70, 115.06, 112.24 ppm; ms: *m/z* 319 $(M)^+$. Anal. Calcd for $C_{16}H_8Cl_2O_3$: C, 60.22; H, 2.53. Found: C, 60.16; H, 2.63.

2-(2,4-Dichlorophenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2v). This compound was obtained as colorless needles (1,4-dioxane); IR (potassium bromide): ν 3050 (CH), 1670 (tropone CO), 1604 (pyran CO), 1550, 1520, 1480, 1380, 1340, 1170, 1110, 890, 870, 820, 700 cm^{-1}; ^1H NMR (CF_3COOD, 400 MHz): δ 7.84–9.06 ppm (m, 8H, ArH, PhH, C=CH); ^{13}C NMR (CF_3COOD, 100 MHz): δ 183.81, 183.60, 168.72, 145.75, 142.19, 139.52, 136.01, 133.45, 130.82, 129.29, 120.66, 117.84, 116.59, 115.03, 112.22 ppm; ms: *m/z* 319 $(M)^+$. Anal. Calcd for $C_{16}H_8Cl_2O_3$: C, 60.22; H, 2.53. Found: C, 60.19; H, 2.66.

2-(3,5-Dichlorophenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2w). This compound was obtained as yellow needles (1,4-dioxane); IR (potassium bromide): ν 3040 (CH), 1650 (tropone CO), 1600 (pyran CO), 1560, 1520, 1425, 1375, 1345, 1250, 1115, 860, 800, 700 cm^{-1}; ^1H NMR (CF_3COOD, 400 MHz): δ 7.30–8.37 ppm (m, 8H, ArH, PhH, C=CH); ^{13}C NMR (CF_3COOD, 100 MHz): δ 183.07, 166.99, 163.04, 161.30, 151.73, 144.40, 138.84, 138.20, 135.02, 134.56, 133.17, 132.06, 130.03, 126.53, 119.94, 118.82, 117.12, 115.99, 114.82, 113.17, 111.49, 110.89 ppm; ms: *m/z* 319 $(M)^+$. Anal. Calcd for $C_{16}H_8Cl_2O_3$: C, 60.22; H, 2.53. Found: C, 60.28; H, 2.51.

2-(3,4-Dichlorophenyl)-4,9-dihydrocyclohepta[*b*]pyran-4,9-dione (2x). This compound was obtained as yellow needles (1,4-dioxane); IR (potassium bromide): ν 3065 (CH), 1650 (tropone CO), 1600 (pyran CO), 1520, 1468, 1410, 1370, 1340, 1180, 1140, 1110, 1030, 900, 820, 710 cm^{-1}; ^1H NMR (CF_3COOD, 400 MHz): δ 7.27–8.32 ppm (m, 8H, ArH, PhH, C=CH); ^{13}C NMR (CF_3COOD, 100 MHz): δ 183.00, 167.52, 163.40, 161.28, 144.41, 140.39, 138.86, 135.91, 135.06, 132.79, 132.08, 130.06, 127.30, 119.99, 117.17, 114.36, 111.54, 110.25 ppm; ms: *m/z* 319 $(M)^+$. Anal. Calcd for $C_{16}H_8Cl_2O_3$: C, 60.22; H, 2.53. Found: C, 60.19; H, 2.65.

2-(3,4,5-Trimethoxyphenyl)-4,9-dihydrocyclohepta[*b*]-pyran-4,9-dione (2y). This compound was obtained as yellow needles (1,4-dioxane); IR (potassium bromide): ν 3060 (CH), 2935 (CH), 1650 (tropone CO), 1610 (pyran CO), 1520, 1470, 1410, 1370 cm^{-1}; ^1H NMR (CF_3COOD, 400 MHz): δ 7.87–8.91 (m, 7H, ArH, PhH, C=CH), 4.48–4.50 ppm (m, 9H, OCH_3); ^{13}C NMR (CF_3COOD, 100 MHz): δ 182.90, 182.58, 169.80, 162.64, 154.64, 144.59, 142.97, 138.79, 135.19, 131.89, 129.56, 126.77, 119.94, 117.12, 114.31, 111.49, 109.61, 106.75, 62.25, 56.98 ppm; ms: *m/z* 341 $(M+1)^+$. Anal. Calcd for $C_{19}H_{16}O_6$: C, 67.05; H, 4.74. Found: C, 66.98; H, 4.87.

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