HETEROCYCLES, Vol. 82, No. 1, 2010, pp. 843 - 850. © The Japan Institute of Heterocyclic Chemistry
Received, 15th May, 2010, Accepted, 14th June, 2010, Published online, 16th June, 2010
DOI: 10.3987/COM-10-S(E)32

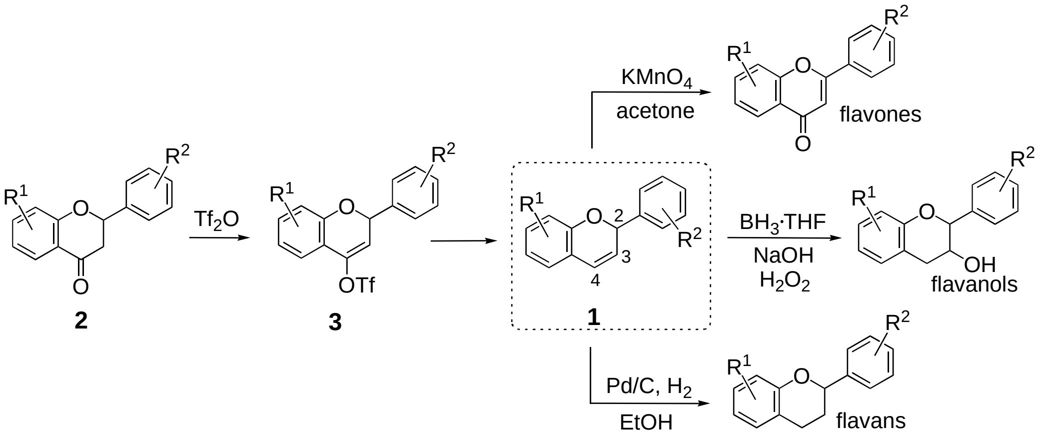
EFFICIENT TRANSFORMATION OF FLAV-3-ENES USING REDUCTIVE ELIMINATION OF FLAV-4-TRIFLATE

Yoshihito Kohari, Yukio Hoshino, Haruo Matsuyama, Hiroto Nakano*

Division of Applied Chemistry, College of Environmental Technology, Graduate School of Muroran Institute of Technology, 27-1 Mizumoto, Muroran, Hokkaido 050-8585, Japan; E-mail: catanaka@mmm.muroran-it.ac.jp

Abstract – Flav-3-enes were prepared in excellent yields (up to 98%) by reductive elimination of flav-3-ene-4-triflates in the presence of palladium acetate, formic acid and tri-*n*-buthylamine.

Flav-3-enes (3-phenyl-2*H*-1-benzopyrans) **1** are the useful intermediates of naturally occurring flavonoids such as flavones (2-phenyl-4*H*-1-benzopyran-4-ones),[1] flavans (2-phenyl-3,4-dihydro-2*H*-1-benzopyrans)[2] and flavanols (3-hydroxy-2-phenyl-3,4-dihydro-2*H*-1-benzopyrans),[3] which have *anti*-allergic, *anti*-inflammatory,[4] *anti*-microbial[5] and *anti*-cancer[6] activities (Scheme 1). It is therefore important to establish an effective synthetic methodology for the ring system **1**. Some synthetic methodologies have been reported previously for the synthesis of this ring system.[7] In particular, the condensation of *α, β*-unsaturated carbonyl compounds with phenols under different reaction conditions represents a largely used and promising route.



Scheme 1. Transformations of flav-3-ene to several flavonoids

---

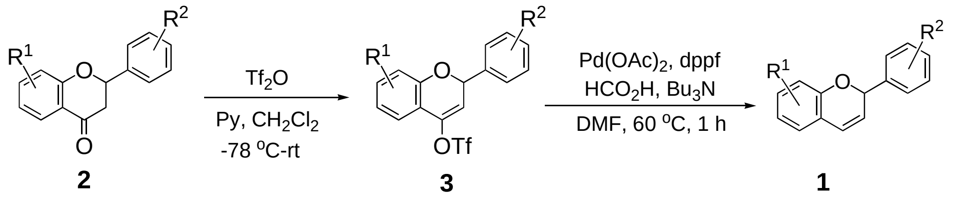
[*] Dedicated to Dr. Albert Eschenmoser on the occasion of his 85th birthday

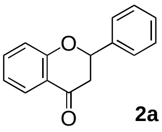
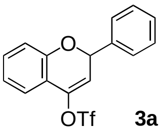
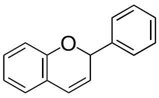
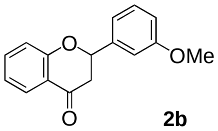
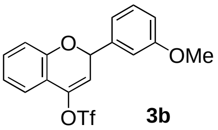
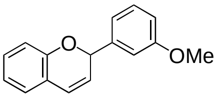
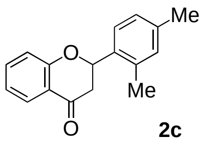
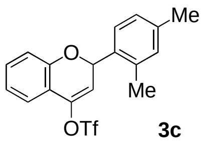
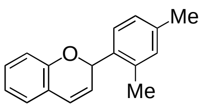
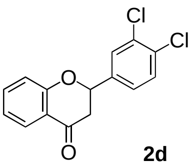
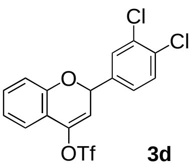
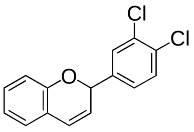
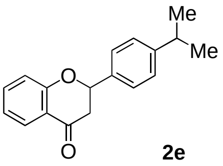
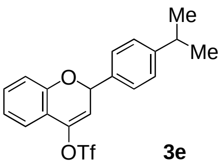
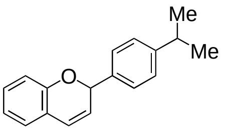
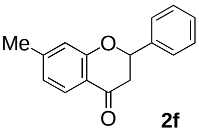
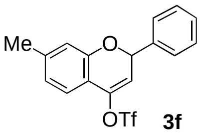
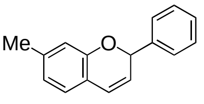
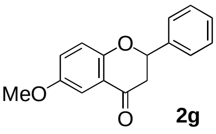
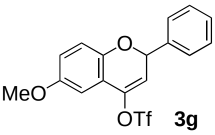
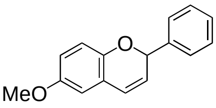
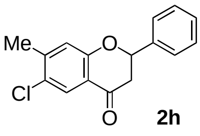
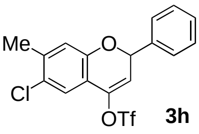
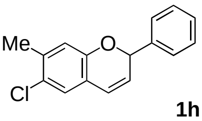
In addition, the methodology using $NaBH_4$ reduction of flavanone **2,** tosylation followed by dehydration of 4-tosylate is also efficient synthetic route.[1-3] The problem with these syntheses, however, relates to both their selectivity and their general applicability; moreover in some cases the overall yields are poor. We planed the new synthetic methodology using the conversion from **3** to vinyl triflate **2**, followed by the reductive elimination of **2** in the presence of palladium acetate, formic acid and tri-*n*-buthylamine (Scheme 1).[8] We describe in this paper the detail of our new and very simple synthetic methodology of **1** based on the reductive elimination of vinyl triflate **2**.

We attempted a conversion from ketones **2a-h** to vinyl triflates **3a-h** (Table 1). The reaction of the simplest ketone **2a** with triflic anhydride was carried out in CH_2Cl_2 in the presence of pyridine as a base at -78 °C. The reaction successfully proceeded to afford the desired triflate **3a** in excellent yield (97%, entry 1). The reactions of several ketones **2b-h** having substituents on the phenyl group at 2-position or benzopyranone ring system, respectively, were also carried out under the same reaction conditions as those used for **2a**. As a result, all of the attempted reactions afforded the desired triflates **3b-h** in fairly good to excellent yields (88-98%, entries 2-8).

Next, the reductive eliminations of triflates **3a-h** were examined (Table 1). The reactions were carried out in the presence of formic acid, tri-*n*-butylamine, and three kinds of Pd catalysts such as $Pd(OAc)_2$-dppf, $Pd(OAc)_2$-$2PPh_3$, and $Pd(PPh_3)_4$ at 60 °C. The reaction of **3a** using $Pd(OAc)_2$-dppf catalyst afforded the desired **1a** in an excellent isolated yield (95%) (entry 1). Although the use of $Pd(OAc)_2$-$2PPh_3$ or $Pd(PPh_3)_4$ as a catalyst, respectively, also afforded satisfactory yields [$Pd(OAc)_2$-$2PPh_3$: 85%, $Pd(PPh_3)_4$: 92%], they did not provide the catalytic activity of $Pd(OAc)_2$-dppf. From the above results, it can be seen that $Pd(OAc)_2$-dppf is a better catalyst for the reductive elimination of triflate **3a**. The reactions of other substrates **2b-h** were also examined under the same reaction conditions as those used for **3a** (entries 2-8). The reactions successively proceeded to afford the desired **1b-h** in moderate to excellent yields, as shown in Table 1. Both the reactions using **3b** with a methoxy substituent or **3c** with a methyl substituent on the phenyl groups as an electron-donating group brought about a decease in chemical yield with a complex mixture, although the reason for this decrease remains unclear (entries 2 and 3). It might be due to the steric and the electric factors of methyl or methoxy substituents. In addition, it might be due to the structural instability[9] of **1b** and **1c**. On the other hand, substrates **3d** or **3h** with a chlorine substituent on the phenyl group as an electron-withdrawing group, respectively, gave chemoselectively **1d** (93%) and **1h** (92%), respectively without dechlorination that is observed under these reaction conditions (entries 4 and 8).

Table 1. Triflation of **2a-h** and reductive elimination of **3a-h**



Entry	Substrate[a] **2a-h**	Time (h)[b]	Product **3a-h**	Yield (%)[c]	Product[d] **1a-h**	Yield (%)[e]
1	 **2a**	4	 **3a**	97	 **1a**	95
2	 **2b**	3	 **3b**	97	 **1b**	61
3	 **2c**	5	 **3c**	94	 **1c**	70
4	 **2d**	72	 **3d**	88	 **1d**	93
5	 **2e**	5	 **3e**	96	 **1e**	86
6	 **2f**	5	 **3f**	87	 **1f**	83
7	 **2g**	4	 **3g**	98	 **1g**	97
8	 **2h**	6	 **3h**	90	 **1h**	92

a. All reactions were carried out on a 2.0 mmol scale with Tf_2O (2.4 mmol) and pyridine (2.4 mmol) in CH_2Cl_2 under nitrogen atmosphere. *b*. Reaction time was determined by monitoring using TLC. *c*. Isolated yield after chromatography. *d*. All reactions were carried out on a 1.0 mmol scale in the presence of $Pd(OAc)_2$ (2 mol%), dppf (4 mol%), HCO_2H (2.0 mmol) and Bu_3N (3.0 mmol) in dry-DMF under nitrogen atmosphere. *e*. Isolated yield after chromatography.

In conclusion, we have developed an efficient synthetic methodology for obtaining the flav-3-enes, which are useful intermediates for the synthesis of flavonids. Thus the conversion from flavanones **2** to flav-3-enes **1** *via* triflates **3** was accomplished in total yields of 61-95% under very mild conditions. This new methodology can be extended to the preparation of still more flav-3-enes having various substituens. Further studies to examine the scope and limitations of our new synthetic methodology for the synthesis of flavonoids are now in progress.

EXPERIMENTAL

All reactions were carried out in anhydrous solvents and under nitrogen atmosphere. Flavanones were prepared from commercially available acetophenones and benzaldehydes according to well-known method. ^{1}H and ^{13}C NMR spectra were recorded at 270 MHz and 67.8 MHz on a JEOL JNM-EX 270 FT NMR SYSTEM in $CDCl_3$ using tetramethylsilane as an internal standard. TLC analyses were performed on commercial aluminum plates bearing a 0.25-mm layer of Merck Silica gel $60F_{254}$. Silica gel (Wakogel 200 mesh) was used for column chromatography.

General procedure for synthesis of flav-3-ene-4-triflates 3a-h. Flavanone **2a** (2.0 mmol) was dissolved in dry CH_2Cl_2 (5.0 mL) along with dry pyridine (2.4 mmol) under nitrogen. The solution was cooled at -78 °C. 2.4 mmol of trifluoromethanesulfonic anhydride was slowly added. The resulting mixture was allowed to warm to 0 °C, stirred at 0 °C for 1 h, then warmed to room temperature, and stirred until flavanone disappeared by monitoring using TLC. The reaction mixture was extracted with Et_2O and the extract was washed with H_2O, 1M aq. HCl and brine, and dried over $MgSO_4$. The solvent was removed and the residue was isolated by silica gel column chromatography (hexane/EtOAc 4:1) to afford **3a**.

2-Phenyl-4-trifluoromethanesulfonyloxy-2*H*-1-benzopyrane (3a). Light yellow oil, *Rf* 0.64 (4:1 hexane/EtOAc), ^{1}H NMR ($CDCl_3$): δ 5.81 (d, 1H, *J* = 3.8 Hz), 6.07 (d, 1H, *J* = 3.8 Hz), 6.82 (d, 1H, *J* = 8.0 Hz), 6.95 (t, 1H, *J* = 7.6 Hz), 7.21 (td, 1H, *J* = 8.0, 1.5 Hz), 7.29 (dd, 1H, *J* = 7.6, 1.5 Hz), 7.34-7.46 (m, 5H), ^{13}C NMR ($CDCl_3$): δ 76.3, 113.1, 116.4, 116.6, 121.6, 121.6, 127.1, 128.3, 128.9, 129.1, 131.8, 138.8, 143.1, 153.8.

3’-Methoxy-2-phenyl-4-trifluoromethanesulfonyloxy-2*H*-1-benzopyran (3b). A Light yellow oil, *Rf* 0.59 (4:1 hexane/EtOAc), ^{1}H NMR ($CDCl_3$): δ 3.78 (s, 3H), 5.83 (d, 1H, *J* = 3.8 Hz), 6.08 (d, 1H, *J* = 3.6 Hz), 6.85 (d, 1H, *J* = 8.3 Hz), 6.89-7.04 (m, 3H), 7.22-7.34 (m, 3H), ^{13}C NMR ($CDCl_3$): δ 55.2, 77.1, 112.5, 113.0, 114.8, 116.4, 116.6, 119.3, 121.6, 121.7, 130.0, 131.8, 140.3, 143.2, 153.8, 160.0.

2',4'-Dimethyl-2-phenyl-4-trifluoromethanesulfonyloxy-2*H*-1-benzopyran (3c). A light yellow oil, *Rf* 0.73 (4:1 hexane/EtOAc), ^{1}H NMR ($CDCl_3$): δ 2.30 (s, 3H), 2.44 (s, 3H), 5.76 (d, 1H, *J* = 3.6 Hz), 6.29 (d, 1H, *J* = 3.6 Hz), 6.79(dd, 1H, *J* = 8.3, 1.0 Hz), 6.80 (td, 1H, *J* = 7.6, 1.0 Hz), 7.00-7.05 (m, 2H), 7.21 (td, 1H, *J* = 7.6, 1.0 Hz), 7.27-7.33 (m, 2H), ^{13}C NMR ($CDCl_3$): δ 19.1, 21.0, 74.9, 113.1, 116.5, 121.5, 121.6, 127.0, 128.0, 131.7, 132.0, 133.3, 136.3, 139.1, 143.4, 154.1.

3',4'-Dichloro-2-phenyl-4-trifluoromethanesulfonyloxy-2*H*-1-benzopyran (3d). A light yellow oil, *Rf* 0.66 (4:1 hexane/EtOAc), ^{1}H NMR ($CDCl_3$): δ 5.80 (d, 1H, *J* = 4.0 Hz), 6.07 (d, 1H, *J* = 4.0 Hz), 6.86 (d, 1H, *J* = 8.3 Hz), 7.00 (td, 1H, *J* = 7.6, 1.0 Hz), 7.29 (dd, 1H, *J* = 8.3, 2.2 Hz), 7.47 (d, 1H, *J* = 8.3 Hz), 7.55 (d, 1H, *J* = 2.2 Hz), ^{13}C NMR ($CDCl_3$): δ 75.0, 116.2, 116.7, 121.9, 122.1, 126.3, 129.2, 131.0, 132.1, 133.1, 133.3, 138.9, 143.7, 153.4.

4'-Isopropyl-2-phenyl-4-trifluoromethanesulfonyloxy-2*H*-1-benzopyran (3e). A light yellow oil, *Rf* 0.73 (4:1 hexane/EtOAc), ^{1}H NMR ($CDCl_3$): δ 1.23 (d, 6H, *J* = 6.9 Hz), 2.90 (q, 1H, *J* = 6.9 Hz), 5.81 (d, 1H, *J* = 3.8 Hz), 6.60 (d, 1H, *J* = 3.8 Hz), 6.82 (dd, 1H, *J* = 8.1, 1.0 Hz), 6.94 (td, 1H, *J* = 7.6, 1.0 Hz), 7.21 (td, 1H, *J* = 7.8, 1.5 Hz), 7.24 (d, 2H, *J* = 8.3 Hz), 7.29 (dd, 1H, *J* = 7.8, 1.5 Hz), 7.37 (d, 2H, *J* = 8.3 Hz), ^{13}C NMR ($CDCl_3$): δ 23.8, 33.9, 77.3, 113.2, 116.4, 116.6, 121.5, 121.6, 127.0, 127.3, 131.7, 136.2, 143.1, 150.0, 153.9.

7-Methyl-2-phenyl-4-trifluoromethanesulfonyloxy-2*H*-1-benzopyran (3f). A light yellow oil, *Rf* 0.65 (4:1 hexane/EtOAc), ^{1}H NMR ($CDCl_3$): δ 2.23 (s, 3H), 5.75 (d, 1H, *J* = 3.8 Hz), 6.04 (d, 1H, *J* = 3.8 Hz), 6.65 (s, 1H), 6.76 (d, 1H, *J* = 7.8 Hz), 7.16 (d, 1H, *J* = 7.8 Hz), 7.33-7.45 (m, 5H), ^{13}C NMR ($CDCl_3$): δ 21.5, 77.3, 111.8, 113.8, 121.4, 127.1, 128.9, 129.0, 139.0, 142.7, 143.4, 153.8.

7-Methoxy-2-phenyl-4-trifluoromethanesulfonyloxy-2*H*-1-benzopyran (3g). A light yellow oil, *Rf* 0.63 (4:1 hexane/EtOAc), ^{1}H NMR ($CDCl_3$): δ 3.76 (s, 3H), 5.86 (d, 1H, *J* = 4.0 Hz), 6.03 (d, 1H, *J* = 3.8 Hz), 6.78-6.83 (m, 3H), 7.35-7.43 (m, 5H), ^{13}C NMR ($CDCl_3$): δ 55.7, 77.1, 106.6, 113.9, 117.1, 117.4, 117.5, 127.1, 128.9, 129.1, 138.7, 143.2, 147.7, 154.3.

6-Chlro-7-methyl-2-phenyl-4-trifluoromethanesulfonyloxy-2*H*-1-benzopyran (3h). A light yellow oil, *Rf* 0.65 (7:1 hexane/EtOAc), ^{1}H NMR ($CDCl_3$): δ 2.29 (s, 3H), 5.83 (d, 1H, *J* = 4.0 Hz), 6.07 (d, 1H, *J* = 4.0 Hz), 6.72 (s, 1H), 7.23 (s, 1H), 7.37-7.41 (m, 5H); ^{13}C NMR ($CDCl_3$): δ 20.3, 77.5, 113.0, 115.5, 119.0, 121.8, 127.0, 127.1, 129.0, 129.3, 138.5, 140.1, 142.2, 152.2.

General procedure for the synthesis of flav-3-enes (2-phenyl-2*H*-1-benzopyrans) 1a-h. To a mixture of **3a** (1.0 mmol) and tri-*n*-butylamine (3.0 mmol) in dry DMF (2.0 mL), formic acid (2.0 mmol) was added in the presence of palladium acetate (0.02 mmol) and 1,1'-bis(diphenylphosphino)ferrocene (0.04 mmol) under nitrogen. The resulting mixture was stirred at 60 °C for 1 h. The reactiom mixture was exracted with Et_2O and the extract was washed with H_2O and brine, and dried over $MgSO_4$. The solvent was removed and the residue was isolated by silica gel column chromatography (hexane/EtOAc 10:1) to afford **1a**.

2-Phenyl-2*H*-1-benzopyran (1a).[10] A light yellow oil, *Rf* 0.55 (4:1 hexane/EtOAc), ^{1}H NMR ($CDCl_3$): δ 5.79 (dd, 1H, *J* = 9.9, 3.5 Hz), 5.91 (dd, 1H, *J* = 3.3, 2.0 Hz), 6.53 (dd, 1H, *J* = 9.8, 1.4 Hz), 6.78 (d, 1H, *J* = 8.8 Hz), 6.86 (td, 1H, *J* = 8.0, 1.5 Hz), 7.29 (dd, 1H, *J* = 7.6, 1.5 Hz), 7.34-7.46 (m, 5H), ^{13}C NMR ($CDCl_3$): δ77.1, 116.0, 121.2, 121.3, 123.9, 124.8, 126.6, 127.0, 128.3, 128.6, 129.4, 140.8, 153.1, HRMS (EI): calcd for $C_{15}H_{12}O$: 208.0880; found: 208.0892.

3'-Methoxy-2-phenyl-2*H*-1-benzopyran (1b). A light yellow oil, *Rf* 0.42 (10:1 hexane/EtOAc); ^{1}H NMR ($CDCl_3$): δ 3.74 (s, 3H), 5.75 (dd, 1H, *J* = 9.7, 3.3 Hz), 5.85 (dd, 1H, *J* = 3.3, 2.0 Hz), 6.48 (dd, 1H, *J* = 9.7, 2.0 Hz), 6.77-7.28 (m, 8H), ^{13}C NMR ($CDCl_3$): δ 55.1, 76.9, 112.5, 113.7, 115.9, 119.2, 121.1, 121.2, 123.9, 124.7, 126.5, 129.4, 129.6, 142.4, 153.1, 159.8, HRMS (EI): calcd for $C_{16}H_{14}O_2$: 238.0994; found: 238.0994.

2',4'-Dimethyl-2-phenyl-2*H*-1-benzopyran (1c). A light yellow oil, *Rf* 0.55 (10:1 hexane/EtOAc), ^{1}H NMR ($CDCl_3$): δ 1.22 (s, 3H), 1.25 (s, 3H), 5.79 (dd, 1H *J* = 9.9, 3.5 Hz), 5.88 (dd, 1H, *J* = 3.5, 1.7 Hz), 6.52 (dd, 1H, *J* = 9.7, 1.6 Hz), 6.77 (d, 1H, *J* = 7.9 Hz), 6.85 (td, 1H, *J* = 7.4, 1.2 Hz), 7.00 (dd, 1H, *J* = 7.4, 1.8 Hz), 7.09 (td, 1H, *J* = 7.9, 1.8 Hz), 7.21 (m, 3H), ^{13}C NMR ($CDCl_3$): δ 23.9, 33.9, 77.1, 116.0, 116.6, 121.1, 121.3, 123.9, 125.0, 127.0, 127.1, 129.1, 131.7, 138.2, 149.1, 153.2, HRMS (EI): calcd for $C_{17}H_{15}O$: 235.1124; found: 235.1127.

3',4'-Dichloro-2-phenyl-2*H*-1-benzopyran (1d). A light yellow oil, *Rf* 0.49 (10:1 hexane/EtOAc), ^{1}H NMR ($CDCl_3$): δ 5.69 (dd, 1H *J* = 9.7, 3.5 Hz), 5.80 (dd, 1H, *J* = 3.5, 1.5 Hz), 6.39 (dd, 1H, *J* = 9.7, 1.5 Hz), 6.77 (d, 1H, *J* = 7.9 Hz), 6.85 (td, 1H, *J* = 7.3, 1.2 Hz), 6.97 (dd, 1H, *J* = 7.4, 1.7 Hz), 7.09 (td, 1H, *J* = 7.8, 1.8 Hz), 7.23 (dd, 1H, *J* = 8.3, 1.9 Hz), 7.36 (d, 1H, *J* = 8.3 Hz), 7.50 (d, 1H, *J* = 1.2 Hz), ^{13}C NMR ($CDCl_3$): δ 75.5, 116.0, 120.9, 121.5, 123.4, 124.7, 126.2, 126.7, 128.9, 129.7, 130.5, 132.2, 132.6, 140.9, 152.6, HRMS (EI): calcd for $C_{15}H_{10}OCl_2$: 276.0109; found: 276.0110.

4'-Isopropyl-2-phenyl-2*H*-1-benzopyran (1e). A light yellow oil, *Rf* 0.58 (10:1 hexane/EtOAc), ^{1}H NMR ($CDCl_3$): δ 1.20 (d, 6H, *J* = 6.9 Hz), 2.85 (q, 1H, *J* = 6.9 Hz), 5.71 (dd, 1H, *J* = 9.9, 3.3 Hz), 5.83 (d, 1H, *J* = 3.3 Hz), 6.45 (d, 1H, *J* = 8.1 Hz), 6.78 (td, 1H, *J* = 7.4, 1.2 Hz), 6.94 (dd, 1H, *J* = 7.3, 1.7 Hz), 7.04 (td, 1H, *J* = 7.6, 1.8 Hz), 7.18 (d, 2H, *J* = 8.1 Hz), 7.34 (d, 2H, *J* = 8.1 Hz), ^{13}C NMR ($CDCl_3$): δ 23.9, 33.8, 77.0, 115.9, 121.0, 121.3, 123.8, 124.9, 126.5, 126.6, 127.1, 129.3, 138.2, 149.0, 153.2, HRMS (EI): calcd for $C_{18}H_{18}O$: 250.1358; found: 250.1360.

7-Methyl-2-phenyl-2*H*-1-benzopyran (1f). A light yellow oil, *Rf* 0.58 (10:1 hexane/EtOAc), ^{1}H NMR ($CDCl_3$): δ 2.24 (s, 3H), 5.70 (dd, 1H, *J* = 9.9, 3.4 Hz), 5.86 (d, 1H, *J* = 3.4 Hz), 6.47 (d, 1H, *J* = 9.9 Hz), 6.61 (s, 1H), 6.65 (d, 1H, *J* = 7.5 Hz), 6.87 (d, 1H, *J* = 7.5 Hz), 7.28-7.44 (m, 5H), ^{13}C NMR ($CDCl_3$): δ 21.4, 77.1, 116.6, 118.6, 121.8, 123.7, 123.8, 126.3, 127.0, 128.2, 128.6, 139.7, 141.0, 153.0, HRMS (EI): calcd for $C_{16}H_{14}O$: 222.1045; found: 222.1045.

7-Methoxy-2-phenyl-2*H*-1-benzopyran (1g). A light yellow oil, *Rf* 0.51 (10:1 hexane/EtOAc), ^{1}H NMR ($CDCl_3$): δ 3.72 (s, 3H), 5.79-5.84 (m, 2H), 6.48 (dd, 1H, *J* = 10.7, 2.8 Hz), 6.57 (d, 1H, *J* = 2.8 Hz), 6.65 (dd, 1H, *J* = 8.7, 2.8 Hz), 6.72 (d, 1H, *J* = 8.7 Hz), 7.28-7.44 (m, 5H), ^{13}C NMR ($CDCl_3$): δ 55.6, 76.9, 111.7, 114.5, 116.5, 122.0, 124.1, 125.8, 127.0, 128.2, 128.6, 140.7, 147.0, 154.0, HRMS (EI): calcd for $C_{16}H_{14}O_2$: 238.0994; found: 238.1002.

6-Chlro-7-methyl-2-phenyl-2*H*-1-benzopyran (1h). A light yellow oil, *Rf* 0.64 (10:1 hexane/EtOAc), ^{1}H NMR ($CDCl_3$): δ 2.27 (s, 3H), 5.80 (dd, 1H, *J* = 9.73, 3.46 Hz), 5.87 (dd, 1H, *J* = 3.5, 1.7 Hz), 6.46 (dd, 1H, *J* =9.7, 1.7 Hz), 6.66 (s, 1H), 6.98 (s, 1H), 7.71-7.44 (m, 5H), ^{13}C NMR ($CDCl_3$): δ 20.1, 77.1, 118.3, 120.4, 123.0, 125.0, 126.0, 126.4, 127.0, 128.5, 128.7, 137.0, 140.4, 151.4, HRMS (EI): calcd for $C_{16}H_{13}OCl$: 256.0655; found: 256.0655.

REFERENCES

1. Y. Ashihara, Y. Nagata, and K. Kurosawa, *Bull. Chem. Soc. Jpn.*, 1977, **50**, 3298.
2. J. L. Asherson, O. Bilgic, and D. W. Young, *J. Chem. Soc., Perkin. Trans. 1*, 1980, 522.
3. (a) M. D. Agli, S. Bellosta, L. Rizzi, G. V. Galli, M. Canavesi, F. Rota, R. Parente, E. Bosisio, and S. Romeo, *Cell. Mol. Life. Sci.*, 2005, **65**, 2896; (b) V. Arnaudinaud, B. Nay, S. Vergé, A. Nuhrich, G. Deffieux, J. M. Mérillon, J. P. Monti, and J. Vercauteren, *Tetrahedron Lett.*, 2001, **42**, 1279; (c) V. Arnaudinaud, B. Nay, S. Vergé, A. Nuhrich, G. Deffieux, J. M. Mérillon, J. P. Monti, and J. Vercauteren, *Tetrahedron Lett.*, 2001, **42**, 5669.
4. Y. Yamamoto and R. B. Gaynor, *J. Clin. Invest.*, 2001, **107**, 135.

5. T. P. T. Cushnie and A. J. Lamb, *Int. J. Antimicrob. Agents,* 2005, **26**, 343.
6. R. R. de Sousa, K. C. Queiroz, A. C. Souza, S. A. Gurgueira, A. C. Augusto, and M. A. Miranda, M. P. Peppelenbosch, C. V. Ferreira, and H. Aoyama, *J. Enzyme Inhib. Med. Chem.*, 2007, **22**, 439.
7. E. Grotewold, '*The Science of Flavonoids*', Springer, Science & Business Media, Inc., New York, 2006.
8. (a) J. Tsuji, '*Transition Metal Reagents and Catalysts: Innovations in Organic Synthesis*.' Wiley: Chichester, U. K., 2000; (b) S. Cacchi, P. G. Ciattini, E. Morera, and G. Ortar, *Tetrahedron Lett*., 1984, **25**, 4821; (c) R. E. Dolle, S. J. Schmidt, and L. I. Kruse, *Tetrahedron Lett*., 1988, **29**, 1581.
9. A reversible mechanism has been reported from a compound similar to **1** to a ring-opened isomer; (a) M. Sakuragi, Y. Kawanishi, Y. Suzuki, and H. Sakuragi, *Bull. Chem. Soc. Jpn.,* 2008, **81,** 641; (b) A. Padwa, A. Au, G. A. Lee and W. Owens, *J. Org. Chem.*, 1975, **40**, 1142; (c) Y. Kodama, T. Nakabayashi, K. Segawa, E. Hattori, M. Sakuragi, N. Nishi, and H. Sakuragi, *J. Phys. Chem., A.* 2000, **104**, 11478.
10. J.-R. Labrosse, P. Lhoste, and D. Sinou, *Synth. Commun*., 2002, **32**, 3667.