Three-Component Barbier Allylation, Friedel–Crafts Alkylation and Intramolecular Hydroalkoxylation in an Ionic Liquid for the Direct Synthesis of 4-Arylchromans

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Abstract: 4-Arylchromans can be synthesized directly using a one-pot Barbier allylation, Friedel–Crafts alkylation and intramolecular hydroalkoxylation of aromatic aldehydes, allylbromides and phenols in an ionic liquid (BPyX–$SnCl_2 \cdot 2H_2O$). The intramolecular hydroalkoxylation of 4-aryl-4-(2-hydroxylphenyl)but-1-enes can be promoted using the Lewis acid $ZnCl_2$ in an ionic liquid.

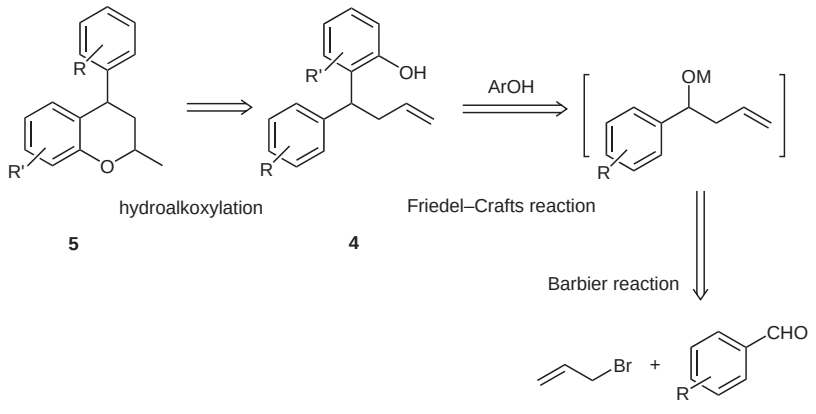
Key words: Barbier, Friedel–Crafts, hydroalkoxylation, one-pot process, 4-arylchroman, ionic liquid

3,4-Dihydro-2*H*-benzopyran (chroman) is an important structural unit in many natural compounds with biological and pharmaceutical activities.[1] Among them, 4-arylchromans have also received considerable attention due to the interest in their biological activities, including inhibition of prostaglandin synthesis,[2] anti-estrogenic and anti-fertility,[3] α_1-adrenoreceptor subtypes,[4] polymerase β-inhibitors and COX-2 inhibitors.[5] A lot of synthetic methods have been developed for the construction of the chroman unit. One of the most convenient and efficient methods is through intramolecular cyclization of an appropriate substrate.[6]

In terms of retrosynthetic analysis, 4-aryl-4-(2′-hydroxylphenyl)but-1-ene (**4**) is a favorable precursor to 4-arylchromans (**5**) with the aid of an intramolecular cyclization reaction. The precursor **4** can be synthesized through the Friedel–Crafts alkylation of phenols with allyl benzyl alcohol derivatives,[7] which in turn can be prepared by Barbier allylation of carbonyl compounds.[8]

Combining sequences of individual transformations into a one-pot process to reduce synthetic steps and enhance synthetic efficiency is challenging in the synthesis of heterocyclics.[9] If the formation of intermediate (**4**) and final product (**5**) can be combined into a one-pot tandem process then the direct synthesis of 4-arylchromans from simple and readily available starting materials can be achieved.

Recently, we reported that Barbier–Prins cyclization reactions can be carried out in a one-pot manner in an ionic liquid to accomplish a direct synthesis of tetrahydropyran compounds.[10] Continuing our interest in one-pot multicomponent reactions in ionic liquids, we report herein a one-pot Barbier allylation, Friedel–Crafts alkylation and intramolecular hydroalkoxylation of allylbromides, aromatic aldehydes and phenols promoted by the ionic liquid BPyX–$SnCl_2 \cdot 2H_2O$ for the direct synthesis of 4-arylchromans (Scheme 1).



Barbier/Friedel–Crafts/hydroalkoxylation in a one-pot process

Scheme 1

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The $SnCl_2$-mediated Barbier-type reaction of allylhalides with carbonyl compounds is an efficient method in the preparation of homoallylic alcohols, although it requires additional catalyst in most cases. Among the catalysts suitable for this type of reaction, quaternary ammonium salts are most convenient.[11] As reported, mixing quaternary ammonium salts, BPyCl or BPyI, with $SnCl_2{\cdot}2H_2O$ (1:2) under solvent-free conditions produced complexes **10a** or **10b** (Figure 1),[12] which were in liquid state at room temperature (so-called room-temperature ionic liquids). It is expected that the ionic liquids (**10a** and **10b**) can serve as both a functionalized reagent with Lewis acidity and as reaction media in the three-component reaction of allylbromide, aromatic aldehydes and phenols.[13]

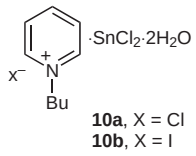
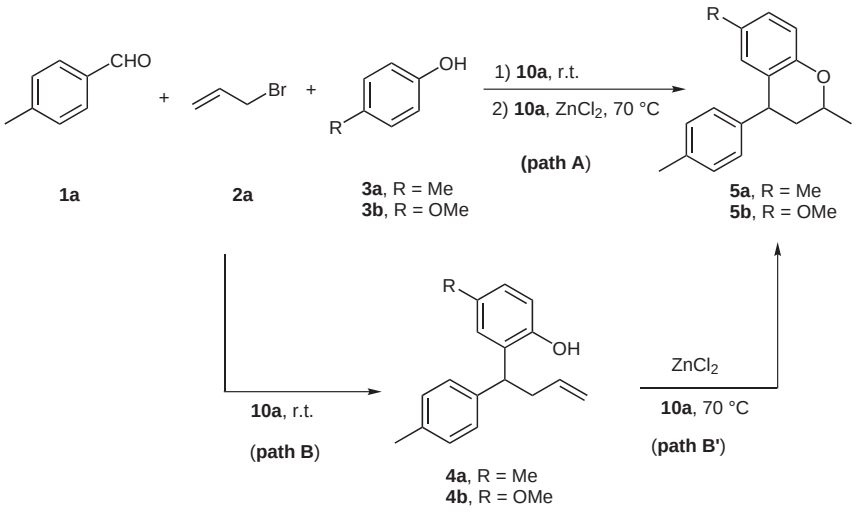


Figure 1

Considering the regioselectivity of the Friedel–Crafts alkylation, the *para*-substituted phenols (**3a**–**b**) were selected as one of the three components for the synthesis of chroman compounds. At first, the three-component reaction of allylbromide **2a**, *p*-methylbenzaldehyde (**1a**) and *p*-methylphenol (**3a**) (R = Me) was attempted in ionic liquid **10a**. There was no organic solvent and the reaction was carried out at room temperature for 24 hours. The Barbier allylation/Friedel–Crafts alkylation product, 4-(4′-methylphenyl)-4-(2′-hydroxyl-4′-methylphenyl)but-1-ene (**4a**) was obtained in 76% yield (Scheme 2, path B). The Friedel–Crafts alkylation occurred at the *ortho*-position of the phenolic hydroxyl group to give exclusively *ortho*-isomers. However, no product of the subsequent intramolecular cyclization was detected. For **3b** (R = OMe) bearing both methoxy and hydroxyl groups in the phenyl ring, the hydroxyl-directed *ortho*-selectivity in the Friedel–Crafts alkylation was still predominate, giving *ortho*-hydroxyl-substituted product **4b** as the sole regioisomer in 64% yield despite the methoxy group being a strong *para*- and *ortho*-directing group.

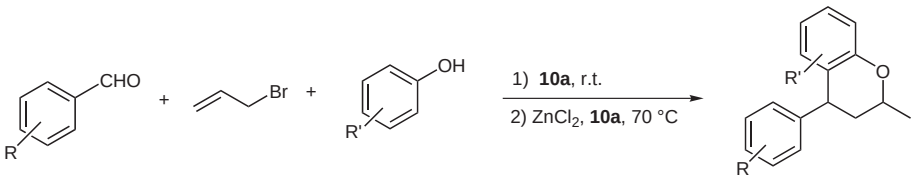
Recently, studies on the addition of an O–H bond to an alkene forming a C–O bond (hydroalkoxylation) have progressed greatly. Intramolecular hydroalkoxylation is an ideal method to use in the synthesis of 4-arylchromans from 4-aryl-4-(2′-hydroxylphenyl)-but-1-enes (for example **4a**–**b**). Various catalysts are suitable for hydroalkoxylation reactions, including protonic acids such as triflic acid (TfOH),[14] Lewis acids such as $AlCl_3$,[15] $FeCl_3$,[16] $Cu(OTf)_2$,[17] $Sn(OTf)_4$[18] and transition-metal reagents,[19] as well as *N*-bromosuccimide (NBS).[20] More recently, Li[21] and Youn[22] reported respectively, that chroman units can be constructed through AgOTf/$AuCl_3$- or AgOTf-catalyzed intramolecular hydroalkoxylation. As reported,[14] hydroalkoxylation reactions depend strongly on the reactivity of the double bond involved in the reaction, which decrease in the following order, trisubstituted > *gem*-disubstituted > monosubstituted. It was found that $Yb(OTf)_3$, $Sc(OTf)_3$, AgOTf, AgOTf–$RuCl_3$, *p*-toluenesulfonic acid and HCl had no catalytic ability in the intramolecular cyclization of **4a** in both CH_2Cl_2 and ionic liquid. This was attributed to the low reactivity of **4a**, which possesses an isolated, monosubstituted terminal double bond. Although TfOH can catalyze the intramolecular hydroalkoxylation of **4a** in CH_2Cl_2 to give cyclization product **5a**, no chroman product was obtained under ionic liquid conditions in the presence of catalytic TfOH. After screening, Lewis acid $ZnCl_2$ was found to be a good catalyst for the hydroalkoxylation reaction of **4a** in **10a**, giving the product **5a** in 82% yield (Scheme 2, path B′). To our delight, after the initial reaction of **1b**, **2a** and **3a** in **10a** at room temperature for 24 hours, $ZnCl_2$ was added to the reaction and the subsequent hydroalkoxylation proceeded smoothly at 70 °C to directly afford product **5a** in 64% yield (Scheme 2, path A).



Scheme 2

Using the optimized experimental procedure, various phenolic compounds (**3a**–**d**) were reacted with **2a** and aromatic aldehydes (**1a**–**b**) in ionic liquid for the direct synthesis of 4-arylchromans. The mixture of three substrates was stirred in **10a** at room temperature for 24 hours and then $ZnCl_2$ (1.2 equiv) was added and the reaction was stirred at 70 °C for six hours, giving 4-arylchromanes (**5a**–**g**) in good yields (54–64%) (Table 1).

Table 1 Three-Component Reactions of Aldehydes, Allyl Bromide, and Phenols in Ionic Liquid **10a**[a]



1a,**b** **2a** **3a**–**d** **5a**–**g**

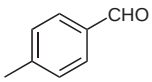
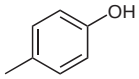
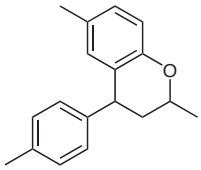
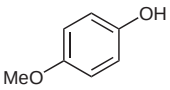
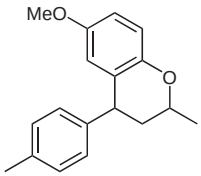
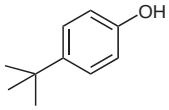
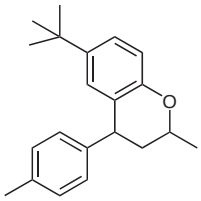
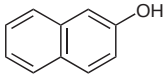
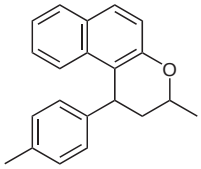
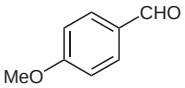
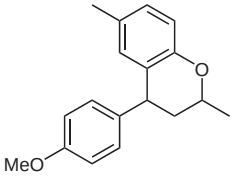
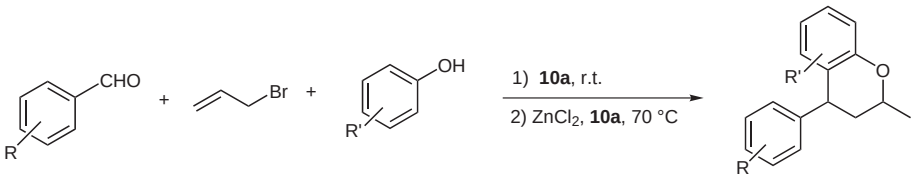
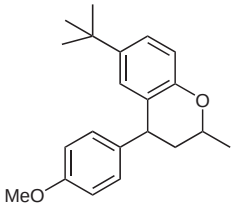
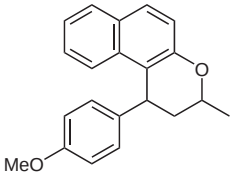
Entry	Aldehyde	Phenol	Product	Yield (%)[b]
1	 **1a**	 **3a**	 **5a**	64
2	**1a**	 **3b**	 **5b**	58
3	**1a**	 **3c**	 **5c**	63
4	**1a**	 **3d**	 **5d**	57
5	 **1b**	**3a**	 **5e**	64

Table 1 Three-Component Reactions of Aldehydes, Allyl Bromide, and Phenols in Ionic Liquid **10a**[a] (continued)



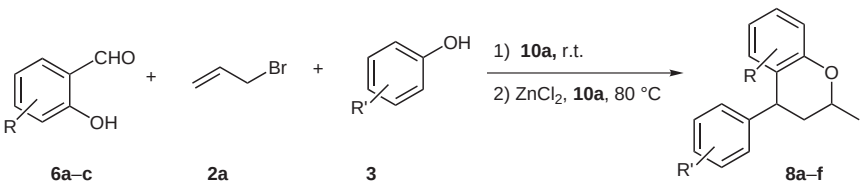
1a,**b** **2a** **3a–d** **5a–g**

Entry	Aldehyde	Phenol	Product	Yield (%)[b]
6	**1b**	**3c**	 **5f**	54
7	**1b**	**3d**	 **5g**	63

[a] (i) 24 h, r.t.; (ii) $ZnCl_2$, 70 °C, 6 h.
[b] Isolated yield.

The use of 2-hydroxylbenzaldehydes (salicylaldehydes, **6a**–**c**) extended the scope of the substrates suitable for the three-component reaction. Phenols without a substituent at the *para*-position of the phenolic hydroxyl group (**3e**–**h**) are also suitable substrates for the three-component reaction in ionic liquid **10a**. Salicylaldehydes not only participated in the Barbier/Friedel–Crafts reaction, but the hydroxyl group in their molecules was also involved in $ZnCl_2$ mediated intramolecular hydroalkoxylation in ionic liquid, giving the cyclization products, 4-arylchromans **8a**–**f** (Table 2).[23] Even anisole (**7**) can be used as a substrate in the three-component reaction to afford the 4-arylchroman product **8g** in 58% yield (Table 2, entry 7). The products (**5a**–**g** and **8a**–**g**) are mixtures of a pair of diastereomers with diastereomeric ratios (dr) in the range of 1:1 to 1:1.2, determined by ^1H NMR spectra.

Table 2 One-Pot Reactions of Aldehydes **6a**–**c**, Allyl Bromide, and Phenols in Ionic Liquid **10a**[a]



6a–c **2a** **3** **8a–f**

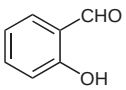
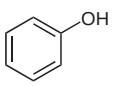
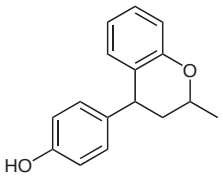
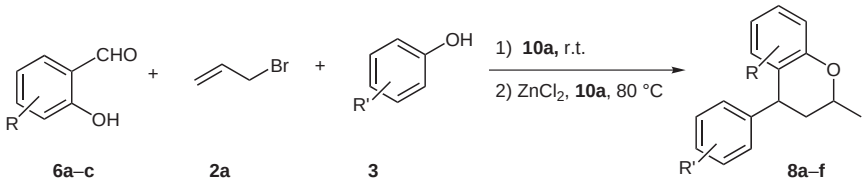
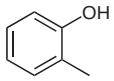
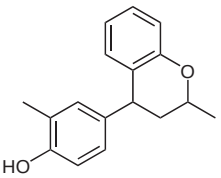
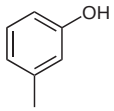
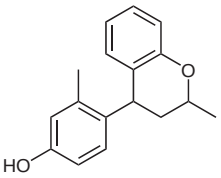
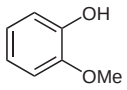
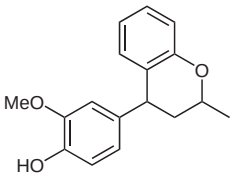
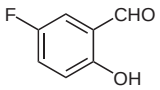
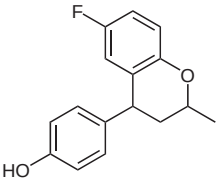
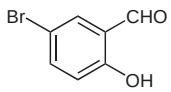
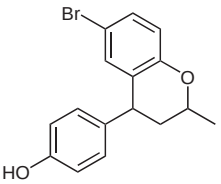
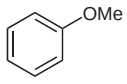
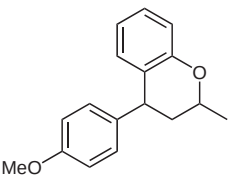
Entry	Aldehyde	Phenol	Product	Yield (%)[b]
1	 **6a**	 **3e**	 **8a**	70

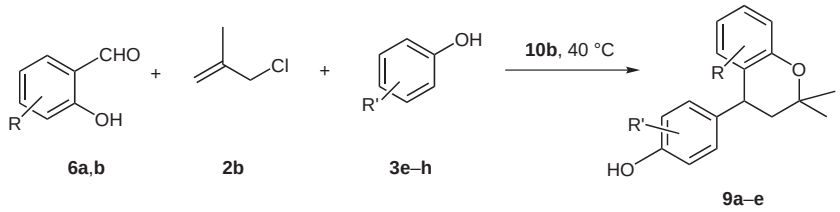
Table 2 One-Pot Reactions of Aldehydes **6a–c**, Allyl Bromide, and Phenols in Ionic Liquid **10a**[a] (continued)



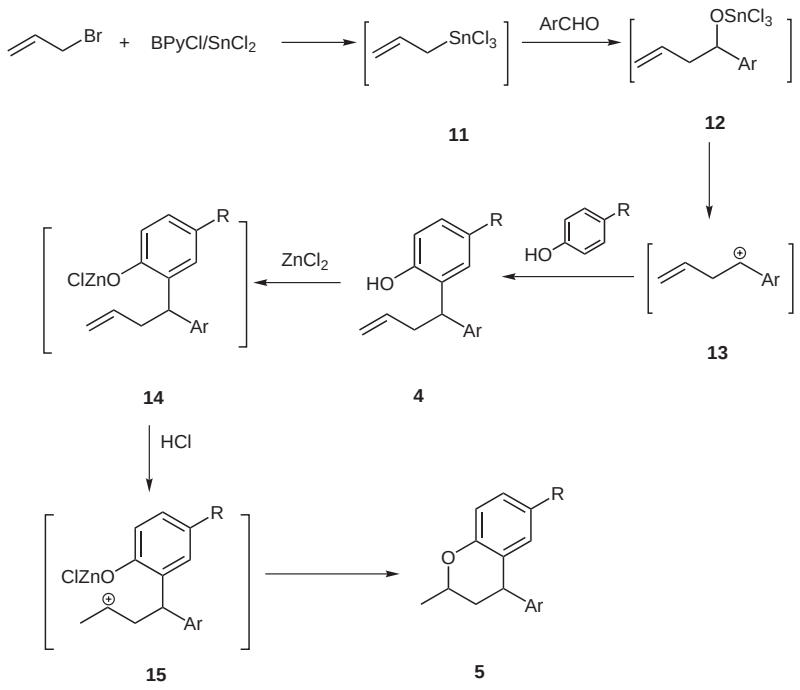
6a–c **2a** **3** **8a–f**

Entry	Aldehyde	Phenol	Product	Yield (%)[b]
2	**6a**	 **3f**	 **8b**	64
3	**6a**	 **3g**	 **8c**	62
4	**6a**	 **3h**	 **8d**	64
5	 **6b**	**3e**	 **8e**	53
6	 **6c**	**3e**	 **8f**	64
7	**6a**	 **7**	 **8g**	58

[a] Reaction conditions: (i) 10 h, r.t.; (ii) 70 °C, 6 h.
[b] Isolated yield.



Scheme 3



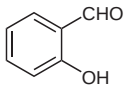
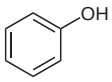
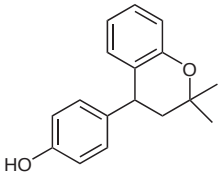
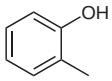
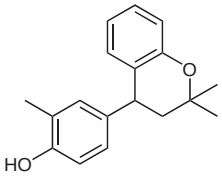
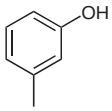
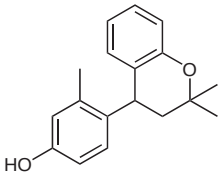
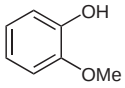
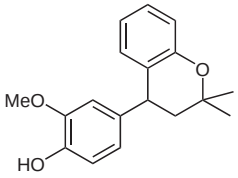
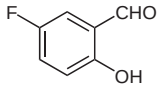
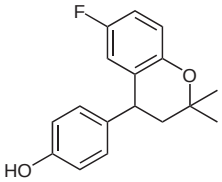
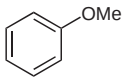
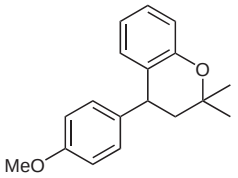
Scheme 4

When 2-methylallylchloride (**2b**) was employed in the reaction of **6a** (R = H) with **3e** (R′ = H) in **10a** at 70 °C, no product was detected and only starting materials were recovered. This was attributed to the low reactivity of allylchloride. Changing **10a** to the iodo analogue **10b**, allowed the three-component reaction to proceed smoothly at 40 °C giving the product of the Barbier/Friedel–Crafts/hydroalkoxylation reaction, 2,2-dimethyl-4-(4′-hydroxylphenyl)chroman (**9a**) in 66% yield (Scheme 3).[24] It was assumed that the transformation of chloride to iodine in allylchloride **2b** could have taken place. The involved intramolecular hydroalkoxylation did not need additional Lewis acid catalyst $ZnCl_2$, probably due to the relatively high reactivity of the *gem*-disubstituted double bond for hydroalkoxylation. The experimental results are listed in Table 3. For anisole **7**, the chroman product **9f** was also obtained in 54% yield (Table 3, entry 6).

The mechanism for the three-component reaction is proposed in Scheme 4. First, a Barbier reaction of allybromide with $SnCl_2$ in the presence of pyridine salt produces the allyltin intermediate **11**,[25] which subsequently undergoes reaction with the aldehyde to generate reactive intermediate **12**. In the reaction media (**10a**), the $OSnCl_3$ group is easily eliminated to form the benzyl carbocation **13**. In the presence of an aromatic carbon nucleophile (phenolic compound), the Friedel–Crafts alkylation of **13** takes place, giving product **4**. At that time, if $ZnCl_2$ is added, the elimination of HCl and formation of an O–Zn bond occur to generate intermediates **14** and **15**, which subsequently undergo intramolecular hydroalkoxylation to form cyclization product **5**. As indicated above, HCl did not catalyze the intramolecular hydroalkoxylation of **4a** in ionic liquid **10a** in the absence of $ZnCl_2$. BPyCl–$ZnCl_2$ does not promote the three-component Barbier, Friedel–Crafts alkylation reaction either, but is able to promote the intramolecular hydroalkoxylation of **4a** at 70 °C, affording the product **5a** in 82% yield. It can be assumed that $SnCl_2$ and $ZnCl_2$ play different roles in the one-pot process.

In summary, the Barbier allylation, Friedel–Crafts alkylation, and intramolecular hydroalkoxylation can be combined into a one-pot process promoted by a Lewis acid ionic liquid. $SnCl_2$ and $ZnCl_2$ played different roles in the one-pot process. This method provides a practical and convenient synthesis of 4-arylchromans starting from simple and commercially available materials.

Table 3 One-Pot Reactions of Aldehydes **6a–c**, Alkenyl Chloride **2b** and Phenols in Ionic Liquid **10b**

Entry	Aldehyde	Phenols	Product	Yield (%)[a]
1	 **6a**	 **3e**	 **9a**	66
2	**6a**	 **3f**	 **9b**	62
3	**6a**	 **3g**	 **9c**	60
4	**6a**	 **3h**	 **9d**	60
5	 **6b**	**3e**	 **9e**	52
6	**6a**	 **7**	 **9f**	54

[a] Isolated yield.

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References and Notes

(1) (a) Browers, W. S.; Ohta, T.; Cleere, J. S.; Marsella, P. A. *Science* **1976**, *193*, 542. (b) Ellis, G. P.; Lockhart, I. M. *Chromanes and Tocopherols*; Wiley-Interscience: New York, **1981**.

(2) Ogundaini, A.; Farah, M.; Perera, P. *J. Nat. Prod.* **1996**, *59*, 587.

(3) Hajela, K.; Pandey, J.; Dwivedy, A.; Dhar, J. D.; Sarkhel, S.; Maulik, P. R.; Velumurugan, D. *Bioorg. Med. Chem.* **1999**, *7*, 2083.
(4) Quaglia, W.; Pigini, M.; Piergentili, A.; Giannella, M.; Gentilli, F.; Marrucci, G.; Carrieri, A.; Carotti, A.; Pogges, E.; Leonardi, A.; Melchiorre, C. *J. Med. Chem.* **2002**, *45*, 1633.
(5) (a) Deng, J.-Z.; Starck, S. R.; Li, S.; Hecht, S. M. *J. Nat. Prod.* **2005**, *68*, 1625. (b) Maloney, D. J.; Starck, S. R.; Gao, Z.; Hechit, S. M. *J. Am. Chem. Soc.* **2005**, *127*, 4140. (c) Sawadjoon, S.; Kittikara, K.; Vichai, V.; Tanticharoen, M.; Thebta-Ranonth, Y. *J. Org. Chem.* **2002**, *67*, 5470.
(6) For example, see: (a) Larock, R. C.; Yang, H.; Pace, P. *Tetrahedron Lett.* **1998**, *39*, 237. (b) Trost, B. M.; Asakawa, N. *Synthesis* **1999**, 1491. (c) Nicolaou, K. C.; Pfefferkorn, J. A.; Barluenga, S.; Mitchell, H. J.; Roecker, A. J.; Cao, G.-Q. *J. Am. Chem. Soc.* **2000**, *122*, 9968. (d) Barluenga, J.; Trincado, M.; Rubio, E.; Gonzalez, J. M. *J. Am. Chem. Soc.* **2004**, *126*, 3416. (e) Merchaet, A.; Delbeke, P.; Daloze, D.; Dive, G. *Tetrahedron Lett.* **2004**, *45*, 4697. (f) Trost, B. M.; Shen, H. C.; Surivet, J.-P. *J. Am. Chem. Soc.* **2004**, *126*, 12565. (g) Vyvyan, J. R.; Oaksmith, J. M.; Parks, B. W.; Peterson, E. M. *Tetrahedron Lett.* **2005**, *46*, 2457.
(7) (a) Shiina, I.; Suzuki, M.; Yokoyama, K. *Tetrahedron Lett.* **2002**, *43*, 6395. (b) Shiina, I.; Suzuki, M.; Yokoyama, K. *Tetrahedron Lett.* **2004**, *45*, 965. (c) Mertines, K.; Iovel, I.; Kischel, J.; Zapf, A.; Beller, M. *Angew. Chem. Int. Ed.* **2005**, *44*, 238.
(8) For a review on the Barbier reaction, see: Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207.
(9) (a) *Multicomponent Reactions*; Zhu, J.; Bienayme, H., Eds.; Wiley-VCH: Weinheim, **2005**. (b) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115.
(10) Zhao, X. L.; Liu, L.; Chen, Y. J.; Wang, D. *Tetrahedron* **2006**, *62*, 7113.
(11) (a) Masuyama, Y.; Kishida, M.; Kurusu, Y. *Tetrahedron Lett.* **1996**, *37*, 7103. (b) Masuyama, Y.; Ito, A.; Kurusu, Y. *Chem. Commun.* **1998**, 315. (c) Masuyama, Y.; Ito, T.; Tachi, K.; Ito, A.; Kurusu, Y. *Chem. Commun.* **1999**, 1261. (d) Ito, A.; Kishida, M.; Kurusu, Y.; Masuyama, Y. *J. Org. Chem.* **2000**, *65*, 494.
(12) Wasserscheid, P.; Waffenschmidt, H. *J. Mol. Catal. A: Chem.* **2000**, *164*, 61.
(13) For examples of three-component reactions in ionic liquid, see: (a) Aza-Diels–Alder reaction: Yadav, J. S.; Reddy, B. V. S.; Reddy, J. S. S.; Rao, R. S. *Tetrahedron* **2003**, *59*, 1599. (b) Coupling reaction of aldehyde, alkyne and amine: Li, Z.; Wei, C.; Chen, L.; Varma, R. S.; Li, C.-J. *Tetrahedron Lett.* **2004**, *45*, 2443. (c) Mannich reaction: Kabalka, G. W.; Venkataiah, B.; Dong, G. *Tetrahedron Lett.* **2004**, *45*, 729. (d) Asymmetric Mannich reaction: Chen, S.-L.; Ji, S.-J.; Loh, T.-P. *Tetrahedron Lett.* **2003**, *44*, 2405. (e) Biginelli reaction: Peng, J.; Deng, Y. *Tetrahedron Lett.* **2001**, *42*, 5917.
(14) (a) Coulombel, L.; Dunach, E. *Green Chem.* **2004**, *6*, 499. (b) Rosenfeld, D. C.; Shekhar, S.; Takemiya, A.; Utsunomiya, M.; Hartwig, J. F. *Org. Lett.* **2006**, *8*, 4179.
(15) Bolzoni, L.; Casiraghi, G.; Casnati, G.; Sartori, G. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 684.
(16) Morimoto, T.; Takaki, K. *Angew. Chem. Int. Ed.* **2006**, *45*, 2930.
(17) Talyor, J. G.; Whittall, N.; Hii, K. K. *Chem. Commun.* **2005**, 5103.
(18) Coulombel Favier, I.; Dunach, E. *Chem. Commun.* **2005**, 2286.
(19) For examples, see: (a) Bienayme, H.; Ancel, J.-E.; Meilland, P.; Simonato, J.-P. *Tetrahedron Lett.* **2000**, *41*, 3339. (b) Qian, H.; Han, X.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2004**, *126*, 9536. (c) Oe, Y.; Ito, Y. *Chem. Commun*. **2004**, 1620. (d) Yang, C.-G.; He, Ch. *J. Am. Chem. Soc.* **2005**, *127*, 6966. (e) Gligorich, K. M.; Schultz, M. J.; Sigman, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 2794.
(20) Talluri, S. K.; Sudalai, A. *Org. Lett.* **2005**, *7*, 855.
(21) Nguyen, R.-V.; Yao, X.; Li, Ch.-J. *Org. Lett.* **2006**, *8*, 2397.
(22) Youn, S. W.; Eom, J. I. *J. Org. Chem.* **2006**, *71*, 6705.
(23) 2-Methyl-4-(4′-hydroxylphenyl)chroman (**8a**): A mixture of salicylaldehyde **6a** (61 mg, 0.5 mmol), allyl bromide (**2a**) (120 mg, 1 mmol) and phenol **3a** (69 mg, 0.75 mmol) in ionic liquid (**10a**) derived from BPyCl–$SnCl_2$·$2H_2O$ was stirred at ambient temperature for 10 h. $ZnCl_2$ (102 mg, 0.75 mmol) was added, followed by stirring at 70 °C for 5 h. The reaction mixture was extracted with Et_2O. The combined Et_2O extracts were washed with aqueous HCl (2 M), and then dried over Na_2SO_4. The solvent was removed under vacuum and the crude product was purified by flash column chromatography on silica gel (EtOAc–PE, 1:30) to afford **8a** as a colorless oil (84 mg, 70%); FTIR (film): 3394, 2971, 1649, 1612, 1581, 1514, 1483, 1455, 1232 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.10–7.30 (m, 6 H), 6.72–7.07 (m, 2 H), 4.12–4.34 (m, 2 H), 1.91–1.26 (m, 2 H), 1.38, 1.48 (2 × d, *J* = 6.9, 6.2 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.9, 153.9 (153.6)*, 138.6, 136.7, 130.5, 129.4, 129.3, 127.2 (127.6), 125.7, 120.0, 116.2 (116.5), 114.8 (115.2), 67.2 (72.2), 41.8 (38.8), 39.7 (37.5), 20.7 (21.1); (* data in parentheses represents diastereomeric peaks); HRMS (EI): *m*/*z* calcd for $C_{16}H_{16}O_2$: 240.1150; found: 240.1149.
(24) 2,2-Dimethyl-4-(4′-hydroxylphenyl)chroman (**9a**): A mixture of salicylaldehyde **6a** (61 mg, 0.5 mmol), 2-methyl-allyl chloride (**2b**) (82 mg, 1.0 mmol) and phenol **3e** (69 mg, 0.75 mmol) in ionic liquid (**10b**) derived from BPyI–$SnCl_2$·$2H_2O$ was stirred at 40 °C for 24 h. The reaction mixture was extracted with Et_2O. The combined Et_2O phase was washed with aqueous HCl (2 M), then dried over Na_2SO_4. The solvent was removed under vacuum and the crude product was purified by flash column chromatography on silica gel (EtOAc–PE, 1:30) to afford **9a** as a colorless oil (83 mg, 66%); FTIR (film): 3394, 2925, 1612, 1571, 1514, 1486, 1449, 1368, 1253, 1124 cm^{-1}; ^1H NMR (300 MHz $CDCl_3$): δ = 7.01–7.16 (m, 3 H), 6.69–6.88 (m, 5 H), 5.63 (br s, 1 H), 4.01 (dd, *J* = 7.2, 4.8 Hz, 1 H), 2.08–2.33 (m, 2 H), 1.43 (s, 3 H), 1.36 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.6, 154.2, 137.1, 129.9, 127.7, 125.0, 119.9, 117.2, 115.5, 74.8, 43.6, 39.1, 30.0, 24.3; HRMS (EI): *m*/*z* calcd for $C_{17}H_{18}O_2$: 254.1307; found: 254.1308.
(25) Ito, A.; Kishida, M.; Kurusu, Y.; Masuyama, Y. *J. Org. Chem.* **2000**, *65*, 494.