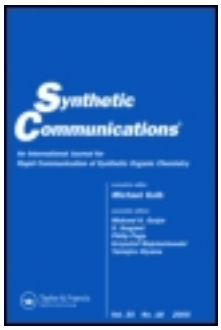
This article was downloaded by: [Mount Royal University]
On: 05 June 2013, At: 17:17
Publisher: Taylor & Francis
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Synthesis of 3-trifluoromethyl Substituted Benzo[F]chromene Derivatives by a One-Pot Reaction

Hua-Fang Fan [a], Xiao-Wei Wang [b], Jing-Wei Zhao [b], Xin-Jin Li [b], Jin-Ming Gao [a] & Shi-Zheng Zhu [b]

[a] Shaanxi Engineering Center of Bioresource Chemistry and Sustainable Utilization, College of Science, Northwest A & F University, Yangling, Shaanxi, China

[b] Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, China

Accepted author version posted online: 31 May 2013.

To cite this article: Hua-Fang Fan, Xiao-Wei Wang, Jing-Wei Zhao, Xin-Jin Li, Jin-Ming Gao & Shi-Zheng Zhu (2013): Synthesis of 3-trifluoromethyl Substituted Benzo[F]chromene Derivatives by a One-Pot Reaction, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, DOI:10.1080/00397911.2012.748074

To link to this article: http://dx.doi.org/10.1080/00397911.2012.748074

Disclaimer: This is a version of an unedited manuscript that has been accepted for publication. As a service to authors and researchers we are providing this version of the accepted manuscript (AM). Copyediting, typesetting, and review of the resulting proof will be undertaken on this manuscript before final publication of the Version of Record (VoR). During production and pre-press, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal relate to this version also.

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.tandfonline.com/page/terms-and-conditions

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae, and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand, or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

ACCEPTED MANUSCRIPT

Synthesis of 3-trifluoromethyl substituted benzo[f]chromene derivatives by a One-Pot Reaction

Hua-Fang Fan[1], Xiao-Wei Wang[2], Jing-Wei Zhao[2], Xin-Jin Li[2], Jin-Ming Gao[1], Shi-Zheng Zhu[2]

[1]Shaanxi Engineering Center of Bioresource Chemistry and Sustainable Utilization, College of Science, Northwest A & F University, Yangling, Shaanxi, China, [2]Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, China

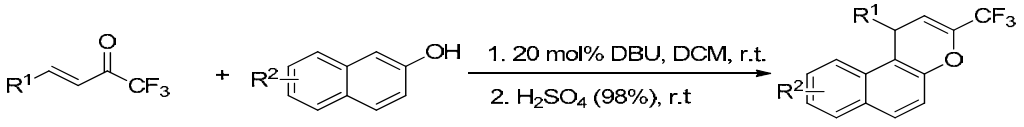
Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032, China Tel: 0086-21-54925185 Fax: 0086-21-64166128 E-mail: zhusz@mail.sioc.ac.cn

Downloaded by [Mount Royal University] at 17:17 05 June 2013

Abstract

In the presence of DBU and concentrated H_2SO_4, 2-naphthol reacted smoothly with α, β-unsaturated trifluoromethyl ketones in CH_2Cl_2 at room temperature affording the 3-trifluoromethyl substituted benzo[f]chromene derivatives in good to excellent yields by a one-pot reaction.

[Supplementary materials are available for this article. Go to the publisher's online edition of *Synthetic Communications*® for the following free supplemental resource(s): Full experimental and spectral details.]



R^1=Ph
- 4-ClC_6H_4
- 4-BrC_6H_4
- 4-EtC_6H_4
- 4-MeC_6H_4
- 2-MeOC_6H_4
- 3-MeOC_6H_4
- 4-MeOC_6H_4

R^2=H
- 9-OMe
- 9-Br
- 8-Br

ACCEPTED MANUSCRIPT

KEYWORDS: 2-naphthol, α,β-unsaturated trifluoromethyl ketone, benzo[f]chromene, one pot reaction.

INTRODUCTION

One of tools used to combine economic aspects with the environmental ones is the tandem reaction strategy, which process consists of two or more synthetic steps which are carried out without isolation of any intermediate thus reducing time, saving money, energy and raw materials. [1]

Benzo[f]chromene derivatives are an important class of compounds with excellent photochromic properties, some of which are also structural motifs present in many biologically active compounds.[2,3] Therefore, the synthesis of such compounds has attracted strong interest.[4–8] In the past few decades, some studies have been reported on the synthesis of Benzo[f]chromenes. Recently, Uemura group reported a ruthenium-catalyzed cycloaddition reaction of propargylic alcohols with phenol derivatives via allenylidene intermediates and obtained the product 1-phenyl-1*H*-naphtho [2,1-*b*]pyran in a yield of 80% (Scheme 1).[9]

As is well known, one of the important methods to introduce the fluorine atom or the fluoroalkyl group into the organic molecular is to use fluorine containing building block, i.e. to prepare the suitable fluorinated compounds which are used to synthesize the target

Downloaded by [Mount Royal University] at 17:17 05 June 2013

molecule. Due to this reaction process do not involve a C-F bond formation or broken, this method generally is carried out with high selectivity and good yield of products.

As part of our current studies on the development of new routes to fluorinated heterocycles, we report the tandem reaction of α,β-unsaturated trifluoromethyl ketones with 2-naphthol catalyzed by DBU and concentrated H_2SO_4 affording the corresponding benzo[f]chromene derivatives in high yields.

Downloaded by [Mount Royal University] at 17:17 05 June 2013

RESULTS AND DISCUSSION

As a test reaction, the reaction of (E)-1,1,1-trifluoro-4-phenylbut-3-en-2-one **1a** and 2-naphthol was initially studied with several different bases as catalysts and different acids as dehydrating agent in CH_2Cl_2 at room temperature (Table 1). The reaction proceeded well at room temperature in CH_2Cl_2 with Et_3N to furnish a Friedel-Craft type addition intermediate **3** in 24 hours. Then compound **3** was dehydrated with a catalytic amount of concentrated H_2SO_4 in a one-pot fashion after completion of the Friedel-Craft type addition step, which provided the benzo[f]chromene derivative **4a** in a yield of 80%. If the base was changed from DMAP to DIPEA or TMEDA, the yield was slightly decreased (Table 1 entries 2-4) and a bit high yield was obtained when Piperdine or DABCO was used (Table 1 entries 5, 7). While strong bases, such as DBU, were used to replace the weak bases, the yield can increase to 97% (Table 1 entry 6). On the contrary, no expected product was monitored by ^{19}F NMR when Na_2CO_3 was used (Table 1 entry 8). When PPA or TsOH was used as dehydrating agent, no better result was observed (Table 1 entries 9, 10).

Next, we examined the influence of solvent and the results were summarized in Table 2. When CH_2Cl_2 was used, the reaction was almost completed after 10 hours monitored by TLC and the product was isolated in a yield of 97%. Slightly lower yield was obtained with the use of $CHCl_3$ or DCE (Table 2 entries 2, 3). When we changed the solvent into ether, such as THF and Et_2O, the yields were around 85% (Table 2 entries 5, 6). However, $PhCF_3$ or *n*-hexane as a solvent, the reaction gave a moderate or a lower yield, respectively, even through longer reaction time was necessary. According to the results, CH_2Cl_2 was proved to be the most efficient solvent (Table 2 entry 1).

The reaction of a series of trifluoromethyl ketones with 2-naphthol derivatives in the presence of DBU and concentrated H_2SO_4 in CH_2Cl_2 at room temperature were also studied (Table 3). According to the results, we found that the CF_3 substituted benzo[f]chromene derivatives were obtained in good to excellent yields when the group R^1 of compound **1** was substituted by phenyl derivatives. However, when R^1 was alkyl, such as Me or Et, the reaction was complicated and no expected product was monitored by ^{19}F NMR. On the other hand, we also got the affording products in good yields when R^2 was 8-Br, 9-Br or 9-OMe, respectively.

All new CF_3 substituted benzo[f]chromene derivatives were confirmed by the NMR, IR and MS. For example, in the ^{13}C NMR of **4a**, the quartet at 119.6 ppm (q, J = 270 Hz) and two quartets at 107.7 ppm and 138.2 ppm were assigned to CF_3 and two sp^2 carbon atoms closed to CF_3, respectively. The singlet at -72.1 ppm in ^{19}F NMR spectrum was

Downloaded by [Mount Royal University] at 17:17 05 June 2013

assigned to the trifluoroacetyl group. And the mass spectrum of **4a** showed a molecular ion peak at m/z = 326 $[M]^+$.

CONCLUSION

In conclusion, a series of 3-trifluoromethyl substituted benzo[f]chromene derivatives were prepared using α, β-unsaturated trifluoromethyl ketones and 2-naphthalenol in present of DBU and concentrated H_2SO_4 at room temperature in CH_2Cl_2 by tandem reaction. Further research and applications of the reaction are in progress in our laboratories.

Downloaded by [Mount Royal University] at 17:17 05 June 2013

EXPERIMENTAL

Melting points were measured in Temp-Melt apparatus and uncorrected. ^1H and ^{19}F NMR spectra were recorded in $CDCl_3$ on Bruker AM-300 instruments with Me_4Si and $CFCl_3$ (with upfield negative) as the internal and external standards, respectively. IR spectra were obtained with a Nicolet AV-360 spectrophotometer. Lower resolution mass spectra or high-resolution mass spectra (HRMS) were obtained on a FinniganMAT-8430 instrument using the electron impact ionization technique (70ev). All reaction as well as column chromatography were monitored routinely with the aid of TLC or ^{19}F NMR spectroscopy.

General Procedure For The Preparation Of Trifluoromethyl-1H-Benzo[F]Chromene (4)

A solution of compound **1** (0.15 mmol), **2** (0.1 mmol) and DBU (0.02 mmol) in DCM (1.0 mL) was reacted at room temperature for 10 hours (monitored by TLC). Then a drop of concentrated H_2SO_4 (98%) was added directly and stirring was continued for 2 hours at room temperature. The crude reaction mixture was directly purified by column chromatography on silica gel using an eluent gradient of petroleum ether to afford the corresponding products.

Downloaded by [Mount Royal University] at 17:17 05 June 2013

1-Phenyl-3-(Trifluoromethyl)-1H-Benzo[F]Chromene 4a

Yield: 97%; yellowish solid; mp: 88-89 ^{o}C; IR (CH_2Cl_2, film): 1601, 1518, 1454, 1311, 1269, 1128, 1035, 950, 869, 699 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.79-7.73 (m, 2H), 7.65-7.61 (m, 1H), 7.36-7.17 (m, 8H), 5.88 (s, 1H), 5.27 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 148.5, 144.3, 138.2 (q, *J* = 37.4 Hz), 131.5, 131.4, 129.6, 129.1, 128.6, 127.7, 127.1, 126.9, 124.7, 123.6, 119.6 (q, *J* = 269.8 Hz), 117.5, 113.4, 107.7 (q, *J* = 3.6 Hz), 38.2; ^{19}F NMR (282 MHz, $CDCl_3$): δ = -72.1 (s, 3F); MS (EI) (m/z): 249 (100), 326 (M^+, 20%), 152 (17), 250 (16), 151 (12), 257 (8), 129 (8), 199 (7); HRMS calcd for $C_{20}H_{13}F_3O$: 326.0918, found: 326.0918.

1-(4-Chlorophenyl)-3-(Trifluoromethyl)-1H-Benzo[F]Chromene 4b

Yield: 93%; yellowish oil; IR (CH_2Cl_2, film): 1601, 1518, 1437, 1310, 1270, 1141, 1034, 951, 854, 695 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.82-7.76 (m, 2H), 7.59-7.56 (m, 1H), 7.39-7.26 (m, 5H), 7.12 (d, *J* = 8.1 Hz, 2H), 5.86 (d, *J* = 5.1 Hz, 1H), 5.28 (d, *J* = 4.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 148.5, 142.7, 138.5 (q, *J* = 33.5 Hz), 133.0, 131.5, 131.1, 129.9, 129.3, 129.0, 128.7, 127.1, 124.9, 123.4, 119.5 (q, *J* = 269.7 Hz),

117.5, 112.8, 107.2 (q, J = 3.6 Hz), 37.5; ^{19}F NMR (282 MHz, $CDCl_3$): δ = -72.6 (s, 3F); MS (EI) (m/z): 249 (100), 360 (M^+, 20%), 152 (17), 250 (16), 291 (13), 151 (12), 293 (8), 146 (8); HRMS calcd for $C_{20}H_{12}ClF_3O$: 360.0529, found: 360.0532.

1-(2-Methoxyphenyl)-3-(Trifluoromethyl)-1H-Benzo[F]Chromene 4c

Yield: 92%; yellowish solid; mp: 132-133 ^oC; IR (CH_2Cl_2, film): 1602, 1516, 1464, 1307, 1269, 1120, 1028, 948, 874, 721 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.78 (d, J = 8.4 Hz, 2H), 7.54 (d, J = 6.0 Hz, 1H), 7.38-7.28 (m, 3H), 7.19-7.13 (m, 1H), 6.93 (d, J = 8.7 Hz, 1H), 6.76-6.67 (m, 2H), 5.96 (d, J = 5.1 Hz, 1H), 5.75 (d, J = 4.8 Hz, 1H), 4.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 155.5, 149.2, 138.7 (q, J = 36.6 Hz), 132.0, 131.4, 131.3, 129.6, 129.2, 128.4, 128.0, 126.9, 124.6, 123.6, 121.3, 119.8 (q, J = 269.8 Hz), 117.4, 113.6, 110.4, 108.9 (q, J = 3.7 Hz), 55.6, 30.9; ^{19}F NMR (282 MHz, $CDCl_3$): δ = -72.6 (s, 3F); MS (EI) (m/z): 249 (100), 356 (M^+, 46%), 287 (37), 152 (22), 151 (22), 250 (17), 325 (16), 357 (10); HRMS calcd for $C_{21}H_{15}F_3O_2$: 356.1024, found: 356.1029.

1-(3-Methoxyphenyl)-3-(Trifluoromethyl)-1H-Benzo[F]Chromene 4d

Yield: 95%; yellowish oil; IR (CH_2Cl_2, film): 1600, 1517, 1465, 1313, 1262, 1137, 1053, 855, 721 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.92 (d, J = 8.7 Hz, 2H), 7.83-7.77 (m, 1H), 7.51-7.48 (m, 2H), 7.45-7.42 (m, 1H), 7.33 (t, J = 7.8 Hz, 1H), 6.93 (d, J = 7.2 Hz, 1H), 6.85 (d, J = 6.6 Hz, 1H), 6.02 (d, J = 4.8 Hz, 1H), 5.40 (d, J = 4.8 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 160.2, 148.2, 145.9, 138.3 (q, J = 36.3 Hz), 131.5, 131.4, 131.1, 130.1, 129.7, 128.5, 126.9, 124.7, 123.6, 120.1, 119.5 (q, J = 269.8 Hz), 117.5, 114.0, 113.2, 111.9, 107.6 (q, J = 3.5 Hz), 55.2, 38.1; ^{19}F NMR (282 MHz,

Downloaded by [Mount Royal University] at 17:17 05 June 2013

$CDCl_3$): δ = -72.6 (s, 3F); MS (EI) (m/z): 249 (100), 356 (M^+, 22%), 250 (15), 152 (15), 151 (11), 199 (7), 287 (7), 201 (5); HRMS calcd for $C_{21}H_{15}F_3O_2$: 356.1024, found: 356.1026.

1-(4-Methoxyphenyl)-3-(Trifluoromethyl)-1H-Benzo[F]Chromene 4e

Yield: 97%; yellowish solid; mp: 97-98 ^oC; IR (CH_2Cl_2, film): 16014, 1515, 1465, 1308, 1261, 1128, 1049, 951, 853, 721 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.82-7.76 (m, 2H), 7.68-7.64 (m, 1H), 7.37-7.28 (m, 3H), 7.12 (d, *J* = 8.1 Hz, 2H), 6.80 (d, *J* = 8.4 Hz, 2H), 5.87 (d, *J* = 4.8 Hz, 1H), 5.25 (d, *J* = 4.5 Hz, 1H), 3.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 156.5, 148.4, 138.0 (q, *J* = 35.7 Hz), 136.6, 131.5, 131.4, 129.5, 128.7, 128.5, 126.8, 124.7, 123.6, 119.6 (q, *J* = 269.8 Hz), 117.5, 114.5, 113.7, 107.9 (q, *J* = 2.9 Hz), 55.2, 37.2; ^{19}F NMR (282 MHz, $CDCl_3$): δ = -71.9 (s, 3F); MS (EI) (m/z): 287 (100), 249 (85), 356 (M^+, 25%), 288 (22), 152 (20), 157 (18), 151 (14), 144 (13); HRMS calcd for $C_{21}H_{15}F_3O_2$: 356.1024, found: 356.1028.

1-(4-Bromophenyl)-3-(Trifluoromethyl)-1H-Benzo[F]Chromene 4f

Yield: 92%; yellowish oil; IR (CH_2Cl_2, film): 1601, 1518, 1437, 1309, 1270, 1141, 1034, 951, 859, 682 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 8.7 Hz, 2H), 7.62-7.56 (m, 1H), 7.44-7.28 (m, 5H), 7.08 (d, *J* = 7.8 Hz, 2H), 5.86 (d, *J* = 4.8 Hz, 1H), 5.29 (d, *J* = 3.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 148.5, 143.2, 138.5 (q, *J* = 36.9 Hz), 132.3, 131.5, 131.1, 129.9, 129.4, 128.7, 127.1, 124.9, 123.4, 121.0, 119.5 (q, *J* = 269.7 Hz), 117.5, 112.7, 107.1 (q, *J* = 3.7 Hz), 37.6; ^{19}F NMR (282 MHz, $CDCl_3$): δ = -72.0 (s, 3F);

Downloaded by [Mount Royal University] at 17:17 05 June 2013

MS (EI) (m/z): 249 (100), 152 (17), 250 (16), 151 (10), 406 (9), 404 (M^+, 9%), 271 (7), 199 (7); HRMS calcd for $C_{20}H_{12}BrF_3O$: 404.0024, found: 404.0021.

1-(4-Ethylphenyl)-3-(Trifluoromethyl)-1H-Benzo[F]Chromene 4g

Yield: 87%; yellowish oil; IR (CH_2Cl_2, film): 1601, 1517, 1437, 1311, 1270, 1139, 1034, 951, 854, 628 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.83-7.75 (m, 2H), 7.68-7.65 (m, 1H), 7.37-7.28 (m, 3H), 7.13-7.07 (m, 4H), 5.89 (d, *J* = 4.8 Hz, 1H), 5.25 (d, *J* = 4.2 Hz, 1H), 2.56 (q, *J* = 7.8 Hz, 2H), 1.17 (t, *J* = 7.8 Hz, 3H), ; ^{13}C NMR (100 MHz, $CDCl_3$): 148.5, 143.0, 141.5, 138.1 (q, *J* = 37.2 Hz), 131.5, 131.4, 129.5, 128.6, 127.7, 126.9, 124.7, 123.7, 119.7 (q, *J* = 269.7 Hz), 117.5, 113.7, 107.9 (q, *J* = 3.7 Hz), 37.7, 28.4, 15.3; ^{19}F NMR (282 MHz, $CDCl_3$): δ = -72.5 (s, 3F); MS (EI) (m/z): 249 (100), 285 (26), 340 (M^+, 22%), 152 (18), 250 (16), 151 (11), 199 (8), 286 (7); HRMS calcd for $C_{22}H_{17}F_3O$: 354.1232, found: 354.1235.

1-(P-Tolyl)-3-(Trifluoromethyl)-1H-Benzo[F]Chromene 4h

Yield: 92%; yellowish solid; mp: 97-98 ^oC; IR (CH_2Cl_2, film): 1599, 1511, 1465, 1310, 1268, 1105, 1026, 948, 860, 727 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.80-7.77 (m, 2H), 7.68-7.65 (m, 1H), 7.37-7.29 (m, 3H), 7.11-7.06 (m, 4H), 5.88 (d, *J* = 5.1 Hz, 1H), 5.27 (d, *J* = 5.4 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 148.4, 141.4, 138.0 (q, *J* = 36.6 Hz), 136.7, 131.4, 131.3, 129.8, 129.5, 128.5, 127.6, 126.9, 123.6, 119.6 (q, *J* = 269.8 Hz), 117.5, 113.6, 107.9 (q, *J* = 3.7 Hz), 37.7, 21.0; ^{19}F NMR (282 MHz, $CDCl_3$): δ = -72.0 (s, 3F); MS (EI) (m/z): 249 (100), 340 (M^+, 32%), 271 (31), 152 (17), 250 (15), 151 (11), 136 (10), 199 (8); HRMS calcd for $C_{21}H_{15}F_3O$: 340.1075, found: 340.1074.

Downloaded by [Mount Royal University] at 17:17 05 June 2013

9-Methoxy-1-Phenyl-3-(Trifluoromethyl)-1H-Benzo[F]Chromene 4i

Yield: 87%; yellowish solid; mp: 125-126 ^{o}C; IR (CH_2Cl_2, film): 1604, 1515, 1454, 1309, 1272, 1136, 1030, 923, 837, 701 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 9.0 Hz, 2H), 7.31-7.17 (m, 6H), 7.02-6.98 (m, 1H), 6.89-6.88 (m, 1H), 5.87 (d, *J* = 5.1 Hz, 1H), 5.19 (d, *J* = 4.2 Hz, 1H), 3.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 158.4, 149.0, 144.3, 138.1 (q, *J* = 36.9 Hz), 132.8, 130.0, 129.2, 129.1, 127.8, 127.1, 126.6, 119.6 (q, *J* = 269.9 Hz), 116.8, 114.9, 112.4, 107.5 (q, *J* = 3.5 Hz), 103.3, 55.1, 38.6; ^{19}F NMR (282 MHz, $CDCl_3$): δ = -72.0 (s, 3F); MS (EI) (m/z): 279 (100), 356 (M^+, 29%), 236 (24), 280 (16), 139 (11), 144 (11), 287 (9), 357 (7); HRMS calcd for $C_{21}H_{15}F_3O_2$: 356.1024, found: 356.1022.

9-Bromo-1-Phenyl-3-(Trifluoromethyl)-1H-Benzo[F]Chromene 4j

Yield: 85%; yellowish solid; mp: 111-112 ^{o}C; IR (CH_2Cl_2, film): 1599, 1500, 1447, 1307, 1266, 1133, 1039, 963, 854, 700 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.80 (s, 2H), 7.73 (d, *J* = 9.0 Hz, 1H), 7.63 (d, *J* = 8.7 Hz, 1H), 7.44-7.41 (m, 1H), 7.32-7.28 (m, 3H), 7.23-7.19 (m, 3H), 5.90 (d, *J* = 5.1 Hz, 1H), 5.19 (d, *J* = 4.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 149.0, 143.7, 138.1 (q, *J* = 37.3 Hz), 132.7, 130.1, 129.9, 129.5, 129.3, 128.2, 127.7, 127.4, 126.1, 121.5, 119.5 (q, *J* = 269.7 Hz), 118.0, 112.9, 107.5 (q, *J* = 3.5 Hz), 38.0; ^{19}F NMR (282 MHz, $CDCl_3$): δ = -71.8 (s, 3F); MS (EI) (m/z): 329 (100), 327 (98), 151 (31), 249 (25), 406 (24), 404 (M^+, 23%), 150 (21), 328 (19); HRMS calcd for $C_{20}H_{12}BrF_3O$: 404.0024, found: 404.0020.

Downloaded by [Mount Royal University] at 17:17 05 June 2013

8-Bromo-1-Phenyl-3-(Trifluoromethyl)-1H-Benzo[F]Chromene 4k

Yield: 85%; yellowish solid; mp: 138-139 ^{o}C; IR (CH_2Cl_2, film): 1590, 1500, 1453, 1306, 1267, 1134, 1037, 947, 862, 699 cm^{-1}; ^{1}H NMR (300 MHz, DCl_3): δ = 7.92 (d, *J* = 1.8 Hz, 1H), 7.68 (d, *J* = 9.0 Hz, 1H), 7.49 (d, *J* = 9.0 Hz, 1H), 7.41-7.38 (m, 1H), 7.38-7.24 (m, 3H), 7.22-7.16 (m, 3H), 5.89 (d, *J* = 5.4 Hz, 1H), 5.24 (d, *J* = 4.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 148.6, 143.9, 138.1 (q, *J* = 37.0 Hz), 132.6, 130.5, 130.2, 129.9, 129.9, 129.2, 128.7, 127.7, 127.3, 125.4, 119.5 (q, *J* = 270.0 Hz), 118.7, 118.6, 113.7, 107.6 (q, *J* = 3.6 Hz), 38.1; ^{19}F NMR (282 MHz, $CDCl_3$): δ = -72.6 (s, 3F); MS (EI) (m/z): 327 (100), 329 (96), 157 (31), 406 (29), 151 (27), 404 (M^+, 27%), 287 (22), 249 (22); HRMS calcd for $C_{20}H_{12}BrF_3O$: 404.0024, found: 404.0022.

Complete experimental and spectral details are available online in the Supplementary Materials.

Downloaded by [Mount Royal University] at 17:17 05 June 2013

ACKNOWLEDGEMENTS

This research was supported by the National Natural Science Foundation of China (No.21032006, 20172064), the QT Program, Shanghai Natural Science Council.

REFERENCES

1. (a) Hall, N. Chemists Clean Up Synthesis With One-Pot Reactions. *Science* **1994**, *266*, 32; (b) Dömling, A.; Herdtweck, E.; Ugi, I. MCR V: [1] the Seven-Component Reaction. *Acta Chem. Scand.* **1998**, *52*, 107.

2. (a) Hepworth, J. D.; Heron, B. M. Progress In Heterocyclic Chemistry; Elsevier: Amsterdam, **2005**, *17*, 33-62; (b) Nakatsuji, S. Recent progress toward the exploitation of organic radical compounds with photo-responsive magnetic properties. *Chem. Soc. Rev.* **2004**, *33*, 348; (c) Shilova, E. A.; Pepe, G.; Samat, A.; Moustrou, C. Synthesis of heterocyclic chromenes via Buchwald C-N coupling and the substituent effect on their photochromic properties. *Tetrahedron* **2008**, *64*, 9977; (d) Kumar, S.; Hernandez, D.; Hoa, B.; Lee, Y.; Yang, J. S.; McCurdy, A. Synthesis, photochromic properties, and light-controlled metal complexation of a naphthopyran derivative. *Org. Lett*. **2008**, *10*, 3761; (e) Malic, N.; Campbell, J. A.; Evans, R. A. Superior Photochromic Performance of Naphthopyrans in a Rigid Host Matrix Using Polymer Conjugation: Fast, Dark, and Tunable. *Macromolecules* **2008**, *41*, 1206.

3. (a) Dell, C. P. Antiproliferative Naphthopyrans: Biological Activity,Mechanistic St udies and Therapeutic Potential. *Curr. Med. Chem.* **1998**, *5*, 179; (b) Karnik, A. V.; Kulkarni, A. M.; Malviya, N. J.; Mourya, B. R.; Jadhav, B. L. Synthesis and in vitro anti-bacterial evaluation of tetracyclic-ortho-fused 4*H*-naphtho [1',2'-5,6] pyrano [3,4-*d*] (1,2,3) selenadiazole and its derivatives. *Eur. J. Med. Chem*. **2008**, *43*, 2615; (c) Hussein, A. A.; Barberena, I.; Capson, T. L.; Kursar, T. A.; Coley, P. D.; Solis, P. N.; Gupta, M. P. Adenaflorins A-D, new cytotoxic naphthopyrane derivatives from Adenaria floribunda. *J. Nat. Prod.* **2004**, *67*, 451; (d) Claessens, S.; Kesteleyn, B.; Van, T. N.; Kimpe, N. D. Synthesis of mollugin. *Tetrahedron* **2006**, *62*, 8419.

4. Markees, D. G. The reaction of ethyl chromone-2-carboxylates with 1,2-diaminobenzene. *J. Heterocycl. Chem.* **1989**, *26*, 29.

Downloaded by [Mount Royal University] at 17:17 05 June 2013

5. Ballini, R.; Bosica, G.; Conforti, M. L.; Maggi, R.; Mazzacani, A.; Righi, P.; Sartori, G. Three-component process for the synthesis of 2-amino-2-chromenes in aqueous media. *Tetrahedron* **2001**, *57*, 1395.

6. Jin, T. S.; Zhang, J. S.; Liu, L. B.; Wang, A. Q.; Li, T. S. Clean, One-Pot Synthesis of Naphthopyran Derivatives in Aqueous Media. *Synth. Commun.* **2006**, *36*, 2009.

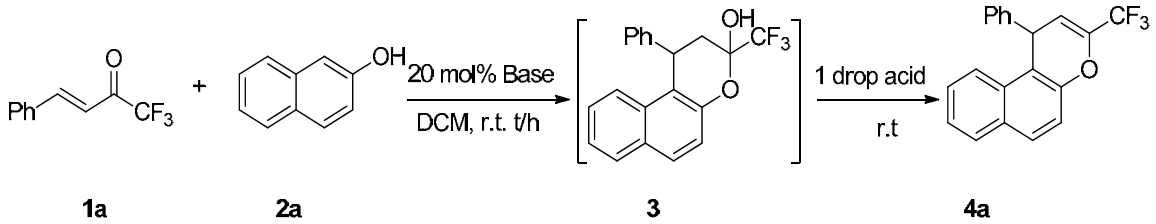
7. Zhang, A. Q.; Zhang, M.; Chen, H. H.; Chen, J.; Chen, H.Y. Convenient Method for Synthesis of Substituted 2-Amino-2-chromenes. *Synth. Commun.* **2007**, *37*, 231.

8. Rawat, M.; Prutyanov, V.; Wulff, W. D. Chromene Chromium Carbene Complexes in the Syntheses of Naphthopyran and Naphthopyrandione Units Present in Photochromic Materials and Biologically Active Natural Products. *J. Am. Chem. Soc.* **2006**, *128*, 11044.

9. Nishibayashi, Y.; Inada, Y.; Hidai, M.; Uemura, S. Ruthenium-Catalyzed Cycloaddition of Propargylic Alcohols with Phenol Derivatives via Allenylidene Intermediates: Catalytic Use of the Allenylidene Ligand as the C_3 Unit. *J. Am. Chem. Soc.* **2002**, *124*, 7900.

Downloaded by [Mount Royal University] at 17:17 05 June 2013

Table 1. Optimization of the tandem reaction[a]



1a **2a** **3** **4a**

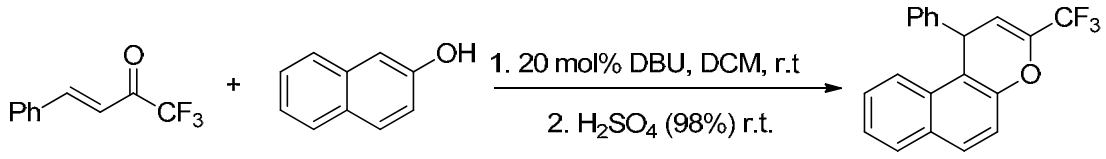
Entry	Base	Acid	t/h	Yield (%)[b]
1	Et_3N	H_2SO_4 (98%)	24	80
2	DMAP	H_2SO_4 (98%)	24	71
3	DIPEA	H_2SO_4 (98%)	24	75
4	TMEDA	H_2SO_4 (98%)	24	72
5	Piperdine	H_2SO_4 (98%)	24	86
6	DBU	H_2SO_4 (98%)	10	97
7	DABCO	H_2SO_4 (98%)	10	90
8	Na_2CO_3	H_2SO_4 (98%)	-	-
9	DBU	TsOH	10	85
10	DBU	PPA	10	72

[a] The reaction was carried out with **1a** (0.15 mmol) and **2a** (0.1 mmol) and base (0.02 mmol) at room temperature in DCM (1.0 mL) .

[b] Yield of the isolated product after column chromatography on silica gel.

Downloaded by [Mount Royal University] at 17:17 05 June 2013

Table 2. Screening of solvent[a]



1a **2a** **4a**

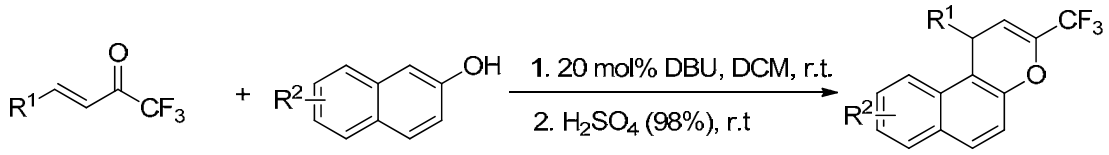
Entry	Solvent	t/h	Yield(%)[b]
1	DCM	10	97
2	$CHCl_3$	10	93
3	DCE	12	92
4	EtOAc	10	77
5	Et_2O	10	85
6	THF	10	88
7	DMF	10	72
8	$PhCF_3$	15	70
9	*n*-hexane	48	45

[a] The reaction was carried out with **1a** (0.15 mmol) and **2a** (0.1 mmol) and base (0.02 mmol) at room temperature in solvent (1.0 mL) .

[b] Isolated yield of the product after column chromatography on silica gel.

Downloaded by [Mount Royal University] at 17:17 05 June 2013

Table 3. Synthesis of 3-trifluoromethyl substituted benzo[f]chromenes [a]



1 **2** **4**

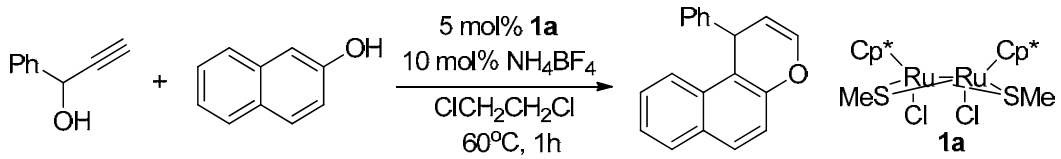
Entry	R^1	R^2	t/h	Product	Yield(%)[b]
1	Ph	H	10	**4a**	97
2	4-ClC_6H_4	H	10	**4b**	93
3	2-$MeOC_6H_4$	H	10	**4c**	92
4	3-$MeOC_6H_4$	H	10	**4d**	95
5	4-$MeOC_6H_4$	H	10	**4e**	90
6	4-BrC_6H_4	H	10	**4f**	92
7	4-EtC_6H_4	H	10	**4g**	87
8	4-MeC_6H_4	H	10	**4h**	92
9	Ph	9-OMe	12	**4i**	87
10	Ph	9-Br	12	**4j**	85
11	Ph	8-Br	12	**4k**	85

[a] The reaction was carried out with **1** (0.15 mmol) and **2** (0.1 mmol) and base (0.02 mmol) at room temperature in solvent (1.0 mL) .

[b] Isolated yield of the product after column chromatography on silica gel.

Downloaded by [Mount Royal University] at 17:17 05 June 2013

Scheme 1



Downloaded by [Mount Royal University] at 17:17 05 June 2013