Hindawi Publishing Corporation
Organic Chemistry International
Volume 2012, Article ID 208948, 4 pages
doi:10.1155/2012/208948

Research Article

Triton-B-Catalyzed, Efficient, Solvent-Free Synthesis of Benzopyrans

Devdutt Chaturvedi,[1] Amit K. Chaturvedi,[2] Nisha Mishra,[2] and Virendra Mishra[2]

[1] *Laboratory of Medicinal Chemistry, Amity Institute of Pharmacy, Amity University Uttar Pradesh, Lucknow Campus, Lucknow 226010, India*
[2] *Synthetic Research Laboratory, Department of Chemistry, B. S. A. College, Mathura 281004, India*

Correspondence should be addressed to Devdutt Chaturvedi, devduttchaturvedi@gmail.com

Received 5 June 2012; Accepted 16 August 2012

Academic Editor: William N. Setzer

A convenient and microwave-promoted novel protocol for the syntheses of diverse kinds of substituted benzopyrans from the corresponding variety of substituted hydroxy acetophenones and keto compounds using benzyltrimethylammonium hydroxide (Triton-B) under solvent-free conditions has been developed. This protocol is mild and efficient than the other reported methods.

1. Introduction

2-*H*-1-benzopyrans, commonly known as 2H-benzopyrans or 2H-chromenes, are an important structural motif present in the varieties of biologically active natural, synthetic drugs, and lead molecules [1, 2]. Interesting chemistry have been exploited to this structural unit for generating diverse series of compounds, which have displayed a wide spectrum of potential biological activities such as anticancer [3, 4], antidiabetic [5, 6], anti-HIV [7], antiinflammatory [8], antimicrobial [9], antibacterial [10], antiarrhythmic [11], and antiestrogenic [12]. Moreover, their use in the synthesis of various kinds of dyes [13] and agrochemicals [14] is well known. Their major use in the development of diverse kinds of potassium channel openers has made further interest for benzopyran chemistry [15]. Furthermore, benzopyran unit has been further explored, as a useful synthon for the generation of diverse kinds of pharmaceutically important complex heterocycles of natural as well as synthetic molecules [16]. Traditional syntheses of substituted benzopyrans involve the reaction of substituted hydroxyl acetophenones with keto compounds using variety of strong bases [17]. Recently, their synthesis has been further achieved through different kinds of starting materials using variety of metallic and nonmetallic basic catalysts either by intramolecular cycloaddition reactions [18, 19] or by condensation reactions [20–22] from the variety of the starting substrates. Furthermore, their solid phase syntheses using various kinds of metallic system were also reported recently [23]. Most of these methods suffer from the limitations such as long-reaction times, use of expensive strongly basic reagents, tedious work-up and low yields. Consequently, there is continued interest in developing new and convenient methods for the synthesis of substituted benzopyrans using mild reaction conditions. Nowadays, microwave-assisted synthesis has become as important tool for the synthesis of various kind of heterocycles [24]. In continuation of our work towards various synthetic transformations employing Triton-B [25–29], we have invented a novel protocol for the syntheses of substituted benzopyrans using Triton-B under solvent-free conditions. Thus, in the present communication, we report herein a novel microwave promoted, one-pot solvent-free protocol for the synthesis of substituted benzopyrans through the direct reaction of corresponding substituted acetophenones and keto compounds mediated by Triton-B under solvent-free conditions.

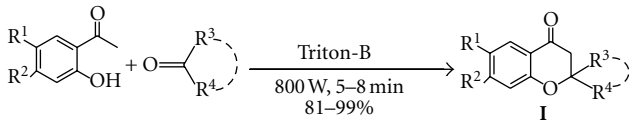
2. Results and Discussion

Initially, the syntheses of various substituted benzopyrans were achieved from the corresponding hydroxy acetophenones and keto compounds using various kinds of solid support like neutral and basic alumina. Better yields of the

Table 1: Conversion of substituted benzophenones into benzopyrans of general formula **I**[a].

Product	R^1	R^2	R^3	R^4	Time/min.	Yields[b]/%	Reference
1	H	H	CH_3	CH_3	5	86	[18, 19]
2	H	OH	CH_3	CH_3	5	89	[18, 19]
3	H	OH	CH_3	C_2H_5	8	85	[20–22]
4	H	OH	$R^3 = R^4$ = Cyclopentyl		7	88	[23]
5	H	OH	$R^3 = R^4$ = Cyclohexyl		6	90	[24]
6	OH	H	CH_3	CH_3	10	81	[23]
7	OH	H	CH_3	C_2H_5	8	82	[23]
8	OH	H	$R^3 = R^4$ = Cyclopentyl		8	89	[24]
9	OH	H	$R^3 = R^4$ = Cyclohexyl		8	86	[25–29]
10	NO_2	H	CH_3	CH_3	8	85	[18, 19]
11	OCH_3	H	CH_3	CH_3	5	91	[23]
12	OCH_3	OH	CH_3	CH_3	5	92	[18, 19]
13	OCH_3	OCH_3	CH_3	C_2H_5	4	94	[24]
14	OCH_3	OCH_3	C_2H_5	C_2H_5	4	99	[25–29]
15	OCH_3	NO_2	n-C_2H_5	CH_3	5	92	[24]
16	OH	OCH_3	n-C_4H_9	n-C_4H_9	5	83	[20–22]

[a]All the products were characterized by IR, NMR, and mass spectroscopic data.
[b]Isolated yields.



Scheme 1

products were obtained in by using basic alumina as a solid support. Moreover, reaction was further carried out without using solid support where minute amount of substituted benzopyrans was observed. Keeping the basic nature of benzyltrimethylammonium hydroxide (Triton-B), we have tried a reaction of hydroxyl acetophenone with a keto compound, where it was realized that there is complete transformation of the starting materials into desired substituted benzopyran derivative. A comparative study of use of various mild bases in caring out this synthetic reaction was studied where it was further realized that best yields were obtained using Triton-B. Moreover, the advantages associated with Triton-B include the easy removal from the reaction mixture by simple filtration. Thus, various substituted hydroxyl compounds were reacted with variety of keto compounds using Triton-B under microwave conditions to afford the clean formation of the corresponding substituted benzopyrans in good to excellent yields. Hence, it was concluded that reaction works using Triton-B under solvent-free conditions and completed in very short time (5–8 min.) afforded very excellent yields (81–99%) of the desired substituted benzopyrans. The results were summarizes in Table 1. It was further realized that the introduction of electron releasing groups at *para* position leads to increase in the yields, while electron withdrawing groups do not have any effect. The whole reaction conditions have been shown in Scheme 1.

In conclusion, we developed a convenient and efficient protocol for the one-pot, two-component coupling of various substituted acetophenones with a variety of keto compounds using basic resin. This method generates the corresponding benzopyrans in good to excellent yields. Furthermore, this method exhibits substrate versatility, mild reaction conditions, and experimental convenience. This synthesis protocol developed is believed to offer a more general method for the formation of substituted benzopyrans essential to numerous organic syntheses.

3. Experimental

Chemicals were procured from Merck, Aldrich, and Fluka chemical companies. Reactions were carried out under Argon. IR spectra 4000–200 cm^{-1} were recorded on Bomem MB-104-FTIR spectrophotometer using neat technique, whereas NMRs were scanned on an AC-300F, NMR (300 MHz) instrument using $CDCl_3$ and *TMS* as internal standard. Elemental analysis was conducted by means of a Carlo-Erba EA 1110-CNNO-S analyzer and agreed favorably with calculated values.

3.1. Typical Experimental Procedure. Substituted hydroxy acetophenone (0.01 mol) was added to a mixture of corresponding ketone (0.01 mol) and Triton-B (0.02 mol). The reaction mixture was irradiated under microwave at 800 W in a sealed tube. The reaction mixture was extracted with ethyl acetate thrice, and organic layer was concentrated to afford the desired substituted benzophenone derivative which was recrystallized with benzene/hexane.

*3.2. 2,2-Dimethyl-Chroman-4-One (**1**).* Mp: 85–87°C; IR (KBr): 2978, 1690, 1604, 1573, 1456 cm^{-1}; ^1H NMR

(300 MHZ, $CDCl_3$) *δ:* 1.48(6H, s, CH_3), 2.75(2H, s, CH_2), 6.90–7.28(1H, m, 6 & 8-H), 7.40–7.56(1H, m, 7-H), 7.91(1H, dd, J = 8.5 Hz & 2.5 Hz, 5-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.49, 48.74, 79.40, 118.18, 120.87, 126.36, 128.48, 136.00, 160.02, 192.12 ppm; MS: *m/z* (%): 176(100), 161(100), 121(100), 92(100), 63(87), 41(48).

*3.3. 7-Hydroxy-2,2-Dimethyl-Chroman-4-One (**2**).* Mp: 168°C; IR (KBr): 3469, 1652, 1611, 1570, 1492, 1459, 1428, 1415 cm^{-1}; ^{1}H NMR (300MHZ, $CDCl_3$) δ: 1.43(6H, s, 2xCH_3), 2.63(2H, s, CH_2), 6.90(1H, d, J = 2.5 Hz, 8-H), 6.56(1H, dd, J = 8.5 Hz & 2.5 Hz, 6-H), 7.83(1H, d, J = 8.5 Hz,5-H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 26.78, 48.55, 79.13, 103.44, 110.14, 114.0, 128.42, 163.12, 164.90, 192.89 ppm; MS: *m/z* (%): 192(51), 177(99), 137(100), 108(58), 80(22).

*3.4. 2-Ethyl 7-Hydroxy-2-Methyl-Chroman-4-One (**3**).* Mp: 98°C; IR(KBr):3128, 2965, 1648, 1574, 1489, 1376 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): 0.93(3H, t, J = 6.5 Hz, CH_3), 1.40 (3H, s, CH_3), 1.73 (2H, q, J = 6.5 Hz, CH_2), 2.73(2H, s, CH_2), 6.53(1H, d, J = 2.5 Hz, 8-H), 6.53(1H, dd, J_1 = 8.5 Hz, J_2= 2.5 Hz, 6-H), 7.90(1H, d, J = 8.5 Hz, 5-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.90, 23.44, 32.13, 46.69, 81.38, 103.65, 110.05, 113.30, 128.66, 162.00, 164.86,192.10, MS at *m/z* (%): 206(22), 191(10), 177(52), 151(26), 137(100), 136(20), 108(19), 81(8), 69(10), 53(11).

Acknowledgments

Author is thankful to Director General, Amity University Uttar Pradesh, Lucknow Campus, Lucknow, U. P., for his constant support and encouragement for research.

Conflict of Interests

The authors confirm that there is no conflict of interests with the commercial identities used inside the paper.

References

[1] M. Curini, G. Cravotto, F. Epifano, and G. Giannone, "Chemistry and biological activity of natural and synthetic prenyloxycoumarins," *Current Medicinal Chemistry*, vol. 13, no. 2, pp. 199–222, 2006.

[2] M. V. Kulkarni, G. M. Kulkarni, C. H. Lin, and C. M. Sun, "Recent advances in coumarins and 1-azacoumarins as versatile biodynamic agents," *Current Medicinal Chemistry*, vol. 13, no. 23, pp. 2795–2818, 2006.

[3] T. C. Wang, I. L. Chen, P. J. Lu et al., "Synthesis, antiproliferative, and antiplatelet activities of oxime- and methyloxime-containing flavone and isoflavone derivatives," *Bioorganic and Medicinal Chemistry*, vol. 13, no. 21, pp. 6045–6053, 2005.

[4] N. Kim, S. Lee, K. Y. Yi et al., "Identification of a novel antiangiogenic agent; 4-(N-imidazol-2-ylmethyl)amino benzopyran analogues," *Bioorganic and Medicinal Chemistry Letters*, vol. 13, no. 10, pp. 1661–1663, 2003.

[5] G. Rastelli, L. Costantino, M. C. Gamberini et al., "Binding of 1-benzopyran-4-one derivatives to aldose reductase: a free energy perturbation study," *Bioorganic and Medicinal Chemistry*, vol. 10, no. 5, pp. 1427–1436, 2002.

[6] L. Tang, J. Yu, Y. Leng, Y. Feng, Y. Yang, and R. Ji, "Synthesis and insulin-sensitizing activity of a novel kind of benzopyran derivative," *Bioorganic and Medicinal Chemistry Letters*, vol. 13, no. 20, pp. 3437–3440, 2003.

[7] Y. R. Lee and X. Wang, "A short synthetic route to biologically active (±)-daurichromenic acid as highly potent anti-HIV agent," *Organic and Biomolecular Chemistry*, vol. 3, no. 21, pp. 3955–3957, 2005.

[8] D. J. Hadjipavlou-Litina, K. E. Litinas, and C. Kontogiorgis, "The anti-inflammatory effect of coumarin and its derivatives," *Anti-Inflammatory and Anti-Allergy Agents in Medicinal Chemistry*, vol. 6, no. 4, pp. 293–306, 2007.

[9] H. Göker, D. W. Boykin, and S. Yildiz, "Synthesis and potent antimicrobial activity of some novel 2-phenyl or methyl-4H-1-benzopyran-4-ones carrying amidinobenzimidazoles," *Bioorganic and Medicinal Chemistry*, vol. 13, no. 5, pp. 1707–1714, 2005.

[10] S. Prado, Y. L. Janin, B. Saint-Joanis et al., "Synthesis and antimycobacterial evaluation of benzofurobenzopyran analogues," *Bioorganic and Medicinal Chemistry*, vol. 15, no. 5, pp. 2177–2186, 2007.

[11] M. Koufaki, C. Kiziridi, P. Papazafiri et al., "Synthesis and biological evaluation of benzopyran analogues bearing class III antiarrhythmic pharmacophores," *Bioorganic and Medicinal Chemistry*, vol. 14, no. 19, pp. 6666–6678, 2006.

[12] A. Gupta, A. Dwivedy, G. Keshri et al., "Rapid synthesis of 4-benzylidene and 4-[bis-(4-methoxyphenyl)-methylene-2-substituted phenyl-benzopyrans as potential selective estrogen receptor modulators (SERMs) using McMurry coupling reaction," *Bioorganic and Medicinal Chemistry Letters*, vol. 16, no. 23, pp. 6006–6012, 2006.

[13] F. Karci and N. Ertan, "Synthesis of some novel hetarylazo disperse dyes derived from 4-hydroxy-2H-1-benzopyran-2-one (4-hydroxycoumarin) as coupling component and investigation of their absorption spectra," *Dyes and Pigments*, vol. 64, no. 3, pp. 243–249, 2005.

[14] T. Kakimoto, F. Koizumi, K. Hirase, S. Banba, E. Tanaka, and K. Arai, "Novel 3,3a,5,9b-tetrahydro-2H-furo[3,2-c][2] benzopyran derivatives: Synthesis of chiral glycol benzyl ether herbicides," *Pest Management Science*, vol. 60, no. 5, pp. 493–500, 2004.

[15] J. Lloyd, K. S. Atwal, H. J. Finlay et al., "Benzopyran sulfonamides as KV1.5 potassium channel blockers," *Bioorganic and Medicinal Chemistry Letters*, vol. 17, no. 12, pp. 3271–3275, 2007.

[16] A. F. E. Mourad, A. A. Aly, H. H. Farag, and E. A. Beshr, "Microwave assisted synthesis of triazoloquinazolinones and benzimidazoquinazolinones," *Beilstein Journal of Organic Chemistry*, vol. 3, p. 11, 2007.

[17] S. S. Joshi and H. Singh, "Nitrohydroxy aromatic ketones. I. Nitrohydroxyacetophenones," *Journal of The American Chemical Society*, vol. 76, no. 19, pp. 4993–4994, 1954.

[18] G. L. Zhao, Y. L. Shi, and M. Shi, "Synthesis of functionalized 2*H*-1-benzopyrans by DBU-catalyzed reactions of salicylic aldehydes with allenic ketones and esters," *Organic Letters*, vol. 7, no. 20, pp. 4527–4530, 2005.

[19] J. L. Portscheller and H. C. Malinakova, "Synthesis of 2H-1-benzopyrans via palladacycles with a metal-bonded stereogenic carbon," *Organic Letters*, vol. 4, no. 21, pp. 3679–3681, 2002.

[20] T. S. Jin, J. C. Xiao, S. J. Wang, T. S. Li, and X. R. Song, "An efficient and convenient approach to the synthesis of benzopyrans by a three-component coupling of one-pot reaction," *Synlett*, no. 13, pp. 2001–2004, 2003.

[21] K. Pachamuthu and R. R. Schmidt, "Diels-Alder reaction of 2-nitro glycals: a new route to the synthesis of benzopyrans," *Synlett*, no. 9, pp. 1355–1357, 2003.

[22] J. S. Yadav, B. V. S. Reddy, M. Aruna, and M. Thomas, "A facile synthesis of trans-fused pyrano[3,2-*c*]benzopyrans catalyzed by scandium triflate," *Synthesis*, no. 2, pp. 217–220, 2002.

[23] J. Y. Hwang, H. S. Choi, J. S. Seo et al., "Construction of a 2,6-difunctionalized 2-methyl-2*H*-1-benzopyran library by using a solid-phase synthesis protocol," *Journal of Organic Chemistry*, vol. 70, no. 24, pp. 10151–10154, 2005.

[24] S. A. Galena, "Microwave Chemistry," *Chemical Society Reviews*, vol. 26, pp. 233–238, 1997.

[25] D. Chaturvedi and S. Ray, "A highyielding, one-pot, triton-B catalyzed, expeditious synthesis of carbamate esters by four component coupling methodology," *Monatshefte fur Chemie*, vol. 137, no. 2, pp. 201–206, 2006.

[26] D. Chaturvedi and S. Ray, "Triton-B catalyzed efficient one-pot synthesis of dithiocarbamate esters," *Monatshefte fur Chemie*, vol. 137, no. 3, pp. 311–317, 2006.

[27] D. Chaturvedi and S. Ray, "Triton-B catalyzed, efficient, one-pot synthesis of carbamate esters from alcoholic tosylates," *Monatshefte fur Chemie*, vol. 137, no. 4, pp. 459–463, 2006.

[28] D. Chaturvedi and S. Ray, "A high yielding, one-pot, triton-B catalyzed synthesis of dithiocarbamates using alcoholic tosylates," *Monatshefte fur Chemie*, vol. 137, no. 4, pp. 465–469, 2006.

[29] D. Chaturvedi, A. K. Chaturvedi, N. Mishra, and V. Mishra, "Triton-B-catalyzed, efficient, one-pot synthesis of carbazates through alcoholic tosylates," *Synthetic Communications*, vol. 38, no. 22, pp. 4013–4022, 2008.