Hindawi Publishing Corporation
Organic Chemistry International
Volume 2011, Article ID 394619, 6 pages
doi:10.1155/2011/394619

Research Article

Microwave-Assisted Improved Regioselective Synthesis of 12*H*-Benzopyrano[3,2-*c*][1]benzopyran-5-ones by Radical Cyclisation

Pradipta Kumar Basu and Amrita Ghosh

Department of Chemistry, Hooghly Mohsin College, P.O. Chinsurah, Dist. Hooghly, West Bengal 712101, India

Correspondence should be addressed to Pradipta Kumar Basu, pkbasu74@gmail.com

Received 25 April 2011; Revised 15 July 2011; Accepted 16 July 2011

Academic Editor: Ashraf Aly Shehata

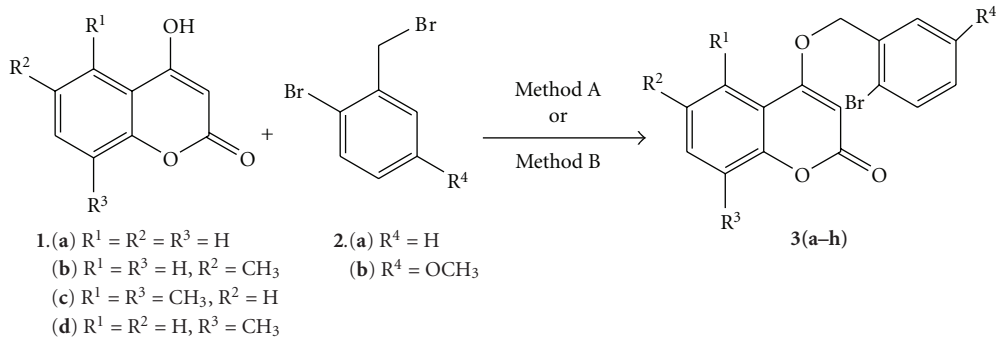
Two new effective methodologies have been adopted for the preparation of 4-(2′-bromobenzyloxy)benzopyran-7-ones **3(a–h)**. In the first methodology, 4-hydroxy[1]benzopyran-2-ones **1(a–d)** was alkylated with 2-bromobenzyl bromide **2a** or 2-bromo-5-methoxy benzyl bromide **2b** under phase transfer catalysis condition using lithium hydroxide/tetrabutyl ammonium bromide in *N,N*-dimethylformamide at 40–50°C and in the second method the microwave irradiation protocol has been exploited by simply mixing of 4-hydroxy[1]benzopyran-2-ones **1(a–d)** with 25% excess of 2-bromobenzyl bromide **2a** or 2-bromo-5-methoxy benzyl bromide **2b**. A catalytic amount of TBAB and potassium carbonate were added and irradiated in an open Erlenmeyer flask in a microwave oven for 4–10 min. The tributyltin-hydride-mediated radical cyclisation of **3(a–h)** was carried out under microwave irradiation to generate 12*H*-benzopyrano[3,2-*c*][1]benzopyran-5-ones **4(a–h)** in 78–88% yield and in this technique yields were significantly improved and reaction time was shortened compared to the previously reported conventional radical cyclisation method.

1. Introduction

In present time, the chemistry of radical cyclisation has been developed as a ripe field in all the aspects starting from polymers to synthesis of organic and inorganic compounds and such reactions have been applied to the synthesis of a number of natural products, pharmaceuticals, and others which mainly include heterocyclic compounds as a core structure [1]. It is now well established that radical chemistry offers a wide array of useful transformations for efficiently constructing complex molecular architectures [2–6] and has become part of the repertoire of the synthetic organic chemist. Radical reactions are of vital importance in biology and medicine. The search for various heterocycles and many new methodologies has been a central goal for free-radical chemists in recent years.

Aryl radical cyclisation has been at the forefront for constructing carbon-carbon bonds in organic synthesis [7–16]. Previously, Majumdar and Mukhopadhyay synthesised [17] 2*H*-benzopyrano[3,2-*c*]quinolin-7(8*H*)-ones by a Bu_3SnH-mediated radical cyclisation of 4-(2′-bromobenzyloxy)quinolin-2(1*H*)-one derivatives. The synthesis of various spiroheterocycles has also been reported [18] by the tri-n-butyltin hydride-induced radical cyclisation of 5-(*o*-bromoaryloxymethylene)-6,7,8-trihydropyrido[2,3-*d*]pyrimidine-2,4-(1*H*, 3*H*)-diones. The synthesis of spiro-[chroman-3,3′(2′*H*)-benzofurans] has also been explored [19] from a number of 3-(2-bromophenoxymethyl) coumarins under similar reaction conditions. But all these methods involve the radical cyclisation procedure under conventional thermal heating technique for a long period of time and long reaction time period makes this process environmentally hazardous. Thus, alternatively a simple, general, and improved methodology for the synthesis of various important heterocyclic systems is required.

Recently, microwave enhancement of organic reactions has attracted the chemists [20] as this technique is extremely useful in organic synthesis and the reactions can be performed with high reaction rates, low byproducts, high yields, and ease of experimental manipulations [21, 22]. It is



1.(**a**) $R^1 = R^2 = R^3 = H$
(**b**) $R^1 = R^3 = H$, $R^2 = CH_3$
(**c**) $R^1 = R^3 = CH_3$, $R^2 = H$
(**d**) $R^1 = R^2 = H$, $R^3 = CH_3$

2.(**a**) $R^4 = H$
(**b**) $R^4 = OCH_3$

3(a–h)

Scheme 1: Method A: LiOH, TBAB, DMF, 40–50°C; Method B: MWI (4–10 min), TBAB, K_2CO_3.

now well established that microwave heating technique is extremely powerful tool to promote a variety of chemical reactions [23–26] and the beauty of such microwave-assisted reaction lies in its dramatically reducing reaction time or sintering time [27], increasing the overall yield and selectivity of the reaction, accelerating the rate of the reaction of various thermally conducted reactions, and the simple and easy work-up procedure. It is obvious that microwave-promoted organic synthesis is an efficient and environmentally friendly synthetic route in modern synthetic organic chemistry as well as in green chemistry and in particular microwave irradiation technique under solvent-free conditions are extremely useful in offering reduced pollution compared to the traditional organic synthesis involving heating by conventional methods [23–31] and in the solvent-free reactions the absorption of microwave irradiation is restricted to the reacting species only [32]. In the conventional heating technique, reactants are slowly activated by a conventional external heat source and the heat penetrates first through the walls of the vessel for reaching the solvent and reactants and therefore is a slow and inefficient method for transferring energy into the reacting system. But, microwaves can create direct coupling with the molecules of the entire reaction mixture and the result is a rapid rise in temperature. There are many organic transformations proceeding through radical chemistry and chemists wonder if microwave irradiation can assist radical formation; microwave-promoted free-radical chemistry is increasingly being explored [33–42].

It is well known that microwave irradiation enhanced the reaction rates of Pd-catalysed C–C coupling such as the Stille, Suzuki, Heck, and Sonogashira reactions [43–57]. With these facts in our mind, we also thought that microwave irradiation might promote Bu_3SnH-annulated radical cyclisation reactions, since metal reagents and catalysts are good candidates to absorb microwaves [58, 59].

In spite of increasing interest of microwave irradiation technique, the use of this methodology in free-radical-based organic synthesis is less common [60–64]. As a part of our recent research activity we became interested in building the 6-membered fused pyran ring by radical cyclisation exploiting microwave irradiation. It is well known that 4-hydroxycoumarins are a class of anticoagulant drug molecules derived from coumarin, and the importance of physiological activity [65, 66] of coumarin and its derivatives motivated us to undertake the synthesis of 12*H*-benzopyrano[3,2-*c*][1]benzopyran-5-ones by aryl radical cyclisation, and in this paper, we will highlight the microwave-assisted one pot facile method compared to our previously described conventional method [67].

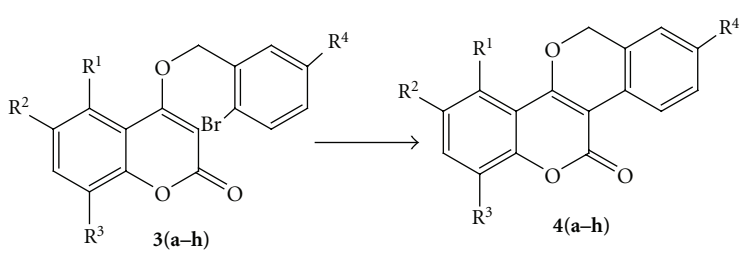
2. Results and Discussion

Previously we prepared [67] 4-(2′-bromobenzyloxy)benzopyran-7-ones **3(a–h)** by refluxing 4-hydroxy[1]benzopyran-2-ones with either 2-bromobenzyl bromide **2a** or 2-bromo-5-methoxy benzyl bromide **2b** in dry acetone in the presence of anhydrous potassium carbonate. Herein, we have established two new more effective methodologies for the preparation of 4-(2′-bromobenzyloxy)benzopyran-7-ones **3(a–h)**. In the first methodology, 4-hydroxy[1]benzopyran-2-ones **1(a–d)** can be successfully alkylated with 2-bromobenzyl bromide **2a** or 2-bromo-5-methoxy benzyl bromide **2b** under phase transfer catalysis condition using lithium hydroxide/tetrabutyl ammonium bromide in *N*,*N*-dimethylformamide at 40–50°C with a shorter reaction time than the conventional acetone-potassium carbonate method (Scheme 1 and Table 1). This new protocol involving reagents (LiOH, TBAB, and DMF) which are apparently little expensive than the previous one, but considering the shorter reaction time and higher yield this new technique is considered to be more effective and energy saving too. In this case, addition of less expensive sodium hydroxide in place of lithium hydroxide would break the lactone ring of the coumarin moiety and thus will be avoided. However, by using less basic LiOH at around 40–50°C, the products **3(a–h)** were obtained in very good yield.

Additionally, we have also exploited the microwave irradiation protocol in synthesising the radical precursor **3(a–h)** under solvent free condition. The syntheses were carried out by simply mixing of 4-hydroxy[1]benzopyran-2-ones **1(a–d)** with 25% excess of 2-bromobenzyl bromide **2a** or 2-bromo-5-methoxy benzyl bromide **2b** and a catalytic amount

Table 1: Preparation of radical precursors 3(**a–h**).

Entry	Product (**3**)	R^1	R^2	R^3	R^4	MWI time (A)	% yield (A)	% yield (B)	mp°C (lit. [67] mp°C)
(1)	**3a**	H	H	H	H	6 min	74	80	143 (142)
(2)	**3b**	H	H	H	OCH_3	4 min	76	82	122 (122)
(3)	**3c**	H	CH_3	H	H	8 min	85	88	157 (158)
(4)	**3d**	H	CH_3	H	OCH_3	8 min	75	81	167 (168)
(5)	**3e**	CH_3	H	CH_3	H	7 min	70	78	164-165 (165)
(6)	**3f**	CH_3	H	CH_3	OCH_3	7 min	82	84	170 (170)
(7)	**3g**	H	H	CH_3	H	10 min	89	93	115 (116)
(8)	**3h**	H	H	CH_3	OCH_3	10 min	76	86	145 (144)



Product **4** (yield)	mp°C (lit. [67] mp°C)
4a (82%)	137 (137)
4b (85%)	141 (142)
4c (80%)	166 (165)
4d (78%)	153 (152)
4e (84%)	185 (185)
4f (88%)	174 (175)
4g (88%)	135 (134)
4h (86%)	171 (172)

Scheme 2: Bu_3SnH, AIBN, PhMe, MWI (2.45 GHz, 1 h) in open vessel.

of tetrabutylammonium bromide (TBAB) (Scheme 1 and Table 1).

The mixtures were adsorbed on potassium carbonate and irradiated in an open Erlenmeyer flask in a microwave oven for 4–10 min (optimized time). The crude reaction mixture after usual workup was purified by column chromatography. Elution of the column with an appropriate mixture of ethyl acetate and petroleum ether gave the required product **3**.

We found that the above alkylation reaction using microwave irradiation (MWI) has advantages over conventional conditions [68] in several aspects including shorter reaction times, cleaner products, and simpler work-up procedures.

Previously we reported [67] the radical cyclisation mediated by tributyltin chloride and sodium cyanoborohydride, which was carried out initially under refluxing benzene conditions, in the reaction mixture maintained by the addition of this reagent via a syringe pump. The reaction furnished 12*H*-benzopyrano[3,2-c][1]benzopyran-5-ones (70–85%), respectively. Performing the cyclisation under microwave heating in an open vessel resulted in some shortening of the reaction time (1 h instead of 3-4 h for complete consumption of starting material, as detected by TLC), but, the important factor is that yields were significantly improved to 78–88% (Scheme 2).

In summary, this paper describes new and efficient methodologies involving microwave irradiation to synthesise 12*H*-benzopyrano[3,2-*c*][1]benzopyran-5-ones via radical cyclisation pathway and the mechanism of all the reactions is already well established [67]. This microwave-assisted free radical cyclisation is proved to be extremely powerful synthetic tool and the beauty of such reactions is improved reaction yields, shortening of reaction time, and being environment friendly. The methodology described here is very simple and general one.

3. Experimental

All the reagents were obtained from commercial sources and used as received. Except methanol (which was HPLC grade), the remaining solvents were dried and distilled before use. Elemental analyses and mass spectra (ESI+) were performed at the Indian Institute of Chemical Biology, Kolkata. UV absorption spectra were recorded in EtOH on a Shimadzu UV-2401 PC spectrophotometer (λ_{max} in nm) and IR spectra on KBr discs on a Perkin Elmer L 120-000A apparatus (ν_{max} in cm^{-1}). Routine ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded with a Bruker DPX-300 MHz instrument and Varian VRX-500 MHz instruments at 298 K. The chemical shifts (δ) are given in ppm and the coupling constants (J) in Hz. In all cases, the solvent for the NMR experiments was $CDCl_3$ (99.9%) and the references were $SiMe_4$ (for ^1H and ^{13}C $\{^1H\}$ NMR experiments). Silica gel ((60–120, 230–400 mesh), SRL, India) was used for chromatographic separation. Silica gel G (E-Merck (India)) and Silica gel 60F 254 (E-Merck (Germany)) were used for TLC. Petroleum ether refers to the fraction boiling between 60 and 80°C. Reaction mixture was irradiated in the CEM Discover microwave synthesis system.

*3.1. Typical Procedure for Synthesis of 4-(2′-Bromobenzyloxy)benzopyran-7-ones **3(a–h)***

Method A. LiOH (1.75 mmol) was added in three portions over 30 min to a solution of **1** (1.0 mmol), TBAB (0.1 mmol), and 2-bromobenzyl bromide **2a** or 2-bromo-5-methoxy benzyl bromide **2b** (1.0 mmol) in DMF (10 mL) at 40–50°C. The mixture was stirred at this temperature for a further 2.5 h, after which the reaction mixture was diluted with EtOAc (10 mL), washed with sat. aq NH_4Cl (20 mL), and extracted with EtOAc (3 × 15 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated by rotavapour. The crude mixture was purified by SiO_2 column chromatography using Petroleum ether : EtOAc = 1 : 1 as eluant to give **3**.

Method B. 4-Hydroxy[1]benzopyran-2-ones **1** (1.0 mmol) was mixed with 25% excess of 2-bromobenzyl bromide **2a** or 2-bromo-5-methoxy benzyl bromide **2b** (1.25 mmol), and a catalytic amount of tetrabutylammonium bromide (TBAB) (0.1 mmol). The mixtures were adsorbed on potassium carbonate (0.5 mmol) and irradiated in an open Erlenmeyer flask in a microwave oven for 4–10 min (optimized time). The residual mass was cooled at room temperature and was extracted with CH_2Cl_2 (2 × 50 mL) and washed with water and then with brine and dried (Na_2SO_4). After removal of dichloromethane solvent, the crude reaction mixture was purified by flash chromatography. Elution of the column with an appropriate mixture of ethyl acetate and petroleum ether gave the required products **3** in excellent yield.

*3.1.1. Typical Procedure for Synthesis of 12H-Benzopyrano [3,2-c][1]benzopyran-5-ones **4(a–h)**.* A mixture of *n*-Bu_3SnH (0.8 mmol, 1.6 equiv) and AIBN (22 mg, 0.13 mmol, 0.25 equiv) in toluene (10 mL) was added via a syringe pump over 1 h with a microwave irradiation at 100–110°C under open-vessel conditions to a solution of **3** (0.5 mmol, 1.0 equiv) and AIBN (22 mg, 0.13 mmol, 0.25 equiv) in toluene (10 mL). The reaction was monitored by TLC and after completion of the reaction solvent was evaporated by rotavapour, and it was extracted with CH_2Cl_2 (2 × 20 mL) and washed with 1% aqueous NH_4OH (2 × 10 mL) and brine. Evaporation of the solvent furnished the residual mass which was then magnetically stirred with saturated solution of potassium fluoride. It was again extracted with CH_2Cl_2 (3 × 10 mL) and was washed several times with water and dried (Na_2SO_4). The residual mass after removal of the solvent (CH_2Cl_2) was subjected to flash column chromatography using petroleum ether/ethyl acetate (1 : 2) as eluant to give cyclised products **4**.

All these products are known compounds and were easily identified by comparison of their spectroscopic data and mp's with those reported [67].

*3.1.2. Compound (**3b**).* White solid; mp 122°C; IR (KBr) (ν_{max}/cm^{-1}): 3030, 1700, 1600, 1450, 1360, 1240, 930, 750. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 3.84 (s, 3H, O–CH_3), 5.25 (s, 2H, –OCH_2), 5.81 (s, 1H, =CH), 6.82–6.85 (m, 1H, ArH), 7.06–7.09 (m, 1H, ArH), 7.28–7.37 (m, 2H, ArH), 7.53–7.61 (m, 2H, ArH), 7.89–7.91 (m, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$): δ_C (ppm) 55.9, 70.9, 91.9, 113.4, 115.7, 115.8, 115.9, 117.2, 123.5, 124.4, 132.9, 134.1, 135.0, 153.8, 159.6, 163.0, 165.4. MS: m/z = 360, 362 [M^+]. (Found: C, 56.58; H, 3.68. Calc. for $C_{17}H_{13}O_4Br$: C, 56.53; H, 3.63%.)

*3.1.3. Compound (**4b**).* White solid, mp 141–42°C; IR (KBr) (ν_{max}/cm^{-1}): 2900, 1710, 1590, 1380, 1080, 740. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H (ppm) 3.87 (s, 3H, O–CH_3), 4.51 (s, 2H, –OCH_2), 6.91–6.94 (dd, 1H, J = 2.5, 8.4 Hz, ArH), 7.13–7.14 (d, 1H, J = 2.5 Hz, ArH), 7.20–7.23 (d, 1H, J = 8.4 Hz, ArH), 7.31–7.36 (m, 1H, ArH), 7.39–7.42 (m, 1H, ArH), 7.53–7.59 (m, 1H, ArH), 7.73 (s, 1H, ArH). MS: m/z = 280 [M^+]. (Found: C, 72.79; H, 4.26. Calc. for $C_{17}H_{12}O_4$: C, 72.85; H, 4.32%.)

Acknowledgments

The authors are grateful to the Department of Science and Technology (New Delhi), Government of India for providing financial support under Fasttrack Scheme (SR/FT/CS-049/2008), and P.K. Basu dedicates this paper in the commemoration of his beloved late father, Sri Bharati Bhusan Basu. A. Ghosh is grateful to DST (New Delhi) for providing research fellowship (JRF). P. K. Basu is thankful to his departmental colleague Professor L. Thander for his continuous help.

References

[1] B. Halliwell and J. M. C. Gutteridge, *Free Radicals in Biology and Medicine*, Oxford University Press, Oxford, UK, 4th edition, 2007.

[2] B. Giese, *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*, Pergamon Press, Oxford, UK, 1986.

[3] C. P. Jasperse, D. P. Curran, and T. L. Fevig, "Radical reactions in natural product synthesis," *Chemical Reviews*, vol. 91, no. 6, pp. 1237–1286, 1991.

[4] G. A. Molander, "Diverse Methods for Medium Ring Synthesis," *Accounts of Chemical Research*, vol. 31, no. 10, pp. 603–609, 1998.

[5] P. Renaud and M. P. Sibi, Eds., *Radicals in Organic Synthesis*, vol. 1 & 2, Wiley-VCH, Weinheim, Germany, 2001.

[6] W. B. Motherwell and D. Crich, *Free Radical Chain Reactions in Organic Synthesis*, Academic Press, London, UK, 1992.

[7] K. C. Majumdar and N. Kundu, "Regioselective synthesis of bioactive spiro heterocyclic compounds containing both indoline and quinoline moieties by aryl radical cyclization," *Journal of Heterocyclic Chemistry*, vol. 46, no. 3, pp. 492–496, 2009.

[8] H. Ishibashi, K. Ohata, M. Niihara, T. Sato, and M. Ikeda, "Regiochemistry in aryl radical cyclisations (5-exo versus 6-endo) of N-vinylic 2-iodobenzamides," *Journal of the Chemical Society, Perkin Transactions 1*, no. 4, pp. 547–553, 2000.

[9] D. P. Curran, "The design and application of free radical chain reactions in organic synthesis. Part 1," *Synthesis*, no. 6, pp. 417–439, 1988.

[10] D. P. Curran, "The design and application of free radical chain reactions in organic synthesis. Part 2," *Synthesis*, no. 7, pp. 489–513, 1988.

[11] C. P. Jasperse, D. P. Curran, and T. L. Fevig, "Radical reactions in natural product synthesis," *Chemical Reviews*, vol. 91, no. 6, pp. 1237–1286, 1991.

[12] K. C. Majumdar, P. Debnath, and S. K. Chattopadhyay, "Aryl radical cyclization: Regioselective synthesis of 6a, 7, 8, 12b-tetrahydro-6Hchromeno[3,4-c]quinolin-6-one," *Synthetic Communication*, vol. 38, no. 11, pp. 1768–1777, 2008.

[13] K. C. Majumdar and P. K. Basu, "Formation of five- and six-membered heterocyclic rings by radical cyclization," *Heterocycles*, vol. 57, no. 12, pp. 2413–2439, 2002.

[14] W. R. Bowman, A. J. Fletcher, and G. B. S. Potts, "Synthesis of heterocycles by radical cyclisation," *Journal of the Chemical Society. Perkin Transactions 1*, no. 24, pp. 2747–2762, 2002.

[15] K. C. Majumdar, P. P. Mukhopadhyay, and P. K. Basu, "Formation of five- and six-membered heterocyclic rings by radical cyclization," *Heterocycles*, vol. 63, no. 8, pp. 1903–1958, 2004.

[16] K. C. Majumdar, P. K. Basu, and P. P. Mukhopadhyay, "Formation of five- and six-membered heterocyclic rings under radical cyclisation conditions," *Tetrahedron*, vol. 60, no. 30, pp. 6239–6278, 2004.

[17] K. C. Majumdar and P. P. Mukhopadhyay, "Regioselective synthesis of 2H-benzopyrano[3,2-c]quinolin-7(8H)-ones by radical cyclization," *Synthesis*, no. 1, pp. 97–100, 2003.

[18] K. C. Majumdar, S. Sarkar, and T. Bhattacharrya, "Studies in pyrimidine-annulated heterocycles: Unusual formation of spiroheterocyclic compounds from acid catalyzed reaction of enol ether," *Tetrahedron*, vol. 59, no. 24, pp. 4309–4314, 2003.

[19] K. C. Majumdar and S. K. Chattopadhyay, "Unusual reduction of a lactone carbonyl in a Bu_3SnCl and $Na(CN)BH_3$ mediated radical cyclization of 3-(o-bromophenoxymethyl) coumarins," *Tetrahedron Letters*, vol. 45, no. 37, pp. 6871–6873, 2004.

[20] H. M. Kingston and S. J. Haswell, *Microwave Enhanced Chemistry, Fundamentals, Sample Preparation and Applications*, American Chemical Society, Washington, DC, USA, 1997.

[21] B. K. Banik, K. J. Barakat, D. R. Wagle, M. S. Manhas, and A. K. Bose, "Microwave-assisted rapid and simplified hydrogenation," *Journal of Organic Chemistry*, vol. 64, no. 16, pp. 5746–5753, 1999.

[22] J. H. M. Lange, P. C. Verveer, S. J. M. Osnabrug, and G. M. Visser, "Rapid microwave-enhanced synthesis of 4-hydroxyquinolinones under solvent-free conditions," *Tetrahedron Letters*, vol. 42, no. 7, pp. 1367–1369, 2001.

[23] S. Caddick, "Microwave assisted organic reactions," *Tetrahedron*, vol. 51, no. 38, pp. 10403–10432, 1995.

[24] L. Perreux and A. Loupy, "A tentative rationalization of microwave effects in organic synthesis according to the reaction medium, and mechanistic considerations," *Tetrahedron*, vol. 57, no. 45, pp. 9199–9223, 2001.

[25] P. Lidström, J. Tierney, B. Wathey, and J. Westman, "Microwave assisted organic synthesis—a review," *Tetrahedron*, vol. 57, no. 45, pp. 9225–9283, 2001.

[26] A. Fini and A. Breccia, "Chemistry by microwaves," *Pure and Applied Chemistry*, vol. 71, no. 4, pp. 573–579, 1999.

[27] R. A. Olofson and R. V. Kendall, "Protection by acylation in the selective alkylation of heterocycles," *Journal of Organic Chemistry*, vol. 35, no. 7, pp. 2246–2248, 1970.

[28] S. A. Galema, "Microwave chemistry," *Chemical Society Review*, vol. 26, pp. 233–238, 1997.

[29] S. K. Srivastava, A. Nema, and S. D. Srivastava, "Conventional as well as microwave assisted synthesis of some new N^9-[hydrazinoacetyl-(2-oxo-3-chloro-4-substituted aryl azetidine)]-carbazoles: Antifungal and antibacterial studies," *Indian Journal of Chemistry B*, vol. 47, no. 4, pp. 606–612, 2008.

[30] A. R. Katritzky and S. K. Singh, "Microwave-assisted heterocyclic synthesis," *Arkivoc*, vol. 2003, no. 13, pp. 68–86, 2003.

[31] V. M. Patel and K. R. Desai, "Eco-friendly synthesis of fluorine-containing pyrazoline derivatives over potassium carbonate," *Arkivoc*, vol. 2004, no. 1, pp. 123–129, 2004.

[32] A. Loupy, L. Perreux, M. Liagre, K. Burle, and M. Moneuse, "Reactivity and selectivity under microwaves in organic chemistry. Relation with medium effects and reaction mechanisms," *Pure and Applied Chemistry*, vol. 73, no. 1, pp. 161–166, 2001.

[33] G. Chen, X. Zhu, Z. Cheng, W. Xu, and J. Lu, "Controlled/"living" radical polymerization of methyl methacrylate using AIBN as the initiator under microwave irradiation," *Radiation Physics and Chemistry*, vol. 69, no. 2, pp. 129–135, 2004.

[34] C. Wetter and A. Studer, "Microwave-assisted free radical chemistry using the persistent radical effect," *Chemical Communications*, vol. 10, no. 2, pp. 174–175, 2004.

[35] Y. Z. Wang, X. X. Zheng, Z. F. Chen, and C. Y. Zheng, "Microwave assisted radical grafting of maleic anhydride onto polyethylene in solution," *Journal of Macromolecular Science: Pure and Applied Chemistry*, vol. 40, no. 7, pp. 739–745, 2003.

[36] Z. Cheng, X. Zhu, M. Chen, J. Chen, and L. Zhang, "Atom transfer radical polymerization of methyl methacrylate with low concentration of initiating system under microwave irradiation," *Polymer*, vol. 44, no. 8, pp. 2243–2247, 2003.

[37] S. Horikoshi, H. Hidaka, and N. Serpone, "Hydroxyl radicals in microwave photocatalysis. Enhanced formation of OH radicals probed by ESR techniques in microwave-assisted photocatalysis in aqueous TiO_2 dispersions," *Chemical Physics Letters*, vol. 376, no. 3-4, pp. 475–480, 2003.

[38] M. Lamberto, D. F. Corbett, and J. D. Kilburn, "Microwave assisted free radical cyclisation of alkenyl and alkynyl isocyanides with thiols," *Tetrahedron Letters*, vol. 44, no. 7, pp. 1347–1349, 2003.

[39] D. D. Wisnoski, W. H. Leister, K. A. Strauss, Z. Zhao, and C. W. Lindsley, "Microwave-initiated living free radical polymerization: rapid formation of custom Rasta resins," *Tetrahedron Letters*, vol. 44, no. 23, pp. 4321–4325, 2003.

[40] W. Xu, X. Zhu, Z. Cheng, G. Chen, and J. Lu, "Atom transfer radical polymerization of n-octyl acrylate under microwave irradiation," *European Polymer Journal*, vol. 39, no. 7, pp. 1349–1353, 2003.

[41] T. Durand-Reville, L. B. Gobbi, B. L. Gray, S. V. Ley, and J. S. Scott, "Highly selective entry to the azadirachtin skeleton via a claisen rearrangement/radical cyclization sequence," *Organic Letters*, vol. 4, no. 22, pp. 3847–3850, 2002.

[42] A. F. Porto, B. L. Sadicoff, M. C. V. Amorim, and M. C. S. De Mattos, "Microwave-assisted free radical bulk-polyaddition reactions in a domestic microwave oven," *Polymer Testing*, vol. 21, no. 2, pp. 145–148, 2002.

[43] N. E. Leadbeater and M. Marco, "Transition-metal-free Suzuki-type coupling reactions," *Angewandte Chemie - International Edition*, vol. 42, no. 12, pp. 1407–1409, 2003.

[44] N. E. Leadbeater and M. Marco, "Transition-metal-free Suzuki-type coupling reactions: scope and limitations of the methodology," *Journal of Organic Chemistry*, vol. 68, no. 14, pp. 5660–5667, 2003.

[45] N. E. Leadbeater, M. Marco, and B. J. Tominack, "First examples of transition-metal free Sonogashira-type couplings," *Organic Letters*, vol. 5, no. 21, pp. 3919–3922, 2003.

[46] J. M. Harris and A. Padwa, "A new β-carbolinone synthesis using a Rh(II)-promoted [3 + 2]-cycloaddition and Pd(0)

cross-coupling/Heck cyclization chemistry," *Organic Letters*, vol. 5, no. 22, pp. 4195–4197, 2003.

[47] K. S. A. Vallin, P. Emilsson, M. Larhed, and A. Hallberg, "High-speed Heck reactions in ionic liquid with controlled microwave heating," *Journal of Organic Chemistry*, vol. 67, no. 17, pp. 6243–6246, 2002.

[48] E. Petricci, M. Radi, F. Corelli, and M. Botta, "Microwave-enhanced Sonogashira coupling reaction of substituted pyrimidinones and pyrimidine nucleosides," *Tetrahedron Letters*, vol. 44, no. 51, pp. 9181–9184, 2003.

[49] M. M. S. Andappan, P. Nilsson, and M. Larhed, "Arylboronic acids as versatile coupling partners in fast microwave promoted oxidative Heck chemistry," *Molecular Diversity*, vol. 7, no. 2-4, pp. 97–106, 2003.

[50] G. K. Datta, K. S. A. Vallin, and M. Larhed, "A rapid microwave protocol for Heck vinylation of aryl chlorides under air," *Molecular Diversity*, vol. 7, no. 2-4, pp. 107–114, 2003.

[51] K. S. A. Vallin, Q. Zhang, M. Larhed, D. P. Curran, and A. Hallberg, "A new regioselective Heck vinylation with enamides. Synthesis and investigation of fluorous-tagged bidentate ligands for fast separation," *Journal of Organic Chemistry*, vol. 68, no. 17, pp. 6639–6645, 2003.

[52] P. Nilsson, H. Gold, M. Larhed, and A. Hallberg, "Microwave-assisted enantioselective Heck reactions: expediting high reaction speed and preparative convenience," *Synthesis*, no. 11, pp. 1611–1614, 2002.

[53] L. Bai, J. X. Wang, and Y. Zhang, "Rapid microwave-promoted Suzuki cross coupling reaction in water," *Green Chemistry*, vol. 5, no. 5, pp. 615–617, 2003.

[54] N. E. Leadbeater and M. Marco, "Rapid and amenable Suzuki coupling reaction in water using microwave and conventional heating," *Journal of Organic Chemistry*, vol. 68, no. 3, pp. 888–892, 2003.

[55] N. E. Leadbeater and M. Marco, "Ligand-free palladium catalysis of the Suzuki reaction in water using microwave heating," *Organic Letters*, vol. 4, no. 17, pp. 2973–2976, 2002.

[56] Y. Gong and W. He, "Direct synthesis of unprotected 4-Aryl phenylalanines via the Suzuki reaction under microwave irradiation," *Organic Letters*, vol. 4, no. 22, pp. 3803–3805, 2002.

[57] M. Melucci, G. Barbarella, and G. Sotgiu, "Solvent-free, microwave-assisted synthesis of thiophene oligomers via suzuki coupling," *Journal of Organic Chemistry*, vol. 67, no. 25, pp. 8877–8884, 2002.

[58] K. Olofsson, S. Y. Kim, M. Larhed, D. P. Curran, and A. Hallberg, "High-speed, highly fluorous organic reactions," *Journal of Organic Chemistry*, vol. 64, no. 12, pp. 4539–4541, 1999.

[59] A. K. Bose, M. S. Manhas, M. Ghosh et al., "Microwave-induced organic reaction enhancement chemistry. 2. Simplified techniques," *Journal of Organic Chemistry*, vol. 56, no. 25, pp. 6968–6970, 1991.

[60] F. Portela-Cubillo, J. S. Scott, and J. C. Walton, "Microwave-assisted preparations of dihydropyrroles from alkenone O-phenyl oximes," *Chemical Communications*, no. 39, pp. 4041–4043, 2007.

[61] J. A. Bull, M. G. Hutchings, and P. Quayle, "A remarkably simple and efficient benzannulation reaction," *Angewandte Chemie - International Edition*, vol. 46, no. 11, pp. 1869–1872, 2007.

[62] C. M. Jessop, A. F. Parsons, A. Routledge, and D. J. Irvine, "Radical addition reactions of phosphorus hydrides: tuning the reactivity of phosphorus hydrides, the use of microwaves and horner-wadsworth-emmons-type reactions," *European Journal of Organic Chemistry*, no. 6, pp. 1547–1554, 2006.

[63] B. Schulte and A. Studer, "Radical carboaminoxylation with subsequent Pd-catalyzed intramolecular allylation for the construction of five- and six-membered carbocycles," *Synthesis*, no. 13, pp. 2129–2138, 2006.

[64] C. Wetter and A. Studer, "Microwave-assisted free radical chemistry using the persistent radical effect," *Chemical Communications*, vol. 10, no. 2, pp. 174–175, 2004.

[65] G. Feur, in *Progress in Medicinal Chemistry*, G. P. Ellis and G. B. West, Eds., North-Holland, New York, NY, USA, 1974.

[66] V. P. Lauger, H. Martin, and P. Muller, "Über Konstitution und toxische Wirkung von natürlichen und neuen synthetischen insektentötenden Stoffen," *Helvetica Chimica Acta*, vol. 27, pp. 892–928, 1944.

[67] K. C. Majumdar, P. K. Basu, P. P. Mukhopadhyay, S. Sarkar, S. K. Ghosh, and P. Biswas, "Regioselective synthesis of *1H,3H,6H*[2]benzopyrano[4,3-*d*]pyrimidine-2,4-diones and 12*H*-benzopyrano[3,2-c][1]benzopyran-5-ones by radical cyclization," *Tetrahedron*, vol. 59, no. 12, pp. 2151–2157, 2003.

[68] A. S. R. Anjaneyulu and B. M. Isaa, "Thermal Claisen rearrangement of allyl ethers of isomeric acetylnaphthols," *Journal of the Chemical Society, Perkin Transactions 1*, vol. 1990, pp. 993–998, 1990.