Available online at www.sciencedirect.com

ScienceDirect

Chinese Chemical Letters 22 (2011) 268–271

CHINESE CHEMICAL LETTERS

www.elsevier.com/locate/cclet

Synthesis of 1,2-allenic ketones through oxidation of homopropargyl alcohols with CrO_3(cat.)/TBHP under MWI

Xin Ying Zhang *, Ying Ying Qu, Yang Yang Wang, Xue Sen Fan *

School of Chemistry and Environmental Science, Henan Key Laboratory for Environmental Pollution Control, Henan Normal University, Xinxiang 453007, China

Received 7 June 2010
Available online 22 December 2010

Abstract

A CrO_3 catalyzed oxidation of homopropargyl alcohols with *tert*-butyl hydroperoxide under microwave irradiation was found to be an efficient and rapid alternative for the preparation of 1,2-allenic ketones. The advantages of this procedure include short reaction time, less adverse impact on the environment and reasonably high efficiency.

Keywords: Allenic ketones; Oxidation; Microwave irradiation; Chromium(VI) oxide; *tert*-Butyl hydroperoxide

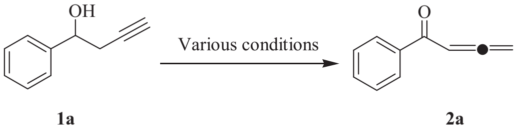
Oxidation is among the most used transformations in organic chemistry and is frequently accomplished by the use of chromium reagents since they are efficient, cheap and readily available. However, many oxidation processes involved chromium agents in quantities ranging from stoichiometric to a large excess, which are unfortunately not compatible with environmental regulations since chromium residues are environmentally hazardous. Therefore, it would be advantageous to develop oxidizing methods requiring only catalytic amounts of Cr(VI) while still exploiting its excellent oxidative capability [1,2]. In the meantime, the utility of microwave energy in synthetic organic chemistry has been increasingly recognized due to the fact that compared with conventional heating, reactions promoted by microwave irradiation (MWI) have shown enhanced reaction rate, greater selectivity and thus an environmentally friendly nature.

1,2-Allenic ketones are an important class of compounds with numerous applications in organic synthesis [3–7]. Due to their importance, various synthetic routes to 1,2-allenic ketones have been reported [8–10]. In particular, one often used protocol involves firstly the reaction of allenylmetals with carbonyl compounds, followed by oxidation of the resulting allenic or homopropargylic alcohols [11]. The oxidant used is usually DMP (Dess–Martin Periodinane). Though Dess–Martin oxidation is an efficient procedure, the formation of 1,2-allenic ketones usually needs extended reaction period and is often contaminated by side products [12]. Therefore, the development of rapid and more efficient procedures for the preparation of 1,2-allenic ketones still remains a challenge.

---

* Corresponding authors.
E-mail addresses: xinyingzhang@henannu.edu.cn (X.Y. Zhang), xuesen.fan@henannu.edu.cn (X.S. Fan).

1001-8417/$ – see front matter © 2010 Published by Elsevier B.V. on behalf of Chinese Chemical Society.
doi:10.1016/j.cclet.2010.09.032



Scheme 1.

As part of our ongoing research efforts towards the development of synthetic methodologies for the preparation of important organic compounds, we envisioned a new route to 1,2-allenic ketone through the oxidation of homopropargyl alcohols under MWI with catalytic CrO_3 together with an environmentally benign oxidant.

Initially, 1-phenylbut-3-yn-1-ol (**1a**, Scheme 1), prepared from benzaldehyde and propargyl bromide in the presence of zinc [13], was used as a model substrate to study the effects of various reaction conditions and different oxidants on this reaction. The results were summarized in Table 1.

Table 1
Optimization of the reaction conditions for the synthesis of **2a**[a].

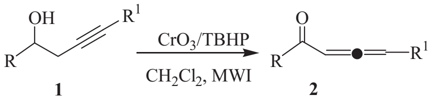
Entry	Solvent	CrO_3 (equiv.)	Oxidant	Time (h)	Temp. (°C)	Yield (%)[e]
1	H_2O[b]	0.03	H_2O_2	5	rt	Trace
2	H_2O[b]	0.03	H_2O_2	5	60	Trace
3	H_2O[b]	0.05	H_2O_2	5	80	21
4	H_2O[b]	0.05	H_2O_2	0.5	MWI	30
5	CH_2Cl_2[b]	0.05	TBHP	5	rt	25
6	CH_2Cl_2[b]	0.05	TBHP	3	reflux	41
7	CH_2Cl_2[b]	0.05	TBHP	0.2	MWI	62
8	CH_2Cl_2[b]	0.05	TBHP	0.5	MWI	63
9	CH_2Cl_2[b]	0.05	TBHP	0.8	MWI	60
10	CH_2Cl_2[b]	0.05	TBHP[d]	0.5	MWI	55
11	CH_3CN[b]	0.05	TBHP	0.5	MWI	42
12	THF[b]	0.05	TBHP	0.5	MWI	36
13	[bmim]BF_4[c]	0.05	TBHP	0.5	MWI	41
14	[bmim]PF_6[c]	0.05	TBHP	0.5	MWI	46

[a] Reaction conditions: 1 mmol of **1a** and 3 equiv. of oxidant were used.
[b] 10 mL of solvent were used.
[c] 1 mL of solvent were used.
[d] 2 equiv. of oxidant were used.
[e] Isolated yields.

Table 2
Synthesis of 1,2-allenic ketones with CrO_3/TBHP under MWI[a].

Entry	R	R^1	Product	Time (min)	Yield (%)[b]
1	C_6H_5	H	**2a**	12	62
2	p-$CH_3C_6H_4$	H	**2b**	12	65
3	p-ClC_6H_4	H	**2c**	10	70
4	p-BrC_6H_4	H	**2d**	10	71
5	p-FC_6H_4	H	**2e**	13	69
6	m-$CH_3C_6H_4$	H	**2f**	10	62
7	m-BrC_6H_4	H	**2g**	13	55
8	m-FC_6H_4	H	**2h**	10	50
9	o-ClC_6H_4	H	**2i**	15	48
10	$C_6H_5CH_2$	H	**2j**	30	18[c]
11	p-BrC_6H_4	Me	**2k**	10	61
12	p-$CH_3C_6H_4$	Me	**2l**	10	62

[a] Reaction conditions: **1** (1 mmol), CrO_3 (0.05 equiv.), TBHP (3 equiv.), MWI, 40 °C.
[b] Isolated yields.
[c] NMR yield.



Scheme 2.

In the first place, aqueous H_2O_2 was chosen as the oxidant. It turned out that with conventional heating, the reaction underwent slowly and the yields of **2a** were low (Table 1, entries 1–3). When MWI was introduced, the time period for a complete conversion shortened, but the yield was still unsatisfactory (entry 4). We then resorted to another kind of peroxide, *tert*-butyl hydroperoxide (TBHP), to replace H_2O_2. Encouragingly, the reactions with TBHP improved significantly compared with that of H_2O_2 (entries 5–7). Various organic solvents were also tried as the reaction medium and CH_2Cl_2 gave the best results (entries 5–12). In CH_2Cl_2, the reaction period for a complete consumption of the starting material at room temperature or under conventional heating was 5 h or 3 h, respectively (entries 5–6). Under MWI, however, the reaction time was strikingly shortened to 12 min, reflecting the specific non-thermal effects under MWI conditions (entry 7). On the other hand, it has been reported that ionic liquids (ILs) are excellent microwave absorbing agents due to their thermal stability, high ionic conductivity and polarizability [14], it was then of our interests to explore MWI technique in two readily available ILs, [bmim][BF_4] and [bmim][PF_6]. However, it turned out the reactions carried out in ILs did not give improved results compared with that with other conventional organic solvents (entries 13–14). Therefore, the optimal conditions were obtained as: the solution of **1a** in CH_2Cl_2 was irradiated with MW at 40 °C for 0.2 h in the presence of 5 mol% of CrO_3 as catalyst and 3 equiv. of TBHP as oxidant (entry 7).

With the optimized reaction conditions, the scope and limitations of this oxidation was evaluated. It was observed that, with aryl substituted homopropargyl alcohols, the reactions underwent smoothly and the corresponding products were obtained in moderate yields [15]. With either electron-withdrawing or electron-donating groups at the *para* position of the phenyl rings, the oxidative reactions were equally efficient (entries 2–5, Table 2). The reactions were slowed with substrate bearing substituent at the *ortho* position (entry 9, Table 2). These results indicated that the electronic effect on the phenyl group did not play a significant role in affecting the oxidation, probably due to their high reactivity. In contrast, steric hindrance seems to be a key factor in affecting the oxidation of these substrates. Moreover, various functional groups, such as alkyl and halide groups on phenyl rings, were well tolerated under these conditions. It is worth to be noted that the oxidation of aliphatic substrate was complicated and the corresponding product was only formed in low yield (entry 10, Table 2). On the other hand, with internal alkyne substrates, the reactions underwent smoothly and afforded the corresponding 1,2-allenic ketones with good yields (entries 11–12, Table 2) (Scheme 2).

In conclusion, we have introduced an efficient and rapid procedure for the preparation of 1,2-allenic ketone through oxidation of propargyl alcohols with TBHP catalyzed by CrO_3 in CH_2Cl_2 under MWI. To the best of our knowledge, this is the first report of synthesis of 1,2-allenic ketone with catalytic Cr(VI) species under MWI and these new reaction conditions open an important alternative to the use of large amount of toxic reagents and long time conventional heating. Further studies to probe the mechanism of this transformation and to broaden the scope of these reactions are currently underway in our laboratory and will be reported in due course.

Acknowledgments

We are grateful to the National Natural Science Foundation of China (Nos. 20772025 and 20972042), Innovation Scientists and Technicians Troop Construction Projects of Henan Province (No. 104100510019), Natural Science Foundation of Henan Province (No. 092300410237) and the Natural Science Foundation of Department of Education of Henan Province (Nos. 2009A150017 and 2008A150013).

References

[1] (a) J. Muzart, Tetrahedron Lett. 28 (1987) 2133;
(b) J. Muzart, O. Piva, Tetrahedron Lett. 29 (1988) 2321;
(c) M.A. Fousteris, A.I. Kousourea, S.S. Nikolaropoulos, A. Riahi, J. Muzart, J. Mol. Catal. A: Chem. 250 (2006) 70.

[2] (a) D.D. Agarwal, J. Mol. Catal. 44 (1988) 65;
(b) D.D. Agarwal, S. Shrivastava, Polyhedron 7 (1988) 2569;
(c) D.D. Agarwal, S. Shrivastava, P. Chadlha, Polyhedron 9 (1990) 487.

[3] N. Krause, A. Hoffmann-Röder, Tetrahedron 60 (2004) 11671.

[4] H.F. Schuster, G.M. Coppola, Allenes in Organic Synthesis, Wiley, New York, 1984.

[5] (a) S.H. Yin, J. Org. Chem. 68 (2003) 8996, and references cited therein;
(b) S.M. Ma, S.C. Yu, W.J. Qian, Tetrahedron 61 (2005) 4157.

[6] (a) J.A. Marshall, G.S. Bartley, J. Org. Chem. 59 (1994) 7169;
(b) S.M. Ma, J.L. Zhang, L.H. Lu, Chem. Eur. J. 9 (2003) 2447;
(c) C.Y. Zhou, P.W.H. Chan, C.M. Che, Org. Lett. 8 (2006) 325.

[7] (a) K. Kumar, A. Kapur, M.P.S. Ishar, Org. Lett. 2 (2000) 787;
(b) N. Krause, A.S.K. Hashmi (Eds.), Modern Allene Chemistry, Wiley-VCH, Weinheim, 2004;
(c) S. Ma, Chem. Rev. 105 (2005) 2829;
(d) S. Ma, Aldrichim. Acta 40 (2007) 91.

[8] P.D. Landor, in: S.R. Landor (Ed.), The Chemistry of Allenes, vol. 1, Academic, London, UK, 1982.

[9] S.M. Ma, L.T. Li, H.Y. Xie, J. Org. Chem. 64 (1999) 5325.

[10] (a) G. Buono, Synthesis (1981) 872;
(b) S.M. Ma, L.T. Li, Org. Lett. 2 (2000) 941;
(c) A. Denichoux, F. Ferreira, F. Chemla, Org. Lett. 6 (2004) 3509;
(d) B.W. Yoo, S.J. Lee, K.H. Choi, et al. Tetrahedron Lett. 42 (2001) 7287.

[11] (a) R. Couffignal, M. Gaudemar, Bull. Soc. Chim. Fr. (1969) 3218;
(b) T. Flood, P.E. Peterson, J. Org. Chem. 45 (1980) 5006;
(c) R.C. Larock, M.S. Chow, S.J. Smith, J. Org. Chem. 51 (1986) 2623;
(d) A.S.K. Hashmi, J.W. Bats, J.H. Choi, L. Schwarz, Tetrahedron Lett. 39 (1998) 7491.

[12] A.S.K. Hashmi, J.-H. Chio, J.W. Bats, J. Prakt. Chem. (1999) 341.

[13] W.L. Wu, Z.J. Yao, Y.L. Li, et al. J. Org. Chem. 60 (1995) 3257.

[14] X.D. Xu, M. Zhang, J. Feng, M.L. Zhang, Mater. Lett. 62 (2008) 2787.

[15] General procedure for the oxidation of homopropargyl alcohols to 1,2-allenic ketones. To a solution containing propargyl alcohol (1 mmol) and CrO_3 (0.05 mmol) in CH_2Cl_2 (10 mL) was added TBHP (3 mmol) at room temperature. The mixture was then put into a commercially available single-mode microwave synthesis apparatus equipped with a high sensitivity infrared sensor for temperature control and measurement (MAS-I, Sineo Microwave Chemical Technology Co. Ltd., Shanghai, P.R. China) and irradiated at 300 W (internal temperature 40 °C) for the time period listed in Table 2. Upon completion, the mixture was filtered over Celite. The solvent was evaporated under reduced pressure and the residue was subjected to flash chromatography (eluted with petroleum ether/ethyl acetate) to afford the corresponding 1,2-allenic ketone product. **2a**: liquid; IR (neat): 2926, 2856, 1961, 1932, 1670 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.27 (d, 2H, $J = 6.4$ Hz, CH_2), 6.46 (t, 1H, $J = 6.4$ Hz, CH), 7.44–7.48 (m, 2H, ArH), 7.55–7.59 (m, 1H, ArH), 7.90–7.92 (m, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 79.2, 93.2, 128.3, 128.7, 132.8, 137.4, 191.0, 217.1. MS: *m/z* 167 $[M+Na]^+$. HRMS (FAB) Calcd. for $C_{10}H_9O$: 145.0653 $(MH)^+$, found: 145.0658. **2c**: liquid; IR (neat): 2920, 2868, 1960, 1932, 1668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.27 (d, 2H, $J = 6.4$ Hz, CH_2), 6.39 (t, 1H, $J = 6.4$ Hz, CH), 7.42 (d, 2H, $J = 8.4$ Hz, ArH), 7.84 (d, 2H, $J = 8.4$ Hz, ArH). 13C NMR (100 MHz, $CDCl_3$): δ 79.5, 93.2, 128.7, 130.1, 135.7, 139.2, 189.8, 217.2. MS: *m/z* 201 $[M+Na]^+$. HRMS (FAB) Calcd. for $C_{10}H_8ClO$: 179.0263 $(MH)^+$, found: 179.0263. **2k**: liquid; IR (neat): 2928, 1960, 1934, 1651 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.99–2.01 (m, 3H, CH_3), 5.04–5.06 (m, 2H, 2× CH), 7.53 (d, 2H, ArH, $J = 8.4$ Hz), 7.63 (d, 2H, ArH, $J = 8.4$ Hz). 13C NMR (100 MHz, $CDCl_3$): δ 14.6, 78.7, 102.0, 126.7, 130.5, 131.1, 136.8, 193.9, 217.5. MS: *m/z* 259 $[M+Na]^+$. HRMS (FAB) Calcd. for $C_{11}H_{10}BrO$: 236.9915 $(MH)^+$, found: 236.9909. **2l**: liquid; IR (neat): 2923, 2870, 1960, 1934, 1665 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.99–2.02 (m, 3H, CH_3), 2.40 (s, 3H, CH_3), 5.02–5.04 (m, 2H, 2× CH), 7.20 (d, 2H, ArH, $J = 8.0$ Hz), 7.70 (d, 2H, ArH, $J = 8.0$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.8, 21.6, 78.2, 101.8, 128.5, 129.5, 135.3, 142.6, 194.7, 217.2. MS: *m/z* 195 $[M+Na]^+$. HRMS (FAB) Calcd. for $C_{12}H_{13}O$: 173.0966 $(MH)^+$, found: 173.0966.