



Received: 03 March 2015
Accepted: 06 August 2015
Published: 07 September 2015

*Corresponding author: Abbas Shockravi, Faculty of Chemistry, Kharazmi University, 49-Mofetteh Ave., Tehran, Iran
E-mail: abbas_shockravi@yahoo.co.uk

Reviewing editor:
George Weaver, University of Loughborough, UK

Additional information is available at the end of the article

ORGANIC CHEMISTRY | RESEARCH ARTICLE

One-pot, solvent-free synthesis via Biginelli reaction: Catalyst-free and new recyclable catalysts

Mahmood Kamali¹, Abbas Shockravi^{1*}, Maryam Saghafi Doost¹ and Seyyed Emad Hooshmand¹

Abstract: Free catalyst one-pot three components coupling of aldehydes, β -dicarbonyl compounds, and urea was performed to afford both the corresponding 3,4-dihydropyrimidine-2-ones (**DHPOs**, (1-9)**a**) and their sulfur analogs 3,4-dihydropyrimidine-2-thiones (**DHPTs**, (1-9)**b**), synthesized in the presence of uranyl acetate (**UA**) and succinimide sulfonic acid (**SuSA**) as catalysts under the same conditions via Biginelli condensation protocol. Interestingly, the free catalyst reactions were performed for 4 h for **DHPOs** with the yields of high to excellent, while in the cases of **DHPTs**, the yield was lower. But when the **UA** or **SuSA** was used, the yields (both of **DHPOs** and **DHPTs**) were high to excellent and the reaction times were either 2.5 or 1 h, respectively. Also, these two catalysts were recyclable for four consecutive runs.

Subjects: Chemistry; Medicinal & Pharmaceutical Chemistry; Organic Chemistry

Keywords: free catalyst; uranyl acetate; succinimide sulfonic acid; 3,4-dihydropyrimidine-2-one; 3,4-dihydropyrimidine-2-thione

1. Introduction

The Italian chemist Biginelli (1891a, 1891b), observed the reaction between an ammonia source and an aldehyde in equimolar ratio and urea in acidic alcoholic solution to obtain new compounds, well known as 3,4-dihydropyrimidine-2(1H)-ones (Kenner & Todd, 1957; Zaugg & Martin, 1965). After years from this discovery, emphasis was on understanding the course of reaction and some emphasis on structural variants as well. Subsequent to these academic developments, the Biginelli scaffold was shown to be of great value from a pharmaceutical point of view; because of this importance, investigations were very fast, and virtually every major journal was flooded with papers on the Biginelli reaction (Biginelli, 1893; Dallinger & Kappe, 2005; Dallinger, Stadler, & Kappe, 2004; Kappe, 1993, 2000a, 2000b, 2003, 2005; Kappe & Stadler, 2004; Kolosov, Orlov, Beloborodov, & Dotsenko, 2009; Phucho,



Mahmood Kamali

ABOUT THE AUTHOR

Mahmood Kamali obtained his PhD in organic chemistry in 2011 from Kharazmi University, Tehran, Iran. Now he is an assistant professor in the Faculty of Chemistry, Kharazmi University. His main interest is designing of new synthetic methodology toward organic compounds with the aim of macrocyclic, polymeric and pharmaceutical targeted molecules.

PUBLIC INTEREST STATEMENT

Considerable attention has been paid to the synthesis of 3,4-dihydropyrimidine-2-ones (-thiones) owing to their significant biological activities. The search continues for better catalysts for the synthesis of and 3,4-dihydropyrimidines in terms of operational simplicity, reusability, economic viability, and greater selectivity. The current work reports efficient new catalysts (**UA** and **SuSA**) and compares these with catalyst free method in the preparation of such products.

Nongpiur, Tumtin, Nongrum, & Nongkhlaw, 2009; Singh, Arorea, & Singh, 2009; Vdovina & Mamedov, 2008; Wan & Liu, 2010). 3,4-Dihydropyrimidine-2-ones (**DHPOs**) were viewed in terms of operational simplicity, reusability, economic viability, and greater selectivity. Although different methods for the synthesis of Biginelli's products were based on the use of strong protic acids such as H_2SO_4 (Folkers & Johnson, 1933a), HCl (Folkers & Johnson, 1933b) and zeolite (Radharani, Srinivas, Radha Kishan, Kulkarni, & Raghavan, 2001) metal triflates (Su, Li, Zheng, & Shen, 2005; Varala, Alam, & Adapa, 2003), varieties of other conditions such as ultrasonic (Gholap, Venkatesan, Daniel, Lahoti, & Srinivasan, 2004; Zhang, Li, Liu, & Wang, 2006), low melting acidic (Sangram, Sundarababu, & Bukhard, 2011) methods and ionic liquid (Valizadeh & Shockravi, 2009) media have been reported in the literature.

Uranyl acetate (**UA**) has been extensively used as a negative stain in the electron microscopy (Lewis & Knight, 1977).

But there are few references for **UA** as catalyst in organic reactions (Jha & Halada, 2011; Wang, Zhao, Li, Wang, & Zhang, 2001). In these works, the **UA** was used along with some other salts. It is vague that the original role is either because **UA** acts as Lewis catalyst or due to other accompanying salt. Also, the researches demonstrate that succinimide sulfonic acid (**SuSA**) efficiency promotes the rates of N-Boc protection of amines, trimethylsilylation of alcohols and phenols, and synthesis of xanthenes (Shirini & Ghaffari Khaligh, 2011, 2012a, 2012b).

In continuation of our investigations on the synthesis of (**DHPOs** and **DHPTs**) via Biginelli protocols (Shockravi, Kamali, Sharifi, Nategholeslam, & PahlavanMoghanlo, 2013), here in, we report efficient new catalysts (**UA** and **SuSA**) and compare with catalyst free method in the preparation of such products.

2. Experimental

2.1. Chemicals and apparatus

All reactions were carried out in an efficient hood. The starting materials were purchased from Merck and Fluka chemical companies. Melting points were determined with a Branstead Electrothermal model 9200 apparatus and are uncorrected. IR spectra were recorded on a Perkin Elmer RX 1 Fourier transform infrared spectrometer. The 1H and ^{13}C NMR spectra were recorded in $DMSO-d_6$, Acetone- d_6 , and $CDCl_3$ on Bruker Avance 300 MHz spectrometers. Elemental analyses were carried out by a Perkin Elmer 2400 series II CHN/O analyzer. In continuation of our investigations on the synthesis of (**DHPOs** and **DHPTs**) via Biginelli protocols, here in, we report efficient new catalysts (**UA** and **SuSA**) and compare with catalyst free method in the preparation of such products.

2.2. Synthesis of 1a as general procedure

A mixture of benzaldehyde (2 mmol, 0.21 g), ethyl acetoacetate (2 mmol, 0.26 g), urea (3 mmol, 0.18 g) and **UA**, $2H_2O$, (1 mol %, 8.5 mg) or **SuSA** (1 mol %, 3.6 mg) (or without catalyst) was heated in an oil bath with stirring at 90°C for corresponding hours (Tables 1 and 2). After cooling, the

Table 1. Free catalyst synthesis of 1a under different conditions for optimization of reactions

Temperature (°C)	Time (h)	Product yield (%)
50	5	30
60	5	35
70	5	55
80	5	67
90	5	95
100	5	95
90	4	95
90	3	85

Table 2. Synthesis of 7b under different conditions for optimization of reactions

Temperature of reaction (°C)	Catalyst (mol %)	UA as catalyst		SuSA as catalyst	
		Time (h)	Product yield (%)	Time (h)	Product yield (%)
80	20	4	75	4	75
90	20	4	95	4	95
100	20	4	95	4	93
90	10	4	95	4	95
90	5	4	95	4	95
90	1	4	95	4	95
90	0.5	4	87	4	85
90	1	2.5	95	2	95
90	1	2	87	1.5	95
90	1	–	–	1	95

Table 3. Details of Biginelli synthesis

Entry	Ar	Urea	Thiourea	Product yield (%) without catalyst	Product yield (%) with UA	Product Yield (%) with SuSA	mp (°C)	
							Found	Lit.
1a	C ₆ H ₅	✓		80	95	90	205–207	204–205 ^a
1b			✓	45	86	85	206–208	206–208 ^b
2a	2-Cl-C ₆ H ₅	✓		95	85	88	221–223	222–224 ^c
2b			✓	62	80	85	216–218	–
3a	4-Cl-C ₆ H ₅	✓		85	84	83	212–214	214–215 ^c
3b			✓	25	81	80	177–180	178–179 ^d
4a	3-(NO ₂)-C ₆ H ₄	✓		70	92	92	227–229	227–228 ^e
4b			✓	45	90	90	210–212	210–212 ^b
5a	4-(NO ₂)-C ₆ H ₄	✓		84	81	84	205–207	207–208 ^f
5b			✓	51	65	75	203–205	204–205 ^g
6a	4-F-C ₆ H ₄	✓		85	90	95	176–178	–
6b			✓	75	85	91	188–190	–
7a	3-HO-C ₆ H ₄	✓		60	95	96	187–189	187–189 ^h
7b			✓	60	95	95	182–184	183–185 ⁱ
8a	4-MeO-C ₆ H ₄	✓		77	81	88	198–200	199–201 ^g
8b			✓	52	80	81	216–218	–
9a	2-Furyl	✓		64	78	85	189–192	–
9b			✓	42	70	80	182–184	185 ^b

^aKumar, Kasthuraiah, Reddy, and Reddy (2001).

^bGhosh, Maiti, and Chakraborty (2004).

^cFu et al. (2002).

^dWang, Qian, Tian, and Ma (2003).

^eKumar, Shanmugam, and Babu (2011).

^fChari, Shobha, Kumar, and Dubey (2005).

^gShaabani, Bazigar, and Teimouri (2003).

^hRussowsky et al. (2006).

ⁱRanu, Hajra, and Jana (2000).

reaction mixture was poured in ice (10 mL) water and the precipitated solid was collected by filtration, washed with distilled water, and dried. The crude product was recrystallized from ethanol to give the corresponding pure product (**1a**). White solid, (Table 3) mp 205–207°C; IR (KBr) ν : 3233, 3101, 2940, 1718, 1697, 1595, 1218 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ : 1.22 (t, $J = 7.0$ Hz, 3H), 2.36 (s, 3H), 4.07 (q, $J = 7.0$ Hz, 2H), 5.29 (s, 1H), 5.91 (s, 1H), 7.09–7.21 (m, 5H), 8.28 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ : 14.1, 18.2, 54.5, 61.1, 102.0, 126.4, 127.3, 128.2, 143.0, 146.5, 163.2 ppm; Anal. Calcd for $\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_3$: C, 64.60; H, 6.20; N, 10.76. Found: C, 64.25; H, 5.99; N, 10.98.

3. Results and discussion

To the best of our knowledge, our first finding was that the free-solvent reaction of benzaldehyde and urea with ethyl acetoacetate without any catalyst afforded the desired **DHPO** in 70% yield (Scheme 1). We then optimized the reaction conditions by conducting the reaction at different temperatures and times. The results are summarized in Table 1, whereby better yields were obtained when the temperature was at 90°C with 4 h reaction time.

Several activated and deactivated aromatic aldehydes underwent the reaction to give the corresponding **DHPOs** in good to excellent yields. The experimental procedure was very simple, convenient, and had the ability to tolerate a variety of other functional groups such as methoxy, nitro, hydroxy, halides, and nitros under the reaction conditions (Table 3).

Our experimental works demonstrated that in the case of **DHPTs**, the yields were generally much lower compared to the reactions which were carried out without a catalyst (Table 3). Therefore, the results, **UA** as Lewis acid and **SuSA** as Brønsted–Lowry acid catalysts, are summarized in Table 2, which clearly indicate the generality and scope of the reaction with respect to various aromatic and heterocyclic aldehydes (Table 3).

Interestingly, both of the catalysts can be recycled for four consecutive runs without significant loss of activity (Table 4).

Scheme 1. Biginelli-type reaction.

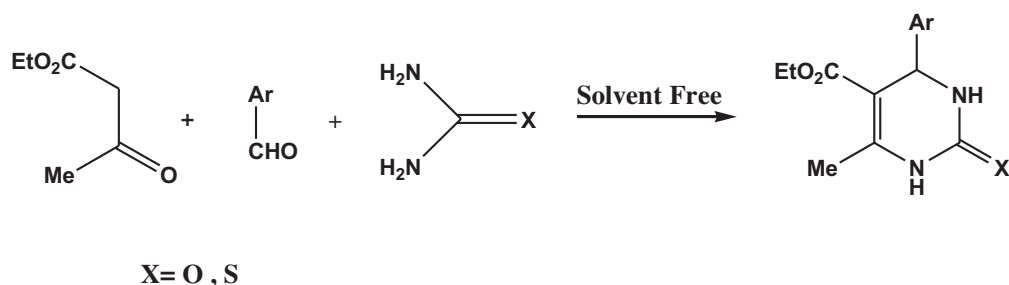


Table 4. Recycled UA and SuSA in the synthesis of Biginelli reactions

Catalyst type	Runs				
	1	2	3	4	5
Product yield (%) with UA	95	88	88	76	45
Product yield (%) with SuSA	95	95	90	75	50

4. Conclusion

In conclusion, we have successfully developed a quick, convenient, and efficient method for the synthesis of DHPs under solvent-free conditions. The environmental advantages include omitting organic solvent, generality and simplicity of procedure, shorter reaction time, simple workup, catalyst-free and reusable catalysts conditions, and pure products in good to excellent yields.

Funding

We appreciate the research council of the Kharazmi University for financial support.

Author details

Mahmood Kamali¹

E-mail: kamali.mahmood@gmail.com

Abbas Shokravi¹

E-mail: abbas_shokravi@yahoo.co.uk

Maryam Saghafi Doost¹

E-mail: maryamsaghafidoost@yahoo.com

ORCID ID: <http://orcid.org/0000-0003-3032-7576>

Seyyed Emad Hooshmand¹

E-mail: emad.hooshmand@yahoo.com

ORCID ID: <http://orcid.org/0000-0001-5573-5539>

¹ Faculty of Chemistry, Kharazmi University, 49-Mofetteh Ave., Tehran, Iran.

Citation information

Cite this article as: One-pot, solvent-free synthesis via Biginelli reaction: Catalyst-free and new recyclable catalysts, Mahmood Kamali, Abbas Shokravi, Maryam Saghafi Doost & Seyyed Emad Hooshmand, *Cogent Chemistry* (2015), 1: 1081667.

References

- Biginelli, P. (1891a). Ueber Aldehyduramide des Acetessigäthers [Treatment of aldehydeuramide with acetoacetic ester]. *Berichte der Deutschen Chemischen Gesellschaft*, 24, 1317–1319. doi:10.1002/cber.189102401228
- Biginelli, P. (1891b). Ueber Aldehyduramide des Acetessigäthers. II [Treatment of aldehydeuramide with acetoacetic ester. II]. *Berichte der Deutschen Chemischen Gesellschaft*, 24, 2962–2967. doi:10.1002/cber.189102402126
- Biginelli, P. (1893). Synthesis of 3,4-dihydropyrimidin-2(1H)-ones. *Gazzetta Chimica Italiana*, 23, 360–413.
- Chari, M. A., Shobha, D., Kumar, T. K., & Dubey, P. K. (2005). Bismuth (III) nitrate catalyzed one-pot synthesis of 3,4-dihydro-pyrimidin-2-(1H)-ones: An improved protocol for the Biginelli reaction. *Arkivoc*, 15, 74–80. doi:10.3998/ark.5550190.0006.f11
- Dallinger, D., & Kappe, C. O. (2005). Creating chemical diversity space by scaffold decoration of dihydropyrimidines. *Pure and Applied Chemistry*, 77, 155–161. doi:10.1351/pac200577010155
- Dallinger, D., Stadler, A., & Kappe, C. O. (2004). Solid- and solution-phase synthesis of bioactive dihydropyrimidines. *Pure and Applied Chemistry*, 76, 1017–1024. doi:10.1002/chin.200452250
- Folkers, K., & Johnson, T. B. (1933a). Researches on pyrimidines. CXXXVI. The mechanism of formation of tetrahydropyrimidines by the Biginelli reaction. *Journal of the American Chemical Society*, 55, 3784–3791. doi:10.1021/ja01336a054
- Folkers, K., & Johnson, T. B. (1933b). Researches on pyrimidines. CXXXIII. Some reactions and derivatives of 2-keto-4-phenyl-5-carboxy-6-methyl-1,2,3,4-tetrahydropyrimidine. *Journal of the American Chemical Society*, 55, 2886–2893. doi:10.1021/ja01334a043
- Fu, N., Yuan, Y., Cao, Z., Wang, S., Wang, J., & Peppe, C. (2002). Indium(III) bromide-catalyzed preparation of dihydropyrimidinones: Improved protocol conditions for the Biginelli reaction. *Tetrahedron*, 58, 4801–4807. doi:10.1016/S0040-4020(02)00455-6
- Gholap, A. R., Venkatesan, K., Daniel, T., Lahoti, R. J., & Srinivasan, K. V. (2004). Ionic liquid promoted novel and efficient one pot synthesis of 3,4-dihydropyrimidin-2-(1H)-ones at ambient temperature under ultrasound irradiation. *Green Chemistry*, 6, 147–150. doi:10.1039/B314015F
- Ghosh, R., Maiti, S., & Chakraborty, A. (2004). In(OTf)₃-catalyzed one-pot synthesis of 3,4-dihydropyrimidin-2(1H)-ones. *Journal of Molecular Catalysis A: Chemical*, 217, 47–50. doi:10.1016/j.molcata.2004.02.025
- Jha, P. K., & Halada, G. P. (2011). Catalytic role of uranyl in formation of polycatechol complexes. *Chemistry Central Journal*, 5, 12–18. doi:10.1186/1752-153X-5-12
- Kappe, C. O. (1993). 100 years of the Biginelli dihydropyrimidine synthesis. *Tetrahedron*, 49, 6937–6963. doi:10.1016/S0040-4020(01)87971-0
- Kappe, C. O. (2000a). Recent advances in the Biginelli dihydropyrimidine synthesis. New tricks from an old dog. *Accounts of Chemical Research*, 33, 879–888. doi:10.1021/ar000048h
- Kappe, C. O. (2000b). Biologically active dihydropyrimidones of the Biginelli-type—A literature survey. *European Journal of Medicinal Chemistry*, 35, 1043–1052. doi:10.1016/S0223-5234(00)01189-2
- Kappe, C. O. (2003). The generation of dihydropyrimidine libraries utilizing Biginelli multicomponent chemistry. *QSAR & Combinatorial Science*, 22, 630–645. doi:10.1002/qsar.200320001
- Kappe, C. O. (2005). The Biginelli reaction. In J. Zhu & H. Bienayme (Eds.), *Multicomponent reactions* (pp. 95–120). Weinheim: Wiley-VCH.
- Kappe, C. O., & Stadler, A. (2004). The Biginelli dihydropyrimidine. Synthesis. *Organic Reactions*, 63, 1–116. doi:10.1002/0471264180.or063.01
- Kenner, G. W., & Todd, A. (1957). Pyrimidine and its derivatives. In R. C. Elderfield (Ed.), *Heterocyclic compounds* (Vol. 6, pp. 239–323). New York, NY: Wiley.
- Kolosov, M. A., Orlov, V. D., Beloborodov, D. A., & Dotsenko, V. V. (2009). A chemical placebo: NaCl as an effective, cheapest, non-acidic and greener catalyst for Biginelli-type 3,4-dihydropyrimidin-2(1H)-ones (-thiones) synthesis. *Molecular Diversity*, 13, 5–25. doi:10.1007/s11030-008-9094-8
- Kumar, J. A., Shanmugam, C., & Babu, P. H. (2011). One pot synthesis of dihydropyrimidinones catalyzed by cyanuric chloride: An improved procedure for the Biginelli reaction. *Der Pharma Chemica*, 3, 292–297.
- Kumar, K. A., Kasthuraiah, M., Reddy, C. S., & Reddy, C. D. (2001). Mn(OAc)₃·2H₂O-mediated three-component, one-pot, condensation reaction: An efficient synthesis of 4-aryl-substituted 3,4-dihydropyrimidin-2-ones. *Tetrahedron Letters*, 42, 7873–7875. doi:10.1016/S0040-4039(01)01603-3
- Lewis, P. R., & Knight, D. P. (1977). Staining methods for sectioned material. In A. M. Glauert (Ed.), *Practical methods in electron microscopy* (Vol. 5, pp. 45–47). North Holland: Amsterdam. doi: 10.1002/jctb.455
- Phucho, I. T., Nongpiur, A., Tumtin, S., Nongrum, R., & Nongklaw, R. L. (2009). Recent progress in the chemistry of dihydropyrimidinones. *Rasayan Journal of Chemistry*, 2, 662–676. doi:10.1002/chin.201447283

- Radharani, V., Srinivas, N., Radha Kishan, M., Kulkarni, S. J., & Raghavan, K. V. (2001). Zeolite-catalyzed cyclocondensation reaction for the selective synthesis of 3,4-dihydropyrimidin-2(1H)-ones. *Green Chemistry*, 3, 305–306. doi:10.1039/B107612B
- Ranu, B. C., Hajra, A., & Jana, U. (2000). Indium(III) chloride-catalyzed one-pot synthesis of dihydropyrimidones by a three-component coupling of 1,3-dicarbonyl compounds, aldehydes, and urea: An improved procedure for the Biginelli reaction. *The Journal of Organic Chemistry*, 65, 6270–6272. doi:10.1021/jo000711f
- Russowsky, D., Canto, R. F. S., Sanches, S. A. A., D'Oca, M. G. M., de Fatima, A., Pilli, R. A., ... Carvalho, J. E. (2006). Synthesis and differential antiproliferative activity of Biginelli compounds against cancer cell lines: Monastrol, oxo-monastrol and oxygenated analogues. *Bioorganic Chemistry*, 34, 173–182. doi:10.1016/j.bioorg.2006.04.003
- Sangram, G., Sundarababu, B., & Bukhard, K. (2011). Efficient synthesis of 3,4-dihydropyrimidin-2-ones in low melting tartaric acid-urea mixtures. *Green Chemistry*, 13, 1009–1013. doi:10.1039/C1CG00009H
- Shaabani, A., Bazigar, A., & Teimouri, F. (2003). Ammonium chloride-catalyzed one-pot synthesis of 3,4-dihydropyrimidin-2-(1H)-ones under solvent-free conditions. *Tetrahedron Letters*, 44, 857–859. doi:10.1016/S0040-4039(02)02612-6
- Shirini, F., & GhaffariKhaligh, N. (2011). Succinimide-N-sulfonic acid: A mild, efficient, and reusable catalyst for the chemoselective trimethylsilylation of alcohols and phenols. *Phosphorus Sulfur Silicon and the Related Elements*, 186, 2156–2165. doi:10.1080/10426507.2011.602377
- Shirini, F., & GhaffariKhaligh, N. (2012a). Succinimide sulfonic acid (SuSA): An efficient and recyclable catalyst for the chemoselective N-Boc protection of amines. *Monatshefte für Chemie*, 143, 631–635. doi:10.1007/s00706-011-0612-5
- Shirini, F., & GhaffariKhaligh, N. (2012b). Succinimide-N-sulfonic acid: An efficient catalyst for the synthesis of xanthen derivatives under solvent-free conditions. *Dyes and Pigments*, 95, 789–794. doi:10.1016/j.dyepig.2012.06.022
- Shockravi, A., Kamali, M., Sharifi, N., Nategholeslam, M., & PahlavanMoghanlo, S. (2013). One-pot and solvent-free synthesis of 1,4-dihydropyridines and 3,4-dihydropyrimidine-2-ones using new synthetic recyclable catalyst via Biginelli and Hantzsch reactions. *Synthetic Communications*, 11, 1477–1483. doi:10.1080/0397911.2011.642923
- Singh, K. D., Arorea, D., & Singh, S. (2009). Genesis of dihydropyrimidinone calcium channel blockers: Recent progress in structure-activity relationships and other effects. *Mini-Reviews in Medicinal Chemistry*, 9, 95–106. doi:10.2174/138955709787001686
- Su, W., Li, J., Zheng, Z., & Shen, Y. (2005). One-pot synthesis of dihydropyrimidones catalyzed by strontium (II) triflate under solvent-free conditions. *Tetrahedron Letters*, 46, 6037–6040. doi:10.1016/j.tetlet.2005.07.021
- Valizadeh, H., & Shockravi, A. (2009). Imidazolium-based phosphinite ionic liquid as reusable catalyst and solvent for one-pot synthesis of 3,4-dihydropyrimidin-2(1H)- (thio)ones. *Heteroatom Chemistry*, 20, 284–288. doi:10.1002/hc.20549
- Varala, R., Alam, M. M., & Adapa, S. R. (2003). Bismuth triflate catalyzed one-pot synthesis of 3,4-dihydropyrimidin-2(1H)-ones: An improved protocol for the Biginelli reaction. *Synlett*, 2003, 67–70. doi: 10.1002/chin.200315157
- Vdovina, S. V., & Mamedov, V. A. (2008). New potential of the classical Biginelli reaction. *Russian Chemical Reviews*, 77, 1017–1053. doi:10.1070/RC2008v077n12ABEH003894
- Wan, J.-P., & Liu, Y. (2010). Synthesis of dihydropyrimidones and thiones by multicomponent reactions: Strategies beyond the classical Biginelli reaction. *Synthesis*, 23, 3943–3953. doi:10.1055/s-0030-1258290
- Wang, L., Qian, G., Tian, H., & Ma, Y. (2003). Lanthanide triflate catalyzed one-pot synthesis of dihydropyrimidin-2(1H)-thiones by a three-component of 1,3-dicarbonyl compounds, aldehydes, and thiourea using a solvent-free Biginelli condensation. *Synthetic Communications*, 33, 1459–1468. doi:10.1002/chin.200334138
- Wang, Y., Zhao, X., Li, F., Wang, S., & Zhang, J. (2001). Catalytic synthesis of toluene-2,4-diisocyanate from dimethyl carbonate. *Journal of Chemical Technology and Biotechnology*, 76, 857–861. doi:10.1002/jctb.455
- Zaugg, H. E., & Martin, W. B. (1965). α -Amidoalkylations at carbon. In R. Adams (Ed.), *Organic reactions* (Vol. 14, pp. 88–90). New York, NY: Wiley.
- Zhang, X., Li, Y., Liu, C., & Wang, J. (2006). An efficient synthesis of 4-substituted pyrazolyl-3,4-dihydropyrimidin-2(1H)-(thio)ones catalyzed by $Mg(ClO_4)_2$ under ultrasound irradiation. *Journal of Molecular Catalysis A: Chemical*, 253, 207–211. doi:10.1016/j.molcata.2006.03.018



© 2015 The Author(s). This open access article is distributed under a Creative Commons Attribution (CC-BY) 4.0 license.

You are free to:

Share — copy and redistribute the material in any medium or format

Adapt — remix, transform, and build upon the material for any purpose, even commercially.

The licensor cannot revoke these freedoms as long as you follow the license terms.

Under the following terms:

Attribution — You must give appropriate credit, provide a link to the license, and indicate if changes were made.

You may do so in any reasonable manner, but not in any way that suggests the licensor endorses you or your use.

No additional restrictions

You may not apply legal terms or technological measures that legally restrict others from doing anything the license permits.

