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Communication

Alginic acid: a highly efficient renewable and heterogeneous bio-polymeric catalyst for one-pot synthesis of the Hantzsch 1,4-dihydropyridines

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Alginic acid, a naturally occurring polysaccharide, in its granular form and without any post-modification was found to be an efficient environmentally benign, easily recoverable and low-cost catalyst for the clean and rapid synthesis of 1,4-dihydropiridine derivatives (DHPs) just based on its polysaccharide architecture. The Hantzsch pseudo-four-component reaction of ethyl or methyl acetoacetate, ammonium acetate and different aldehydes is catalyzed by alginic acid efficiently under mild conditions to afford desired products in high to quantitative yields and clean reaction profiles. Avoiding the use of any transition-metal, the use of a one-pot and multi-component procedure for the synthesis of DHPs, reusability of the catalyst and operational simplicity are important features of this methodology.

Designing and application of new eco-friendly chemicals and processes have almost been mandatory to keep and increase human health standards due to growing environmental pollution arising from industrial activities and their intensive impact on living systems as well as economic point of view.[1] Therefore, science and technology has shifted toward green processes nowadays.[2] Consequently, developing chemical processes using more environmentally acceptable catalysts, chemicals and atom efficient procedures have been emerged as subjects of innovation in green chemistry. For instance, the terrible impact of non-biodegradable wastes is still an open challenge in either developed or developing countries.[3] In this regard, great efforts have been performed to use different bio-based feedstocks such as chitosan,[4] chitin,[5] starch,[6] cellulose,[7] gelatin,[8] wool[9] and alginates[10] as biopolymeric support in the transition metal-based heterogeneous catalytic systems. However, complete replacement of transition metal-based heterogeneous catalytic systems by the metal-free biopolymeric analogues is of significant importance because of both toxicity and difficulty in separation of metal catalysts from the final products, especially in the pharmaceutical industry.[11]

Alginic acid, also called algin or alginate, is a naturally occurring anionic polysaccharide distributed widely in the cell walls of brown algae. It can also be produced by a microbial fermentation using special bacteria including *Azotobacter* and *Pseudomonas*. Alginic acid is an acidic form of alginate and has a plenty of both exposed carboxylic acid and hydroxyl groups inside its backbone. Alginic acid and its salts are linear copolymer with homopolymeric blocks of (1→4)-linked α-L-guluronic acid (G) and β-D-mannuronic acid (M) residues (Fig. 1).[12] Therefore, it can activate the reaction components by not only Bronsted acid centers but also hydrogen bonding, as a heterogeneous organocatalyst.[13] The catalytic activity of alginic acid can also be intensified by the hydrophilic/hygroscopic nature of these polymers when organic reactions produce water as their byproducts. It is noteworthy that alginic acid is capable of absorbing 200-300 times its own weight in water.[4d,10,14] These requirements are fully met in the multicomponent reaction (MCR) for synthesis of the Hantzsch 1,4-dihydropyridines (1,4-DHPs).

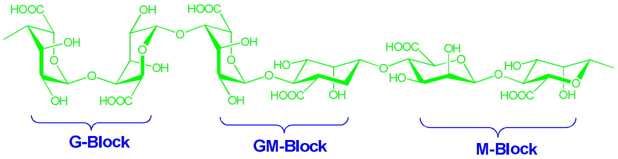


Fig. 1. Chemical structure of alginic acid (**1**).

The Hantzsch pseudo-four-component reaction is the oldest and most general known method for the synthesis of 1,4-DHPs and their derivatives which are medicinally and pharmacologically very important molecules. Indeed, commercial drugs such as nifedipine, amlodipine, nicardipine and felodipine constitute a major class of ligands for L-type Ca^{2+} channels (LTCC) blockers that are widely used to treat conditions such as hypertension and angina (Fig. 2).[15] Therefore, the attempts to modify the conditions of the Hantzsch reaction are still of growing importance.

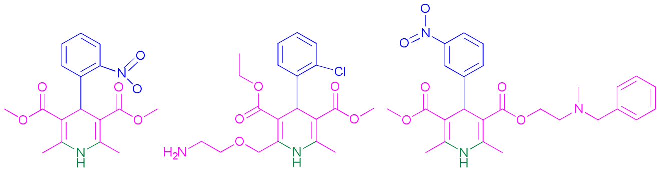


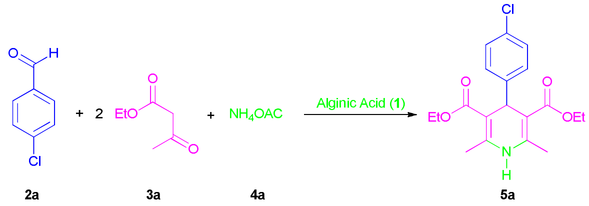
Fig. 2. Selected examples of 1,4-dihydropyridines demonstrating pharmacological activity.

Literature survey shows that several modified methods for Hantzsch reaction have been reported using different catalysts mostly consisting of Bronsted or Lewis acids in recent years.[16] For example, homogeneous catalytic systems such as *p*-TSA,[17a] 3,4,5-trifluorobenzeneboronic acid in ionic liquid or $InCl_3$,[17b] $Cd(NO_3)_2.4H_2O$,[17c] $Yb(OTf)_3$,[17d] $Sc(OTf)_3$,[17e] hafnium (IV) bis(perfluorooctanesulfonyl)imide complex $[Hf(NPf_2)_4]$[17f] and $Zn[(L)proline]_2$,[17g] can be mentioned. On the other hand, organic Lewis bases such as PPh_3[18a] and TMS-protected prolinol[18b] as well as bifunctional *L*-proline under ultrasound irradiation[18c] have also been reported. Furthermore, enzymes such as *candida antarctica* lipase B[19a] or baker's yeast,[19b] ionic liquids,[19c] and non-ionic surfactant Triton X-100[19d] demonstrated catalytic activity for DHP synthesis. In spite of their merits, most of these methods suffer from the use of hazardous or expensive catalysts or solvents, long reaction times, high temperature and complicated workup. Although some heterogeneous catalysts such as sulfonic acid supported γ-Fe_2O_3[20a] or cellulose,[20b] silica supported 12-tungstophosphoric acid,[20c] preyssler heteropolyacids,[20d] $Ce(SO_4)_2$-SiO_2,[20e] self-assembled tinphosphonate nanoparticles,[20f] Zn-VCO_3 hydrotalcite,[20g] and hydromagnesite[20h] have been introduced in the recent years but there is still room to improve the reaction conditions in terms of the use of renewable biopolymeric and transition metal-free heterogeneous catalysts under mild conditions. In continuation of our interest to explore application of biopolymers in different fields, especially their catalytic activity without any post-modification as well as MCRs,[4d,21] we wish herein to report the first catalytic activity of alginic acid (**1**) as a mild, highly effective and convenient bifunctional heterogeneous biopolymeric catalyst for the one-pot synthesis of 1,4-dihydropyridines *via* Hantzsch reaction in EtOH (Scheme 1).

Scheme 1. Pseudo-four-component reaction of different aldehydes **2**, β-ketoesters **3**, and nitrogen sources **4** catalysed by alginic acid (**1**) in EtOH under reflux conditions.

To evaluate the catalytic activity of alginic acid (**1**) for the synthesis of 1,4-DHPs, first the reaction of 4-chlorobenzaldehyde (**2a**), ethyl acetoacetate (**3a**), and ammonium acetate (**4a**) (2:1:1.2 mole ratio) was investigated as the model reaction in EtOH. The results are summarized in Table 1. In the absence of any catalyst, only a poor yield of the corresponding 1,4-DHP **5a** was obtained after 4 h (entry 1). Interestingly, the yield of the desired product **5a** was significantly improved in shorter reaction times when catalytic amounts of **1** were added to the reaction mixture in EtOH (entries 2-5). The model reaction was also studied in other solvents such as 50% aqueous EtOH (v/v), H_2O and EtOAc using alginic acid (**1**) loading of 10 mol% (entries 6-8). The obtained yield of the desired product **5a** in H_2O was significantly less than compared to EtOH under similar catalyst loading and reflux conditions (entries 3 and 6). This may be attributed to both lower solubility of the reactants and rendering the established equilibriums between the reactants and reaction intermediates or desired product **5a** to the left side in H_2O compared to EtOH (Scheme 4). Finally, the effect of temperature on the obtained yield and required reaction time was also examined (entries 9, 10). The obtained results demonstrated higher yields in shorter reaction times can be obtained in EtOH under reflux conditions.

Table 1 Optimization of the Hantzsch pseudo-four-component reaction for the synthesis of **5a** catalyzed by alginic acid (**1**)[a]



Entry	Catalyst loading (mol%)	Solvent	Temp. (°C)	Time (min)	Yield[b] (%)
1	-	EtOH	Reflux	4 h	46
2	20	EtOH	Reflux	40	98
3	15	EtOH	Reflux	40	98
4	10	EtOH	Reflux	50	96
5	5	EtOH	Reflux	2 h	63
6	10	H_2O	Reflux	3 h	65
7	10	Aqueous EtOH[c]	Reflux	2 h	77
8	10	EtOAc	Reflux	5 h	62
9	10	EtOH	25	3.5 h	89
10	10	EtOH	50	2 h	92
11[d]	10	EtOH	Reflux	60	92

[a] Reaction conditions: 4-Chlorobenzaldehyde (**2a**, 1 mmol), ethyl acetoacetate (**3a**, 2 mmol), ammonium acetate (**4a**, 1.2 mmol). [b] Isolated yields. [c] (50% v/v). [d] The scale up of model reaction using 4-chlorobenzaldehyde (**2a**,10 mmol), ethyl acetoacetate (**3a**, 20 mmol), and ammonium acetate (**4a**, 11 mmol).

Furthermore, the catalytic activity of the alginic acid (**1**) was examined in the next step to prove its feasibility as a heterogeneous biopolymeric catalyst for scale up of the Hantzsch reaction (entry 11). Interestingly, the alginic acid was found to be an efficient catalyst for performing of the Hantzsch reaction at higher scales. Therefore, alginic acid (**1**) loading of 10 mol% (17.6 mg per 1 mmol of aldehyde 2) in EtOH under reflux conditions, as the optimized reaction conditions, was developed to other derivatives of aromatic and α,β-unsaturated carbonyl compounds (**2b–p**) and amines (**4a–c**) for the synthesis of the desired 1,4-DHPs **5** (Fig. 3 and Scheme 2).

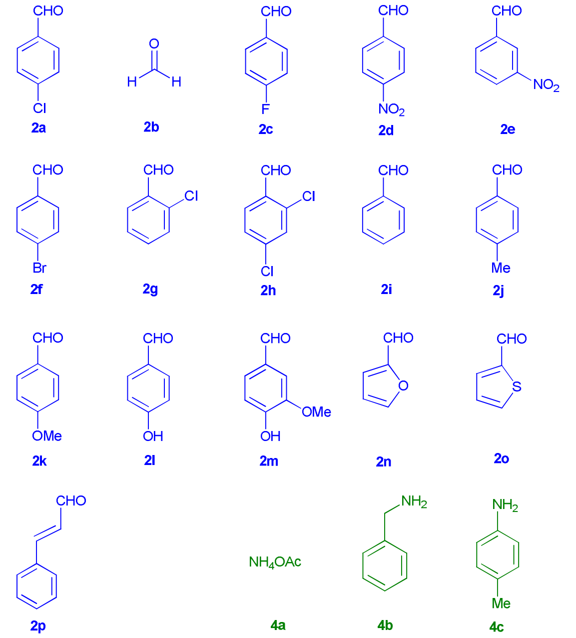
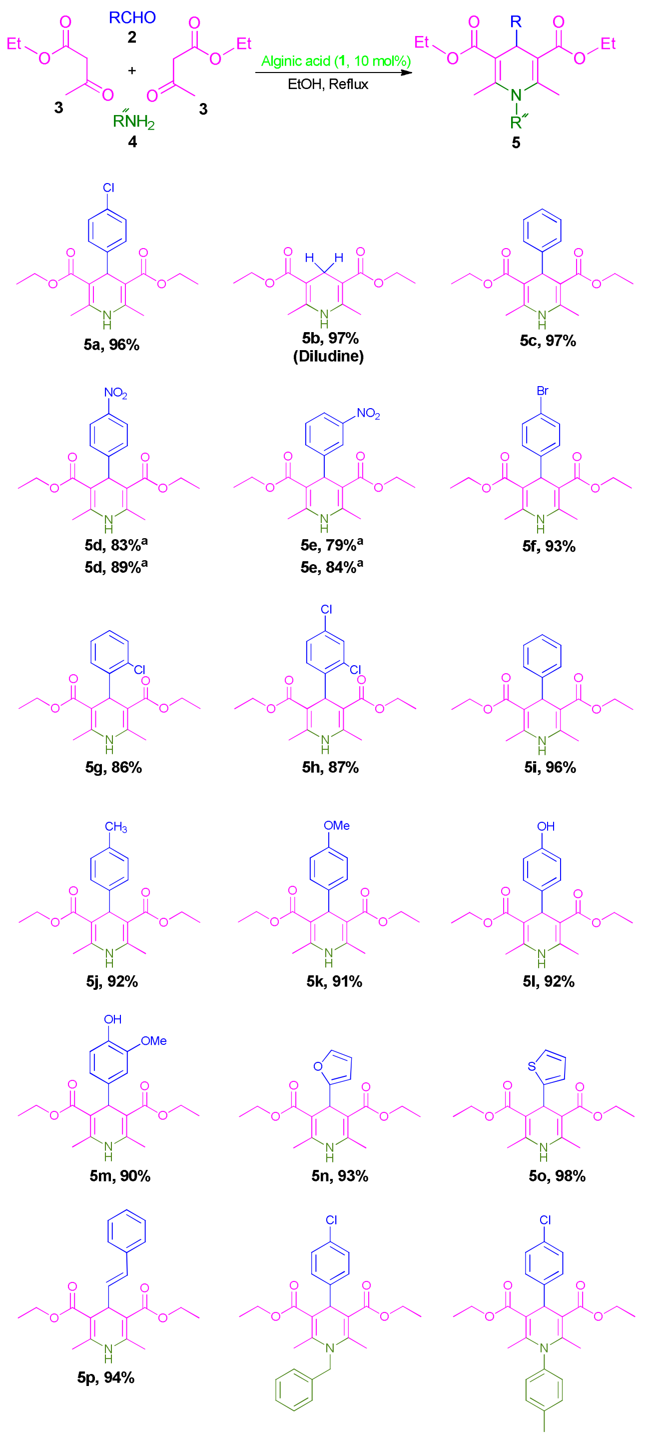


Fig. 3. Different aldehydes (**2a-p**) and ammonia derivatives (**4a-c**) examined in the Hantzsch MCR catalysed by alginic acid (**1**).

To our delight, the diludine (**5b**), a substance with noteworthy pharmaceutical and food applications as well as organic reductive agent,[15,22] was prepared in short reaction time and excellent yield (See also ESI). Moreover, all the aromatic aldehydes having either electron-withdrawing substitutes (**2c-2h**) or electron-donating ones (**2j-2o**) reacted smoothly to provide the corresponding Hantzsch esters (**5c-5o**) in good to excellent isolated yields. However, the aldehydes carrying nitro groups (**2d**, **2e**) afforded lower yields compared to those having other electron-withdrawing substituents rather than nitro group or even electron-donating ones. Lower yields obtained for aldehydes having *meta*- and *para*-nitro substituents (**2d**, **2e**) may be attributed to the competitive formation of less reactive corresponding imines.[23] The obtained yields in these cases were improved somewhat by late addition of aldehydes **2d** or **2e** to the reaction mixture (89% and 84%, respectively). On there hand, the effect of nitrogen source in the Hantzsch reaction catalysed by alginic acid (**1**) was also examined. It has been reported that ammonium salts of carbonate or bicarbonate show somewhat higher efficiency than the acetate salt in hot water.[24] However, it should be noted that those former salts produce CO_2 on their decomposition as reaction proceeds (Scheme 4). The greenhouse effect of CO_2 is well known. Therefore, ammonium acetate is one of the best choice as ammonia source in the Hantzsch reaction. Furthermore, aliphatic or aromatic amines including benzyl amine (**4b**) and *p*-toluidine (**4c**) were also examined. Lower yields of the desired DHPs (**5q** and **5r**, respectively) can be attributed to the more steric hindrance and stronger resonance effect of these amines compared to ammonium acetate.[25]

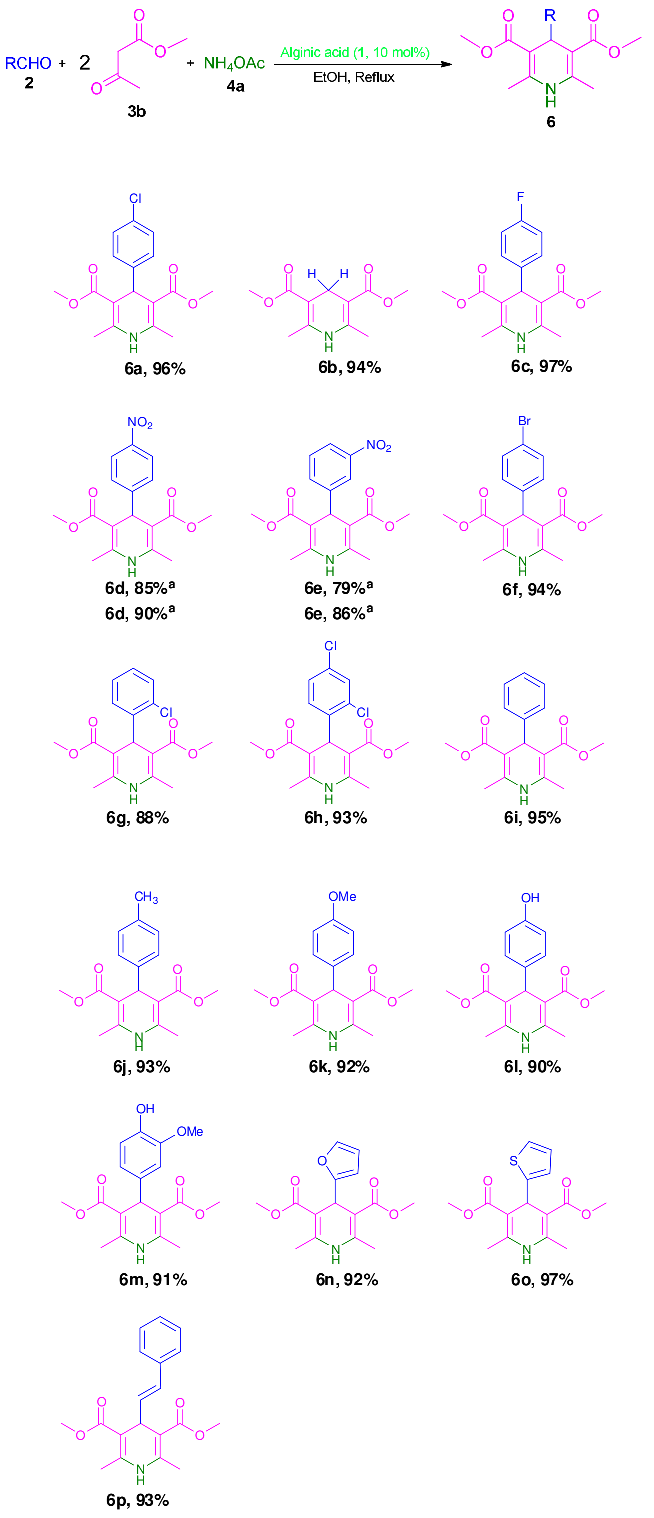


[a] One step, one-pot reaction

[b] Two step, one-pot reaction

Scheme 2. Pseudo-four-component synthesis of different diethyl 1,4-DHP-3,5-dicarboxylate (**5a-r**) catalysed by alginic acid (**1**) in EtOH under reflux conditions.

In the next stage, the size effect of the alkyl group of ester moiety in the β-ketoester **3** on the yield of the expected 1,4-DHPs was also investigated using methyl acetoacetate (**3b**) instead of ethyl acetoacetate (**3a**). Corresponding 1,4-DHPs **6a-p** were obtained in good to excellent yields (Scheme 3, See also ESI). In all of studied cases, similar trend of reactivity were observed compared to ethyl acetoacetate (**3a**).



a One step, one-pot reaction

b Two step, one-pot reaction

Scheme 3. Pseudo-four-component synthesis of different dimethyl 1,4-DHP-3,5-dicarboxylate (**6a-p**) catalysed by alginic acid (**1**) in EtOH under reflux conditions.

According to obtained results, the following mechanism can be proposed for the synthesis of 1,4-DHPs **5**-**6** through MCR of aldehydes **2**, β-ketoesters **3**, and nitrogen sources **4** catalysed by alginic acid (**1**) (Scheme 4). First, alginic acid (**1**) activates the carbonyl functional group of aldehyde **2** for the next addition of enol form of β-ketoesters **3** on it to form the corresponding Kenovenagle intermediate (II). This intermediate is also protonated by alginic acid (**1**) to be activated for the next Michael addition of enol form of β-ketoesters **3**. Then, one of the keto functional groups in the intermeadiate (IV) is activated through proton transfer from alginic acid (**1**) to react with the nitrogen source **4** and give imine intermediate (V). This later intermediate is also activitaed through proton transfer from alginic acid (**1**) to facilitate its subsequent tautomerision to the corresponding enamine (VI). In the next step, alginic acid (**1**) activates the remaining keto functional group for ring closure by amino group of the enamine moiety. Finally, elimination of third H_2O molecule is catalysed by alginic acid (**1**) to afford the desired 1,4-DHP **5-6.** Furthermore, all the above steps can be competitively catalysed through hydrogen bonding rather than proton transfer with weaker interactions. On the other hand, ring closure may take place from position 4- of 1,4-DHP rather than its 1-position, alternatively. This means that enamine formation and condensation with the second molecule of β-ketoesters **3** can take place prior to Micaheal addition in the above proposed mechanism.

On the other hand, the reusability of alginic acid (1) was also investigated for at least 6 runs. The results are summarised in Fig. 4. The obtained results demonstrated that alginic acid (**1**) is reusable for the practical applications in the Hantzsch 1,4-DHPs synthesis.

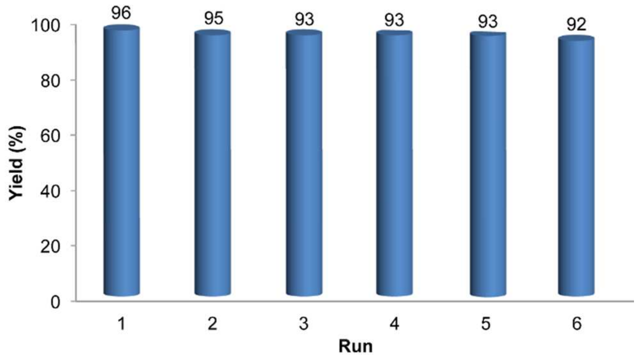


Fig. 4. Reusability of alginic acid catalyst (**1**) for the Hantzsch MCR to afford **5a**.

In conclusion, a new, renewable and readily recoverable biopolymeric catalyst for the MCR Hantzsch reaction has been described which displays particularly high efficiency just based on polysaccharide architecture of alginic acid. Avoiding the use of any transition-metal, clean reaction profiles, the use of a one-pot and multi-component procedure for the synthesis of DHPs, reusability of the catalyst and operational simplicity are the important features of this methodology. Further developemet of this methodology to bicyclic and tricyclic derivatives of DHPs are currently underway and will be presented in due course.

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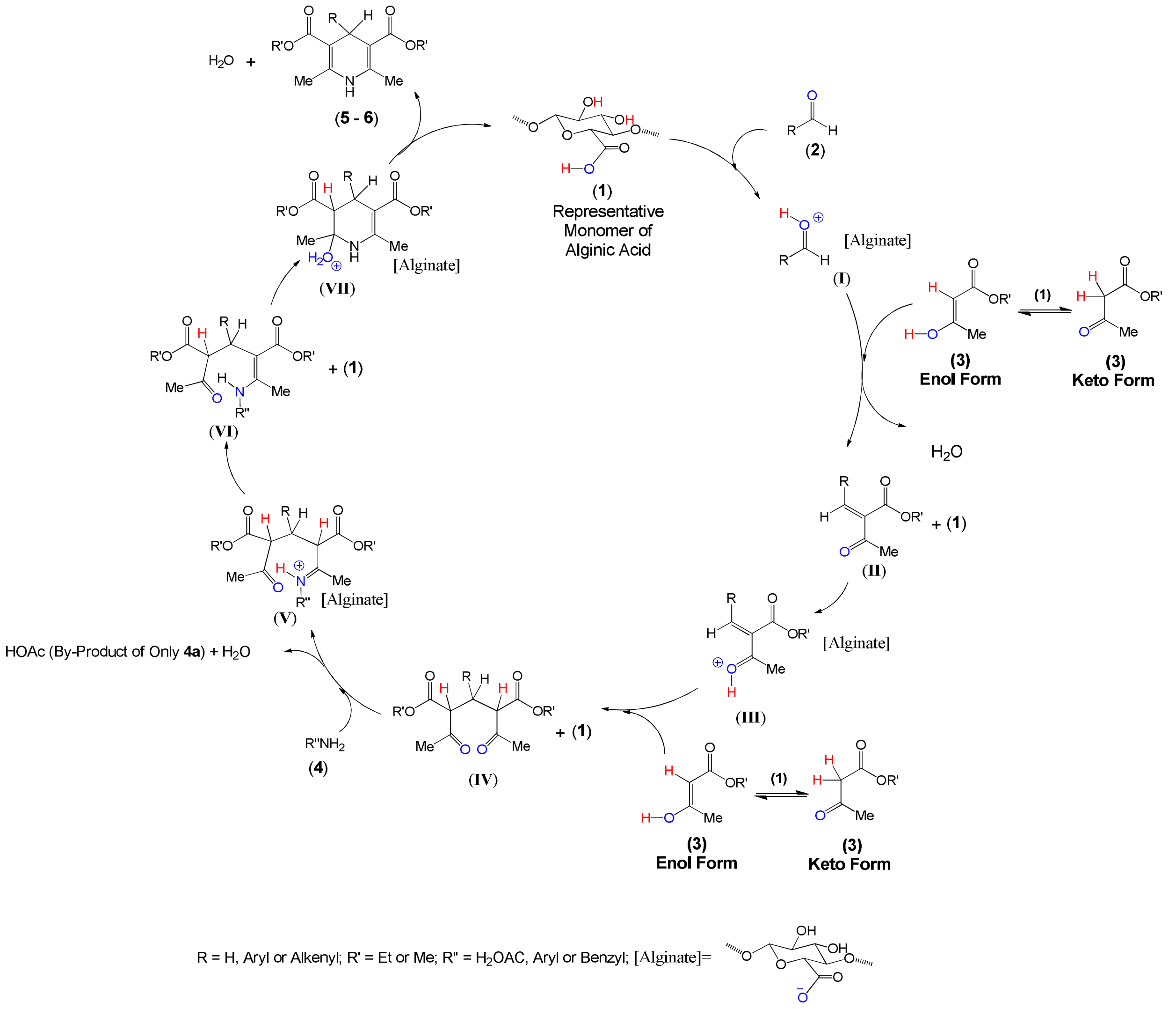

Scheme 4. Plausible mechanism for the Hantzsch pseudo-four-component reaction of different aldehydes **2**, β-ketoesters **3**, and nitrogen sources **4** catalysed by alginic acid (**1**).

Notes and references

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† Electronic Supplementary Information (ESI) available: [Experimental procedure, characterization data, IR and ^{1}H NMR spectra of products, and IR spectra and TGA of catalyst]. See DOI: 10.1039/b000000x/

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1 (a) K. Sanderson, *Nature*, 2011, **469**, 18; (b) R. A. Sheldon, I. Arends and U. Hanefeld, *Green Chemistry and Catalysis*, Wiley-VCH, 2007, Ch. 1, pp 1-47; (c) F. M. Kerton, Y. Liu, K. W. Omaria and K. Hawboldt, *Green Chem.*, 2013, **15**, 860; (d) J. H. Clark, *J. Chem. Technol. Biotech.*, 2007, **82**, 603; (e) L. Qian and H. Zhang, *Green Chem.*, 2010, **12**, 1207.

2 (a) R. A. Sheldon, *Chem. Soc. Rev.*, 2012, **41**, 1437; (b) J. H. Clark, F. E. I. Deswarte and T. J. Farmer, *Biofuels, Bioprod. Bioref.*, 2009, **3**, 72.

3 (a) G. Steinhauser and T. M. Klapötke, *Angew. Chem. Int. Ed.*, 2008, **47**, 3330; (b) Y. C. Sharma, B. Singh and J. Korstad, *Green Chem.*, 2011, **13**, 2993; (c) A. Gandini, *Green Chem.*, 2011, **13**, 1061.

4 (a) M. Chtchigrovsky, A. Primo, P. Gonzalez, K. Molvinger, M. Robitzer, F. Quignard and F. Taran, *Angew. Chem. Int. Ed.*, 2009, **121**, 6030; (b) C. Jouannin, C. Vincent, I. Dez, A. C. Gaumont, T. Vincent and E. Guibal, *J. Appl. Polymer Sci.*, 2013, **128**, 3122; (c) R. B. N. Baig and R. S. Varma, *Green Chem.*, 2013, **15**, 1839; (d) M. G. Dekamin, M. Azimoshan and L. Ramezani, *Green Chem.,* 2013, **15**, 811.

5 (a) B. M. L. Dioos, I. F. J. Vankelecom and P. A. Jacobs, *Adv. Synth. Catal.*, 2006, **348**, 1413; (b) E. S. Medeiros, A. S. F. Santos, A. Dufresne, W. J. Orts and L. H. C. Mattoso, in *Polymer Composites*, Wiley-VCH, 2013, pp. 361.

6 (a) S. Verma, S. L. Jain and B. Sain, *ChemCatChem*, 2011, **3**, 1329; (b) A. Pourjavadi, F. Seidi, S. S. Afjeh, N. Nikoseresht, H. Salimi and N. Nemati, *Starch*, 2011, **63**, 780.

7 (a) B. R. Vaddula, A. Saha, R. S. Varma and J. Leazer, *Eur. J. Org. Chem.*, 2012, **34**, 6707; (b) H. S. Chandak, N. P. Lad and P. P. Upare, *Catal. Lett*., 2009, **131**, 469; (c) F. Quignard and A. Choplin, *Chem. Commun*., 2001, 21.

8 X. Zhang, Y. Geng, H. Han, M. Y. Ying, M. U. Huang and Y. Y. Jiang, *Polym. Adv. Technol*., 2001, **12**, 642.

9 X. Wang, D. Sui, M. Huang and Y. Jiang, *Polym. Adv. Technol.*, 2006, **17**, 163.

10 (a) K. R. Reddy, K. Rajgopal and M. L. Kantam, *Catal. Lett*., 2007, **114**, 36; (b) P. L. Boey, S. Ganesan, G. P. Maniam, M. Khairuddean and S. E. Lee, *Appl. Catal. A: Gen*., 2012, **12**, 433.

11 (a) A. Daştan, A. Kulkarnia and B. Török, *Green Chem.*, 2012, **14**, 17; (b) C. J. Li and B. M. Trost, *Proc. Natl. Acad. Sci. USA*, 2008, **105**, 13197.

12 (a) K. Y. Lee, D. J. Mooney, *Prog. Polym. Sci*., 2012, **37**, 106; (b) H. Daemi, M. Barikani and M. Barmar, *Carbohydr. Polym*., 2013, **92**, 490.

13 (a) Z. Du and Z. Shao, *Chem. Soc. Rev.*, 2013, **42**, 1337; (b) P. I. Dalko and L. Moisan, *Angew. Chem. Int. Ed.*, 2004, **43**, 5138; (c) P. R. Schreiner, *Chem. Soc. Rev.*, 2003, **32**, 289; (d) C. Thomas and B. Bibal, *Green Chem*., 2014, **16**, 1687.

14 K. Etzenbach-Effers and A. Berkessel, *Noncovalent Organocatalysis Based on Hydrogen Bonding: Elucidation of Reaction Paths by Computational Methods*, Vol. 291 (Ed.: B. List), Springer-Verlag, Heidelberg, 2010, pp. 1-27.

15 (a) D. J. Triggle, *Drug Dev. Res.*, 2003, **58**, 5; (b) J. C. Liang, J. L. Yeh, C. S. Wang, S. F. Liou, C. H. Tsai and I. J. Chen. *Bioorg. Med. Chem*., 2002, **10**, 719; (c) N. Edraki, A. R. Mehdipour, M. Khoshneviszadeh and R. Miri, *Drug Discov. Today*, 2009, **14**, 1058; (d) M. F. Litvić, M. Litvić, I. Cepanec and V. Vinković, *Molecules*, 2007, **12**, 2546.

16 J. P. Wan and Y. Liu, *RSC Adv*., 2012, **2**, 9763.

17 (a) S. R. Cherkupally and R. Mekalan, *Chem. Pharm. Bull*., 2008, **56**, 1002; (b) R. Sridhar and P. T. Perumal, *Tetrahedron*, 2005, **61**, 2465; (c) R. Tafer, R. Boulcina, B. Carboni and A. Debache, *J. Chin. Chem. Soc*., 2012, **59**, 1555; (d) L. M. Wang, J. Sheng, L. Zhang, J. W. Han, Z. Fan, H. Tian and C. T. Qian, *Tetrahedron*, 2005, **61**, 1539; (e) J. L. Donelson, R. A. Gibbs and S. K. De, *J. Mol. Catal. A Chem*., 2006, **256**, 309; (f) M. Hong, C. Cai and W. B. Yi, *J. Fluorine Chem*., 2010, **131**, 111; (g) V. Sivamurugan, R. S. Kumar, M. Palanichamy and V. Murugesan, *J. Heterocycl. Chem.*, 2005, **42**, 969.

18 (a) A. Debache, W. Ghalem, R. Boulcina, A. Belfaitah, S. Rhouati and B. Carboni, *Tetrahedron Lett*., 2009, **50**, 5248; (b) P. T. Franke, R. L. Johansen, S. Bertelsen and K. A. Jørgensen, *Chem. Asian J*., 2008, **3**, 216; (c) S. Guo and Y. Yuan, *Chin. J. Chem*., 2010, **28**, 811.

19 (a) J. L. Wang, B. K. Liu, C. Yin, Q. Wu and X. F. Lin, *Tetrahedron*, 2011, **67**, 2689; (b) J. H. Lee, *Tetrahedron Lett.*, 2005, **46**, 7329; (c) J. S. Yadav, B. V. S. Reddy, A. K. Basak and A. V. Narsaiah, *Green Chem*., 2003, **5**, 60; (d) P. P. Ghosh, P. Mukherjee and A. R. Das, *RSC Adv*., 2013, **3**, 8220.

20 (a) N. Koukabi, E. Kolvari, M. A. Zolfigol, A. Khazaei, B. S. Shaghasemi and B. Fasahati, *Adv. Synth. Catal.*, 2012, **354**, 2001; (b) J. Safari, S. H. Banitaba and S. D. Khalili, *J. Mol. Catal. A Chem*., 2011, **335**, 46; (c) E. Rafiee, S. Eavani, S. Rashidzadeh and M. Joshaghani, *Inorg. Chim. Acta*., 2009, **362**, 3555; (d) A. Gharib, M. Jahangir, M. Roshani and J. W. Scheeren, *Synth. Commun.*, 2012, **42**, 3311; (e) W. Pei, Q. Wang, X. Li and L. Sun, *Chin. J. Chem.*, 2010, **28**, 483; (f) M. Pramanik and A. Bhaumik, *J. Mater. Chem. A*, 2013, **1**, 11210; (g) R. Pagadala, S. Maddila, V. D. B. C. Dasireddy and S. B. Jonnalagadda, *Catal. Commun*., 2014, **45**, 148; (h) U. C. Rajesh, S. Manohar and D. S. Rawat, *Adv. Synth. Catal.*, 2013, **355**, 3170.

21 (a) M. G. Dekamin and M. Eslami, *Green Chem.,* 2014, DOI: 10.1039/c4gc00411f; (b) M. G. Dekamin and Z. Mokhtari, *Tetrahedron*, 2012, **68**, 922; (c) M. G. Dekamin, M. Eslami and A. Maleki, *Tetrahedron*, 2013, **69**, 1074; (d) H. Daemi, R. R. Rad, M. Barikani and M. Adib, *Appl. Catal. A: Gen.*, 2013, **468**, 10; (e) H. Daemi, M. Barikani and M. Barmar, *Int. J. Biol. Macromol.*, 2014, **66**, 212; (f) H. Daemi, M. Barikani and M. Barmar, *Carbohydr. Polym.*, 2013, **95**, 630; (g) H. Daemi and M. Barikani, Carbohydr. Polym., 2014, 112, 638; (h) M. G. Dekamin, Z. Mokhtari and Z. Karimi, *Sci. Iran.*, 2011, **18**, 1356.

22 (a) J. Stemper, K. Isaac, J. Pastor, G. Frison, P. Retailleau, A. Voituriez, J. F. Betzer and A. Marinetti, *Adv. Synth. Catal.*, 2013, **355**, 3613; (b) D. B. Ramachary, M. Kishor and Y. V. Reddy, *Eur. J. Org. Chem.*, 2008, 975.

23 (a) A. T. Khan, M. M. Khan and K. K. R. Bannuru, *Tetrahedron*, 2010, **66**, 7762; (b) J. Li, P. He and C. Yu, *Tetrahedron*, 2012, **68**, 4138.

24 F. Tamaddon, Z. Razmi and A. A. Jafari, *Tetrahedron Lett.*, 2010, **51**, 1187.

25 (a) Y. P. Liu, J. M. Liu, X. Wang, T. M. Cheng and R. T. Li, *Tetrahedron*, 2013, **69**, 5242; (b) S. Balalaie and E. Kowsari, *Monatsh. Chem*., 2001, **132**, 1551.

Graphical Abstract

Alginic acid: a highly efficient renewable and heterogeneous bio-polymeric catalyst for one-pot synthesis of the Hantzsch 1,4-dihydropyridines

Mohammad G. Dekamin, Siamand Ilkhanizadeh, Zahra Latifidoost, Hamed Daemi, Zahra Karimi and Mehdi Barikani

Alginic acid was found to be an efficient, environmentally benign, easily recoverable and low-cost catalyst for clean synthesis of 1,4-dihydropiridine derivatives (DHPs).