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Boric acid an effective catalyst for Knoevenagel condensation

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Abstract:

A green approach for Knoevenagel condensation of 4-oxo-4*H*-benzopyran-3-carbaldehydes with Meldrum's acid in the presence of catalytic amount of boric acid [H_3BO_3] in water at room temperature has been reported. The most significant feature of this methodology is simple work-up procedure, mild reaction conditions, short reaction times and good yield of products. Additionally, boric acid has emerged as an efficient, non-toxic and inexpensive commercially available catalyst.

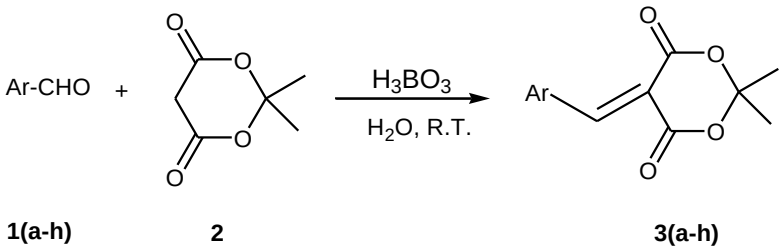
Keywords: Knoevenagel reaction; boric acid; 4-oxo-(4*H*)-1-benzopyran-3-carbaldehyde; Meldrum's acid.

Introduction

A Knoevenagel condensation is one of the most important methods for the preparation of substituted alkenes by a nucleophilic addition of an active methylene compounds to a carbonyl group followed by a dehydration reaction.[1] This reaction found many applications such as, in the synthesis of intermediate of fine chemicals[2], intermediates like coumarin and benzofuran[3,4].

Compounds having a chromone moiety are synthetically versatile molecules with a reactive carbonyl group. They have considerable significance for their biological activities [5] and for their reactivity towards nucleophiles, which allow the synthesis of a wide variety of heterocycles. The condensation reactions of 4-oxo-(4*H*)-1-benzopyran-3-carbaldehyde with active methylene compounds are well known.[6] It is well known that 2,2-dimethyl-5- [(4-oxo-4*H*-chromen-3-yl) methylene]-1, 3-dioxane-4, 6-diones is synthesized by condensation of 4-oxo-4*H*-benzopyran-3-carbaldehyde with Meldrum's acid in presence of alumina under microwave irradiation.[7]

Water is unique solvent due to easy availability, cheap, non-toxic, safer to organic solvents and environmental benign[8]. Boric acid [H_3BO_3]) has exploited in the organic synthesis as a non-toxic, inexpensive, eco-friendly nature, easy handling and Lewis acid mild catalyst[9].



Scheme

Experiment

Materials

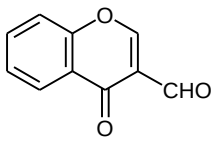
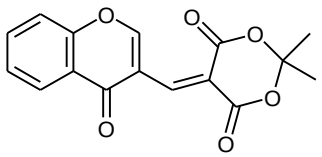
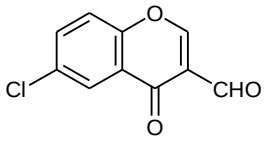
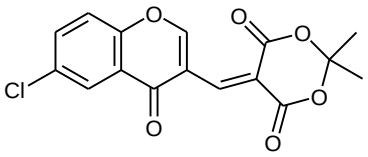
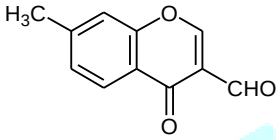
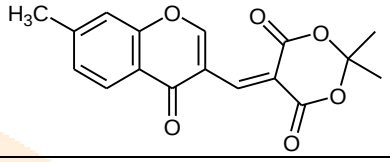
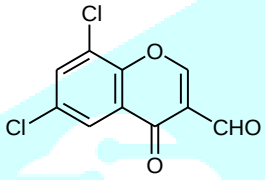
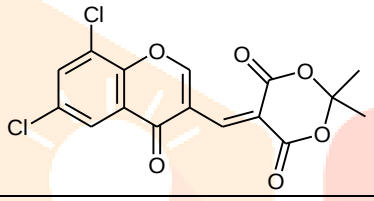
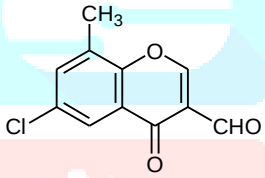
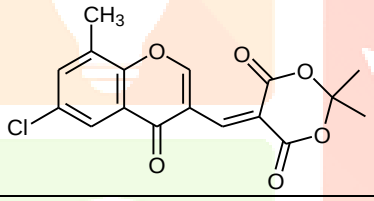
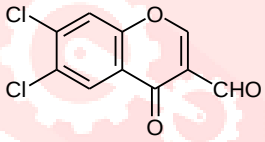
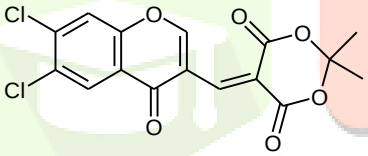
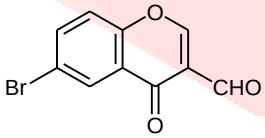
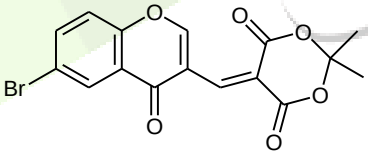
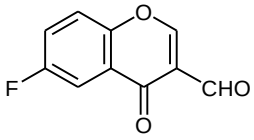
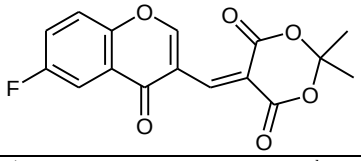
The uncorrected melting points of compounds were taken in an open capillary in a paraffin bath. The progress of the reactions was monitored by TLC (Thin Layer Chromatography). IR spectra were recorded on Perkin-Elmer FTIR spectrophotometer in KBr disc. ^{1}H NMR spectra were recorded on an 300 MHz FT-NMR spectrometer in $CDCl_3$ as a solvent and chemical shift values are recorded in units δ (ppm) relative to tetramethylsilane (Me_4Si) as an internal standard.

The required 4-oxo-4*H*-benzopyran-3-carbaldehydes was prepared by Vilsmeir-Haack reaction.[10]

General procedure

A mixture of 4-oxo-*4H*-benzopyran-3-carbaldehyde (1 mmol), Meldrum's acid (1 mmol) and water (10mL) were taken in single neck round bottom flask and to this boric acid (10 mol%) was added. The flask with the reaction mixture was stirred at room temperature. The progress of reaction was monitored by TLC. After the completion of the reaction, The crude product was recrystallized from ethanol to afford pure corresponding compounds 3(a-h) in good to excellent yield.

Table I. Knoevenagel condensation of 4-oxo-4*H*-benzopyran-3-carbaldehydes with Meldrum's acid in presence of boric acid at room temperature[a].

Entry	Ar	Product	Time (min)	Yield (%)[b]	M.p.(°C) Found	M.p.(°C) Reported
3a			20	90	180-182	182[11]
3b			15	92	198-200	198[11]
3c			30	87	184-186	186[11]
3d			25	89	176-178	180[11]
3e			20	91	198-200	200[11]
3f			15	88	240-242	242[11]
3g			20	90	200-202	205[11]
3h			10	92	198-200	-

[a] All the products were characterized by IR, ^{1}H NMR, and mass spectra; [b] Isolated yields based upon starting aldehyde.

Result and Discussion

In continuation of our work on Knoevenagel condensations and the development of novel synthetic methodologies,[11] herein, we would like to report a simple, efficient and green methodology for the synthesis of 2,2-dimethyl-5- [(4-oxo-4*H*-chromen-3-yl) methylene]-1, 3-dioxane-4, 6-diones. The synthetic route has been shown in Scheme.

For the search of best experimental condition, the reaction of 4-oxo-4*H*-benzopyran-3-carbaldehyde **1a,** Meldrum's acid **2** and boric acid in water at room temperature has been considered as the model reaction. The different heteroaromatic aldehydes containing electron-withdrawing or electron-donating compounds were reacted with Meldrum's acid. They all gave the expected products with good yields in short reaction times. All the results are listed in Table I.

We have developed a newer route for the condensation of various 4-oxo-(4*H*)-1-benzopyran-3-carbaldehyde with Meldrum's acid in the presence of boric acid in water at room temperature. (Table I). For 4-oxo-(4*H*)-1-benzopyran-3-carbaldehyde, which has three active sites, the reactions selectively occurred at the formyl group. All the reactions were carried out using mild reaction conditions at room temperature with constant stirring. Using this methodology, condensation reactions were completed in shorter reactions times (10-30 min) with excellent yield (87-92%).

Conclusion

In conclusion, we developed a efficient and green methodology for the synthesis of 2, 2-dimethyl-5- [(4-oxo-4*H*-chromen-3-yl) methylene]-1, 3-dioxane-4, 6-dione from the condensation of substituted 4-oxo-4*H*-benzopyran-3-carbaldehyde with Meldrum's acid in the presence of boric acid in water at room temperature. The prominent merits offered by this methodology are mild reaction conditions, simple procedures, cleaner reaction, short reactions time and good yield of products.

Spectral data ofrepresented compounds

(3a) IR (KBr, cm^{-1}): 3062, 2996, 1732, 1670 1396, 1251. ^1H NMR (300 MHz, $CDCL_3$) δ (ppm): 1.8 (6H, s, 2×CH_3), 7.2-8.1 (4H, m, aromatic), 8.7 (1H, s, olefinic), 9.6 (1H, s, C_2-H of chromone moiety). EIMS (m/z, %): = 301 [M+1].

(3e) IR (KBr, cm^{-1}): 3060, 2996, 1718, 1649, 1396, 1283, 796. ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.5 (3H, s, Ar–CH_3), 1.9 (6H, s, 2-CH_3), 7.2-7.5 (2H, s, aromatic), 8.6 (1H, s, olefinic), 9.5 (1H, s, C_2-H of chromone moiety). EIMS (m/z, %): = 349 [M+1].

References

1. Jones G, 1967, Visible Light Induced Knoevenagel Condensation Catalyzed by Starfruit Juice of Averrhoa carambola, *Organic Reactions*, 15, 204-599.
2. Freeman F, 1980, Properties and reactions of arylidenemalononitriles, *Chem Rev*, 80, 329-50.
3. Chavan H. V., Bandgar B. P., 2013, Aqueous Extract of Acaciaconcinna Pods: An Efficient Surfactant Type Catalyst for Synthesis of 3-Carboxycoumarins and Cinnamic Acids via Knoevenagel Condensation, *ACS Sustainable Chem Eng* 1, 929-36.
4. Weclawski M. K., Meiling T. T., Leniak A, Cywinski P. J., Gryko D. T., 2015, Planar, Fluorescent Push-Pull System That Comprises Benzofuran and Iminocoumarin Moieties, *Org Lett*, 17, 4252-55.
5. Gerwick W. H., Lopez A., Van Duyne G. D., Clardy J., Ortiz W., Buez A., 1979, *Tetrahedron Lett*, 27,(18), 1979-1982.

6. (a) Prousek J., Czech C., 1993, *Chem. Commun.* 58, 3014; (b) Rama Sarma G. V. S., Reddy V. M., 1993, Hormothamnione, a novel cytotoxic styrylchromone from the marine cyanophyte hormothamnion enteromorphoides grunow, *Ind. J. Hetero. Chem.*, 3, 111.
7. Shindalkar S. S., Madje B. R., Shingare M. S., 2007, Microwave Induced, Solvent-Free Knoevenagel Condensation of 4-Oxo(4H)-1-benzopyran-3-carbaldehyde with Meldrum′s Acid Using Alumina Suppor, *Ind. J. Chem. Sec. B*, 45, 2571.
8. (a) Brahmachari G., Nurjamal K., Karmakar I., Begam S., Nayek N., Mandal B. 2017, Development of a Water-Mediated and Catalyst-Free Green Protocol for Easy Access to a Huge Array of Diverse and Densely Functionalized Pyrido [2,3-d:6,5-d′]dipyrimidines via One-Pot Multicomponent Reaction under Ambient Conditions, *ACS Sustainable Chem. Eng.* , 5, 10, 9494-9505; (b) Li G., Wang B., Resasco D. E., 2020, Water-Mediated Heterogeneously Catalyzed Reactions, *ACS Catal.*, 10, 2, 1294; (c) Shi L., Ying Z., Xu A., Cheng Y., 2020, Unraveling the Water-Mediated Proton Conduction Mechanism along the Surface of Graphene Oxide, *Chem. Mater.*, 32, 14, 6062-6069.
9. (a) Shelke K. F., Badar A. D., Devhade J. B., 2016, An Efficient Synthesis of 5-Arylidene-2,4-Thiazolidinedione Catalyzed by Boric acid in Aqueous media under Ultrasound-Irradiation, *Chemistry & Biology Interface*, 6, 6, 410-415; (b) Pal R., 2018, Boric acid in organic synthesis: scope and recent developments, *Arkivoc*, 1, 346; (c) Shahebaaz K. Pathan P., Mahaparale S., Deshmukh H., Arote R., Sangshetti J., 2020, *Applications of Nanotechnology for Green Synthesis*, 457-483; (d) Nguyen T. B., Sorres J., Tran M. Q., Ermolenko L., Mourabit A. A., 2012, *Boric Acid: A Highly Efficient Catalyst for Transamidation of Carboxamides with Amines*, *Org. Lett.*, 14, 12, 3202-3205; (e) Bhattacharyya D., Nandi S. Adhikari P., Sarmah B. K., Konwara M., Das A, 2020, Boric acid catalyzed chemoselective reduction of quinolones, *Org. Biomol. Chem.*, 18, 1214-1220.
10. Nohara A., Umetani T., Sanno Y., 1974, Studies on antianaphylactic agents—I : A facile synthesis of 4-oxo-4H-1-benzopyran-3-carboxaldehydes by Vilsmeier reagents, *Tetrahedron*, 30, 3553-3561.
11. (a) Shelke, K. F.; Khadse, R. E., 2015, Ionic liquid is an efficient catalyst for Knoevenagel condensation under grinding method, *Der Pharma Chemica*, , 7(1),191-196; (b) Shelke, K. F.; Khadse, R. E., 2015, Ultrasound-assisted an efficient Knoevenagel reaction catalyzed by ionic liquid, *J. Applicable Chem*, 4(6), 1804-1810; (c) Shelke, K. F.; Idhole, S. S.; Badar, A. D.; Devhade, J. B., 2016, A facile & efficient synthesis of 5-arylidene 2,4-thiazolidinedione catalyzed by ionic liquid, *Der Pharmacia Letter*, 8(5),72-75; (d) K. F. Shelke; Badar, A. D.; Devhade, J. B.,2016, Ultrasound assisted an efficient synthesis of Azalactone derivatives catalysed by ionic liquid, *Chem & Bio. Interface*, 6(3), 157-161; (e) Gholave J. V., Gadhari N. S., Patil S. S., Upadyay S. S., Patil V. R., Shelke K. F., 2020, Development and Validation of a Stability-indicating RP-HPLC Method for the Simultaneous Determination of Telmisartan and its Related Substances in Telmisartan Bulk Drug Substance, *Analytical Chemistry Letter*, 10 (5), 577-589.