Send Orders for Reprints to reprints@benthamscience.ae

Letters in Organic Chemistry, **2016**, *13*, 231-235

New Facile, Eco-Friendly and Rapid Synthesis of Trisubstituted Alkenes Using Bismuth Nitrate as Lewis Acid

Munira T. Muhammad[a], Khalid M. Khan[a,*], Muhammad Taha[b,c], Tariq Khan[a], Shafqat Hussain[a,d], Muhammad I. Fakhri[a], Shahnaz Perveen[e] and Wolfgang Voelter[f]

[a]*H. E. J. Research Institute of Chemistry, International Center for Chemical and Biological Sciences, University of Karachi, Karachi-75270, Pakistan;* [b]*Atta-ur-Rahman Institute for Natural Product Discovery, Universiti Teknologi MARA (UiTM), Puncak Alam Campus, 42300 Bandar Puncak Alam, Selangor D. E. Malaysia;* [c]*Faculty of Applied Science Universiti Teknologi MARA, 40450 Shah Alam, Malaysia* [d]*Department of Chemistry, Karakoram International University, Gilgit-15100, Gilgit-Baltistan, Pakistan;* [e]*PCSIR Laboratories Complex, Karachi, Shahrah-e-Dr. Salimuzzaman Siddiqui, Karachi-75280, Pakistan;* [f]*Interfakultäres Institut für Biochemie, Universität Tübingen, Hoppe-Seyler-Str. 4, D-72076 Tübingen, Germany*

Khalid M. Khan

Received July 22, 2015: Revised November 26, 2015: Accepted December 14, 2015

Abstract: ***Background*:** For the synthesis of tri and tetra-substituted alkenes, Knoevenagel condensations have previously been performed in solvents like dichloromethane, DMF, toluene, acetonitrile, DMSO *etc*. These conditions suffer from certain limitations like long reaction times are required in DMSO or harsh heating conditions are necessary using DMF as a solvent decreasing the yields to below 50%. Tedious work up is required after long reaction times or/and high temperatures, if the reaction is performed in toluene.

***Methods*:** In a typical reaction, 1 mmol of aromatic aldehyde with 1.1 mmol of malanonitrile in the presence of bismuth nitrate (3 mmol%) was refluxed in water (10 ml) for 25-30 min. After completion of the reaction (TLC analysis), excess bismuth nitrate was filtered for next use and the filtrate was kept at room temperature over night for crystallization. Crystals were filtered, washed with water and dried. In a separate reaction the catalyst was re-used for the one of the same reactions and found satisfactory results.

***Results*:** In order to generalize our newly developed methodology, we selected a variety of aldehydes to synthesize different trisubstituted alkenes and found that this method can also be applied on aromatic aldehydes. For comparison purposes, the reaction was carried out in ethanol in parallel to water and found that water is the best solvent for this reaction.

***Conclusion*:** In summary, we have discovered a facile and rapid method for Knoevenagel condensations using bismuth nitrate as Lewis acid. The advantages of bismuth nitrate as a catalyst are: easy to remove from the reaction mixture by simple filtration, recyclable, requires water as solvent, is eco-friendly and afforded high yields (90-97%).

Keywords: Bismuth nitrate, eco-friendly, knoevenagel, trisubstituted alkenes.

1. INTRODUCTION

Knoevenagel condensation is a well-established method for carbon-carbon bond formation: Compounds containing active methylene groups are condensed either with aldehydes or ketones to trisubstituted and tetrasubstituted alkenes, respectively [1]. Alkenes are present in numerous naturally occurring compounds such as α-carotene, β-carotene, vitamin A, macrocycles, polycycles, terpenes, *etc*. It is also reported that compounds containing longer conjugated unsaturated carbon chains have redox activity in the living system and may serve as anticancer agents [2, 3]. Compounds containing active methylene moieties like malononitrile, when condensed with aldehydes, yield trisubstituted alkenes serving as important intermediates in many reactions [4-9]. For the synthesis of such trisubstituted alkenes, Knoevenagel condensations have previously been performed in solvents like dichloromethane, DMF, toluene, acetonitrile, DMSO *etc*. [10, 11]. These conditions suffer from certain limitations like long reaction times are required in DMSO [12, 13] or harsh heating conditions are necessary using DMF as a solvent decreasing the yields to below 50%. Tedious work up is required after long reaction times or/and high temperatures, if the reaction is performed in toluene. Also, under solvent-free conditions using microwave irradiation only 50-75% yield in 15-180 minutes have been achieved [14, 15]. Additionally, catalysts like morphine, pyridine, piperidine, piperazine, I_2, PPh_3, in the presence of Pd, Cu (I) mediated, Tf_2NH Catalysed, alkali metal hydroxides (KOH, NaOH), basic zeolites (Cs, lanthanum-impregnated mesoporous) MCM-41, alkali-exchanged zeolites or biocata-

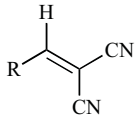
*Address correspondence to this author at the H. E. J. Research Institute of Chemistry, International Center for Chemical and Biological Sciences, University of Karachi, Karachi-75270, Pakistan; Tel: 0092-21-34824910; Fax: 0092-21-34819018-9; E-mails: khalid.khan@iccs.edu, and hassaan2@super.net.pk

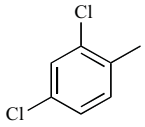
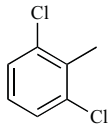
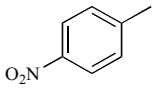
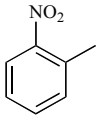
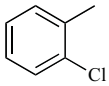
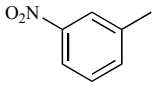
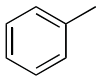
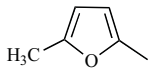
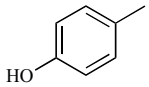
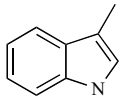
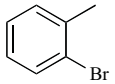
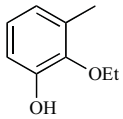
1875-6255/16 $58.00+.00

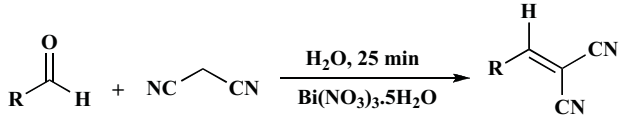
lysts like lipase were also used but found inappropriate [16-18]. The major problems using these catalysts are not to be active in all solvents, to require tedious work up, and sometimes suffer from poor yields. High costs, poor yields along with troublesome isolation procedures are the disadvantages of applying biocatalysts. These limitations clearly indicate that a Knoevenagel condensation under conventional conditions is a limited approach for the synthesis of trisubstituted alkenes [19].

In continuation of our work on bismuth-containing Lewis acids as catalyst and other catalysts for Knoevenagel condensations [19-21], we herein want to report an improved, facile, expeditious and high yielding method for the synthe-

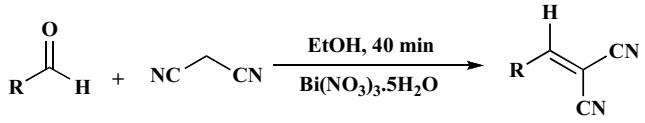
Table 1. Synthesized Trisubstituted Alkene 1-12.



Comp. No.	R	H_2O		EtOH	
		Yield (%)	Time (min)	Yield (%)	Time (min)
1		94	30	92	34
2		90	28	82	32
3		95	24	90	27
4		88	26	80	25
5		89	25	84	30
6		89	30	85	34
7		93	24	88	22
8		95	20	82	20
9		94	24	82	28
10		89	30	80	35
11		89	24	80	30
12		95	30	85	34



Scheme 1.



Scheme 2.

sis of trisubstituted alkenes using bismuth nitrate in water or ethanol (Schemes **1** and **2**, Table **1**).

2. RESULTS AND DISCUSSION

During a total synthesis of a bioactive natural product, we found that bismuth nitrate can catalyze Knoevenagel condensations, and to the best of our knowledge, bismuth nitrate is used for the first time for this condensation.

In order to generalize our newly developed methodology, we selected a variety of aldehydes to synthesize different trisubstituted alkenes and found that this method can be applied also on aromatic aldehydes. For comparison purposes, the reaction was carried out in ethanol in parallel to water and found that water is the best solvent for this reaction (Scheme **1** and **2**).

In a typical reaction, 1 mmol of aromatic aldehyde with 1.1 mmol of malanonitrile in the presence of bismuth nitrate (3 mmol%) was refluxed in water (10 ml) for 25-30 min. After completion of the reaction (TLC analysis), excess bismuth nitrate was filtered for next use and the filtrate was kept at room temperature over night for crystallization. Crystals were filtered, washed with water and dried. In a separate reaction the catalyst was re-used for the one of the same reactions and found satisfactory results.

The reaction between malononitrile and aldehydes was explored by using different bases which abstract the acidic proton from malononitrile, however, in the newly developed method, $Bi(NO_3)_3$ acts as a Lewis acid and activates the aldehydic carbon. As water (Pka 15.7) as well as ethanol (Pka 15.9) are basic enough to de-protonate malononitrile, and due to the presence of $Bi(NO_3)_3$, the aldehydic carbon becomes more electrophillic. Thus, the attack of the anion of malononitrile results in the formation of an alkoxide bonded to bismuth nitrate. As soon as this oxygen atom abstracts a proton from the solvent, $Bi(NO_3)_3$ departs and forms an alcohol. Elimination of a water molecule from the alcohol and formation of a trisubstituted alkene takes place. Almost all aromatic aldehydes, either having electron- withdrawing or -donating groups are activated nearly to the same extent with $Bi(NO_3)_3$, and the reaction times (below 40 min) for all reactions were nearly the same (Fig. **1**). Some experiments were also carried out in dichloromethane and acetonitrile, but found to be ineffective.

3. CONCLUSION

In summary, we have discovered a facile and rapid method for Knoevenagel condensations using bismuth nitrate as Lewis acid. The advantages of bismuth nitrate as a catalyst are: easy to remove from the reaction mixture by simple filtration, recyclable, requires water as solvent, is eco-friendly, and afforded high yields (90-97%).

4. EXPERIMENTAL

4.1. General Procedure for the Synthesis of Compounds 1-12

In a round-bottomed flask corresponding aldehydes (1 mmol) and a catalytic amount (3 mol%) of $Bi(NO_3)_3$ in water/ethanol (10 mL) were stirred for 2 minutes at room temperature, and then malononitrile (1.1 mmol) was added. The reaction mixture was refluxed for 20 minutes. After completion of the reaction (TLC analysis), $Bi(NO_3)_3$ was filtered

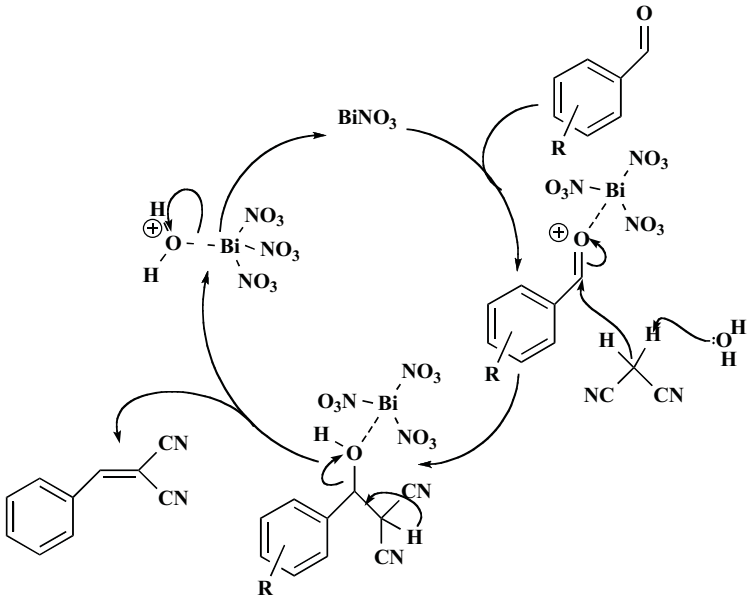


Fig. (1). Plausible mechanism of $BiNO_3$ catalyzed Knoevenagel condensation.

for the next use and the filtrate was kept at room temperature over night for crystallization. Crystals were filtered, washed with water, dried, and were re-crystallized from hot ethanol. All aldehydes and other starting materials were used as received from the supplier. Nuclear magnetic resonance spectra were recorded on Bruker 300 MHz and 500 MHz spectrometers and mass spectra were recorded at JEOL JMS-HX110 mass spectrometer using FABMS-H. Thin layer chromatography was carried out on aluminum plates precoated with silica gel (Kieselgel 60, E. Merck, Darmstadt, Germany). UV light at 254 and 365 nm was used for chromatograms visualization.

4.1.1. 2-(2, 4-Dichlorobenzylidene)malononitrile (1)

Yield: 94%; M.p. 149°C; UV $\lambda_{max\ (MeOH)}$ nm (log ε): 310 (13.02); IR (KBr) ν_{max} cm^{-1}: 3746, 3044, 1738, 1376, 1264; ^{1}H-NMR; (300 MHz, DMSO-d_6) δ 8.62 (s, 1H, H-8), 8.045 (d, 1H, J = 8.4 Hz, H-2), 7.92 (d, 1H, J = 1.8 Hz, H-3), 7.72 (dd, 1H, J = 6.6, 10.5 Hz, H-5); MS: *m/z* 223 (100%), 195 (20%), 187(100%), 124 (10%), 83 (60%); ^{13}C-NMR; (75 MHz, DMSO-d_6) δ 156.7 (C-1), 130.9 (C-3), 130.0 (C-5), 128.3 (C-6), 138.6 (C-2), 135.5 (C-4), 113.3 (C-1′), 112.2 (C-2’), 87.1 (C-1″).

4.1.2. 2-(2, 6-Dichlorobenzylidene)malononitrile (2)

Yield: 90%; M.p. 94°C; UV $\lambda_{max\ (MeOH)}$ nm (log ε): 287 (37.36); IR (KBr) ν_{max} cm^{-1}: 3746, 3076, 2236, 1796, 1325; ^{1}H-NMR; (300 MHz, DMSO-d_6) δ 8.62 (s, 1H, H-8), 7.70 (d, 2H, J = 1.8 Hz, H-4, 5), 7.62 (m, 1H, H-3); MS: *m/z* 223 (100%), 195 (20%), 187 (100%), 124 (10%), 83 (60%); ^{13}C-NMR; (75 MHz, DMSO-d_6) δ 159.5 (C-1), 133.4 (C-2, C-6), 129.1 (C-4), 128.9 (C-5, C-3), 112.0 (C-3′), 111.0 (C-4′), 93.0 (C-2′).

4.1.3. 2-(4-Nitrobenzylidene) malononitrile (3)

Yield: 95%; M.p. 135°C; UV $\lambda_{max\ (MeOH)}$ nm (log ε): 307 (3.14); IR (KBr) ν_{max} cm^{-1}: 3745, 3084, 2226, 1595, 1151; ^{1}H-NMR; (300 MHz, DMSO-d_6) δ 8.83 (s, 1H, H-8), δ 8. 43 (d, 2H, J = 9.0 Hz, H-5, 6), 8.14 (d, 2H, J = 9.0 Hz, H-2, 3); MS: *m/z* 199 (100%), 169 (40%), 153 (90%), 126 (90%), 114 (50%); ^{13}C-NMR; (75 MHz, DMSO-d_6) δ 159.2 (C-1′), 149.6 (C-1), 136.6 (C-4), 131.4 (C-5, C-3), 124.3 (C-2- C-6), 113.5 (C-3′), 112.4 (C-4′), 85.9 (C-2′).

4.1.4. 2-(2-Nitrobenzylidene)malononitrile (4)

Yield: 88%; M.p. 130°C, UV $\lambda_{max\ (MeOH)}$ nm (log ε): 254 (5.82); IR (KBr) ν_{max} cm^{-1}: 3735, 3047, 1567, 1346, 1211; ^{1}H-NMR; (300 MHz, DMSO-d_6) δ 8.96 (s, 1H, H-8), 8.34 (d, 2H, J = 0.8 Hz, H-2, 3), 8.00 (m, 2H, H-4, 5); MS: 199 *m/z* 199 (90%), 144 (50%), 126 (90%), 114 (85%), 92 (100%), 75 (50%); ^{13}C-NMR; (75 MHz, DMSO-d_6) δ 161.3 (C-1′), 135.0 (C-2), 133.3 (C-5), 130.4 (C-4), 127.1 (C-1), 125.4 (C-6), 113.0 (C-3′), 111.7 (C-4′), 87.0 (C-2′).

4.1.5. 2-(2-Chlorobenzylidene)malononitrile (5)

Yield: 89%; M.p. 90°C, UV $\lambda_{max\ (MeOH)}$ nm (log ε): 287 (5.61); IR (KBr) ν_{max} cm^{-1}: 3745, 3049, 1635, 1358, 1210; ^{1}H-NMR; (300 MHz, DMSO-d_6) δ 8.669 (s, 1H, H-8), 8.034 (d, 1H, J = 7.5 Hz), 7.713 (m, 1H); MS: *m/z* 188 (90%), 134 (50%), 114 (90%), 102 (85%), 90 (100%), 65(50%); ^{13} C-NMR; (75 MHz, DMSO-d_6) δ 157.9 (C-1′), 134.8 (C-3), 130.3 (C-6), 129.8 (C-5), 127. 9 (C-4), 134.2 (C-2), 129.6 (C-1), 113.4 (C-2’’), 112.3 (C-1″).

4.1.6. 2-(3-Nitrobenzylidene)malononitrile (6)

Yield: 89%; M.p. 133°C, UV $\lambda_{max\ (MeOH)}$ nm (log ε): 268 (5.83); IR (KBr) ν_{max} cm^{-1}: 3746, 3049, 1577, 1348, 1210; ^{1}H-NMR; (300 MHz, DMSO-d_6) δ 8.76 (s, 1H, H-8), 8.71 (s, 1H, H-6), 8.49 (dd, 1H, J = 9.9 Hz, 6.3 Hz, H-4), 8.33 (d, 1H, J = 7.8 Hz, H-2) *7.91* (t, 1H, J = 15.9 Hz, H-3); MS: *m/z* 199 (85%), 153 (100%), 126 (50%), 75 (15%); ^{13} C- NMR; (75 MHz, DMSO-d_6) δ 159.2 (C-1′), 135.8 (C-2), 131.1 (C-2), 127.9 (C-5), 124.8 (C-6), 148.0 (C-3), 132.4 (C-4), 113.6 (C-2’’), 112.5 (C-1″), 84.9 (C-1).

4.1.7. 2-Benzylidenemalononitrile (7)

Yield: 93%; M.p. 80°C, UV $\lambda_{max\ (MeOH)}$ nm (log ε): 344 (5.92); IR (KBr) ν_{max} cm^{-1}: 3747, 2219, 1549, 1346, 1211; 1H-NMR; (300 MHz, DMSO-d_6) δ 8.53 (s, 1H, H-8), 7. 95 (d, 2H, J=7.2 Hz, H-5, 6), 7.96 (m, 3H, H-2, 3, 4); MS: *m/z* 154 (100%), 123 (70%), 103 (50%), 44 (70%); ^{13}C-NMR; (75 MHz, DMSO-d_6) δ 161.5 (C-1’), 134.3 (C-4), 131.2 (C-1), 130.4 (C-6, C-2), 129.5 (C-3, C-5), 114.1 (C-1’), 113.1 (C-2’), 81.6 (C-2”).

4.1.8. 2-[(5-Methyl-2-furyl)methylene]malononitrile (8)

Yield: 95%; M.p. 98°C, UV $\lambda_{max\ (MeOH)}$ nm (log ε): 358 (8.93); IR (KBr) ν_{max} cm^{-1}: 3747, 3129, 2217, 1545; ^{1}H-NMR; (300 MHz, DMSO-d_6) δ 8.13 (s, 1H, H-6), 7.39 (d, 1H, J = 3.6 Hz, H-3), 6.61 (d, 1H, J = 3.6 Hz, H-4), 2.44 (s, 3H, H-10); MS: *m/z* 158 (100%), 131 (60%), 103 (25%), 53 (15%); ^{13}C-NMR; (75 MHz, DMSO-d_6) δ 162.1 (C-4), 147.0 (C-1), 143.4 (C-1′), 128.0 (C-2), 114.9 (C-3′), 113.6 (C-4′), 112.2 (C-3), 72.1 (C-2′), 14.0 (C-1″).

4.1.9. 2-(4-Hydroxybenzylidene)malononitrile (9)

Yield: 94%; M.p. 185°C, UV $\lambda_{max\ (MeOH)}$ nm (log ε): 354 (6.392); IR (KBr) ν_{max} cm^{-1}: 3746, 3351, 1610, 1322, 1172; ^{1}H-NMR; (300 MHz, DMSO-d_6) δ 8.290 (s, 1H, H-8), δ 7.894 (d, 2H, J = 8.7 Hz , H-5, 6), 6.971 (d, 2H, J = 8.7 Hz, H-2, 3); MS: *m/z* 170 (100%), 142 (80%), 115 (60%), 91 (25%), 63 (15%); ^{13}C-NMR; (75 MHz, DMSO-d_6) δ 163.8 (C-1′), 160.4 (C-4), 133.8 (C-2, C-6), 122.7 (C-1), 116.6 (C-3, C-5), 115.0 (C-3′), 114.1 (C-4′), 75.0 (C-2′).

4.1.10. 2-(1H-Indol-3-ylmethylene)malononitrile (10)

Yield: 89%; M.p. 220°C, UV $\lambda_{max\ (MeOH)}$ nm (log ε): 287 (9.26); IR (KBr) ν_{max} cm^{-1}: 3722, 2234, 1610, 1358; ^{1}H-NMR; (300 MHz, DMSO-d_6) δ 8.69 (s, 1H,H-10), 8.52 (s, 1H, H-2), 8.04 (dd, 1H, J = 17.4, 4.2 Hz, H-6), 7.58 (dd, 1H, J = 8.4 Hz, 4.5 Hz, H-9),7.32 (m, 2H, H-7, 8); MS: *m/z* 193 (100%), 166 (65%), 139 (25%), 88 (10%); ^{13}C-NMR; (75 MHz, DMSO-d_6) δ 160.4 (C-1′), 139.4 (C-1), 129.3 (C-6), 120.9 (C-5), 123.6 (C-3), 121.3 (C-4), 114.8 (C-3′), 113.4 (C-4′), 112.5 (C-2), 90.0 (C-2′).

4.1.11. 2-(2-Bromobenzylidene)malononitrile (11)

Yield:89%; M.p. 92°C, UV $\lambda_{max\ (MeOH)}$ nm (log ε): 298 (10.44); IR (KBr) ν_{max} cm^{-1}: 3741, 2229, 1645, 1322, 1348, 1241; ^{1}H-NMR; (300 MHz, DMSO-d_6) δ 8.59 (s, 1H, H-8), 7.98 (dd, 1H, J = 9Hz, 6Hz, H-6), 7.87 (dd, 1H, J = 9Hz , 6.6 Hz, H-3), 7.64 (m, 2H, H-4, 5); MS: *m/z* 233 (100%), 153

(100%), 126 (85%), 99 (65%), 75 (70%);^{13}C-NMR; (75 MHz, DMSO-d_6) δ 157.3 (C-1′), 135.1 (C-2), 132.3 (C-6), 129.4 (C-4), 128.2 (C-5), 126.1 (C-3), 123.2 (C-1), 114.2 (C-3′), 115.4 (C-4′), 80.2 (C-2′).

4.1.12. 2-(3-Ethoxy-4-hydroxybenzylidene)malononitrile (12)

Yield: 95%; M.p. 134°C, UV $\lambda_{max\ (MeOH)}$ nm (log ε): 295 (7.44); IR (KBr) ν_{max} cm^{-1}: 3747, 2219, 1555, 1346, 1348; ^{1}H-NMR; (300 MHz, DMSO-d_6) δ 10.70 (s, 1H, OH), 8. 24 (s, 1H, H-11), 7.61 (s, 1H, H-6), 7.48 (d, 1H, J = 6.9 Hz, H-4) , 6.98 (d, 1H, J = 8.4, H-3), 4.07 (q, 2H, J = 6.9, H-8), 1.37 (t,3H, J = 13.8 Hz, H-9); MS: *m/z* 214(40 %), 193 (55%), 154 (35%), 132 (20%); ^{13}C-NMR; (75 MHz, DMSO-d_6) δ 162.1 (C-1′), 149.3 (C-3), 148.1 (C-4), 128.7 (C-1), 123.3 (C-6), 117.2 (C-5), 114.1 (C-2), 114.1 (C-3′), 115.2 (C-4′), 81.3 (C-2′).

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

ACKNOWLEDGEMENTS

The authors are thankful to Higher Education Commission (HEC) Pakistan for financial support to Project No. 20-2073 under National Research Program for Universities and DAAD (Deutscher Akademischer Austauschdienst), Bonn, (Germany) for granting a fellowship to Prof. Dr. Khalid M. Khan.

REFERENCES

[1] Guanyinsheng, Q., Qiuping, D., Yiyuan, P., Jie, W. Synthesis of (*Z*)-1-benzylidene- 3-(1*H*-indol-1-yl)-1*H*-indene-2,2(3*H*)-dicarbonitriles *via* three-component reaction of 2 alkynylbenzaldehyde, malononitrile, and indole, *Tetrahedron Lett.,* **2010**, *51,* 4391-4394.

[2] Paola, P., Can *β*-carotene regulate cell growth by a redox mechanism, *Biochim. Biophys. Acta*, **2005**, *17,* 215-221.

[3] Mayne S.T. Beta-carotene, carotenoids and disease prevention in humans, *FASEB J*., **1996,** *10*, 690-701.

[4] Ghozlan, S.A.; Abdelhamid, I.A.; Gaber, H.; Elnagdi, M.H. Studies with functionally substituted enamines: Synthesis of new aminoazolo-pyrimidines and -1,2,4-triazines. *J. Chem. Res*., **2004**, *12*, 789-793.

[5] Lingaiah, B.P.V.; Reddy, G.V.; Yakaiah, T.; Narsaiah, B.; Reddy, S.N.; Yadla, R.; Rao, P.S. Efficient and convenient method for the synthesis of poly-functionalized 4*H*-pyrans. *Synth. Commun.,* **2004**, *34*, 4431-4437.

[6] Balalaie, S.; Ramezanpour, S.; Bararjanian, M.; Gross, J.H. DABCO-catalyzed efficient synthesis of naphthopyran derivatives *via* one-pot three-component condensation reaction at room temperature. *Synth. Commun*. **2008**, *38*, 1078-1089.

[7] Abdel-Galil, F.M.; Abdel-Motaleb, R.M.; Elnagdi, M.H. Nitriles in heterocyclic synthesis: The reaction of acetophenonylidene-malononitrile with some active methylene reagents and acrylonitrile derivatives. *An. Quim. Ser. C.,* **1988**, *84*, 19-21;

[8] Stoyanov, E.V.; Ivanov, I.C.; Heber, D. General method for the preparation of substituted 2-amino-4*H*,5*H*-pyrano[4,3-*b*]pyran-5-ones and 2-amino-4*H*-pyrano[3,2-c]pyridine-5-ones. *Molecules,* **2000**, *5*, 19-32.

[9] Nagarajan, A.S.; Reddy, B.S. Synthesis of substituted pyranopyrazoles under neat conditions *via* a multicomponent reaction. *Synlett.,* **2009**, *12*, 2002-2004.

[10] Bernasconi, C.F.; Ali, M.; Nguyen, K.; Ruddat, V.; Rappoport, Z. Kinetics and mechanism of reactions of substituted (methylthio)benzylidene Meldrum's acids with primary amines in aqueous DMSO. *J. Org. Chem*., **2004**, *69*, 9248-9254.

[11] Lee, A.; Michrowska, A.; Sulzer-Mosse, S.; List, B. The catalytic asymmetric Knoevenagel condensation, *Angew. Chem. Int. Ed.,* **2011**, *50*, 1707-1710.

[12] Taha, N., Sasson, Y., Chidambaram, M. Phase transfer methodology for the synthesis of substituted stilbenes under Knoevenagel condensation condition. *Appl. Catal. A: General.,* **2008**, *350*, 217-224.

[13] Trilleras, J. E., Velasquez, K. J., Pacheco, D. J., Quiroga, J., Ortíz, A. Microwave-assisted synthesis under solvent-free conditions of (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-arylacrylonitriles. *J. Braz. Chem. Soc.*, **2011**, *22*, 2396-2402.

[14] Sonawane, Y.A., Phadtare S.B., Borse B.N., Jagpit, A.R. and Shankarling G.S. Synthesis of diphenyl amine- based novel fluorescent styryl colorants by knoevengel condensation using a conventional method, biocatalyst and deep eutectic solvent. *Org. Lett.*, **2010,** *12*, 1456-1459.

[15] Khan, K.M.; Ali, M.; Farooqui, T.A.; Khan, M.; Taha, M.; Perveen, S. An improved method for the synthesis of 5-arylidene barbiturates using $BiCl_3$.*J. Chem. Soc. Pak.*, **2009**, *31*, 823-828.

[16] Sonawane, Y.A.; Phadtare, S.B.; Borse, B.N.; Jagpit, A.R.; Shankarling, G.S. Synthesis of diphenylamine-based novel fluorescent styryl colorants by Knoevenagel condensation using a conventional method, biocatalyst, and deep eutectic, *Org. Lett*., **2010**, *12*, 1456-1459 and references quoted therein.

[17] Xie, M., Wang, J., Fang, K., Wang, S., Yan, L. A convenient hydroiodination of alkynes using I_2/PPh_3/H_2O and its application to the one-pot synthesis of trisubstitutedalkenes *via* iodoalkenes using Pd-catalyzed cross-coupling reactions. *Tetrahedron Lett.,* **2014**, *55*, 6779-6783.

[18] Belaid M., Ashwini A. G., Rajib C., Alexander G. Air–water interface effects on the regioselectivity of singlet oxygenations of a trisubstituted alkene, *Tetrahedron Lett.*, **2015**, *56,* 4505-4508.

[19] Khan, K.M.; Ali, M.; Farooqui, T.A.; Khan, M.; Taha, M.; Perveen, S. An improved method for the synthesis of 5-arylidene barbiturates using $BiCl_3$, *J. Chem. Soc. Pak.,* **2009**, *31,* 823-828 and references quoted therein.

[20] Khan, K.M.; Muhammad, M.T.; Khan, I.; Perveen, S.; Voelter, W. Rapid cesium fluoride catalyzed Knoevenagel condensation to synthesize highly functionalized 4,4′-(arylmethylene)*bis*(1*H*-pyrazol-5-ol) derivatives. *Monatsch. Chem-Chem. Mon.,* **2015**, 146, 1587-1590.

[21] Khan, K.M.; Khan, I.; Perveen, S.; Malik, M. I. A rapid and efficient CsF catalyzed tandem Knoevenagel-Michael reaction, *J. Fluorine Chem.,* **2014**,*158*, 1-5.