Microwave Assisted Knoevenagel Condensation: Synthesis and Antimicrobial Activities of Some α-Cyanoacrylates

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Abstract. A series of α-cyanoacrylates (**1-9**) were prepared by Knoevenagel condensation of ethyl cyanoacetate with corresponding aromatic aldehydes in presence of ammonium acetate (NH_4OAc) using microwave irradiation under solvent free condition. The reactions were completed in 20-60 sec with excellent yield. These compounds were screened for their antibacterial activities against five pathogenic organisms: *Bacillus cereus, Staphylococcus aureus* (ATCC 6538)*, Vibrio cholerae*, *Shigella dysenteriae* (AE 14396) and *Salmonella typhi* (AE 14612) and antifungal activity against two organisms: *Aspergillus flavus* and *Saccharomyces cerevisiae* using disc diffusion method and poisoned-food technique, respectively. Some of them were found to possess significant activity, when compared to standard drugs.

Keywords: Knoevenagel condensation, microwave irradiation, α-cyanoacrylates, antimicrobial activity

Introduction

Carbon-carbon double bond formation (Shen, 1998) is one of the useful and fundamental reactions in synthetic organic chemistry, particularly in the synthesis of complex natural products with biological activity. The Knoevenagel condensation is one of the most important, useful and widely employed methods for the formation of carbon-carbon bonds. It has been used for the preparation of a range of substituted alkenes and bioactive molecules, as a key step in natural product synthesis and important intermediate for the synthesis of cosmetic, perfume, agrochemicals and pharmaceuticals (Tietze and Beifuss, 1991). Active methylene compounds such as malononitrile, ethyl cyanoacetate, malonic ester etc., are largely used in the Knoevenagel condensation. The ylidenemalononitriles thus obtained have found increasing applications in industry, agriculture, medicine, biological science and in the elegant synthesis of fine chemicals (Freeman, 1980; Fatiadi, 1978a, 1978b). They are important intermediates for the synthesis of various organic compounds, mainly by cyclization reactions (Campaigne and Schneller, 1976). Knoevenagel condensation products with ethyl cyanoacetate have been utilized successfully in the synthesis of mercaptopyrimidine as an intermediate for an antimetabolite, substrates for Guareschi reaction, indanone derivatives for diterpene alkaloid, cyano-

coumarins (Kumar, 2009; Bigi *et al*., 1999) and versatile precursors for the synthesis of substituted heterocycles (Kandeel *et al*., 1996).

The Knoevenagel condensation is generally carried out in the presence of weak organic bases such as aliphatic amines, ethylenediamine and piperidine or their corresponding ammonium salts, Lewis bases and acids including $ZnCl_2$, CdI_2, $TiCl_4$, Al_2O_3, MgO, ZnO, $AlPO_4–Al_2O_3$, $KF–Al_2O_3$, natural hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$) (Mallouk *et al*., 2010), tetra-*n*-butylammonium hydroxide (TBAH) (Balalaie and Bararjanian, 2006), *N*-methylpiperazine (Mukopadhyay and Datta, 2008), 1,1,3,3-tetramethyl-guanidium lactate (Zhang *et al*., 2006), polyacrylonitrile fibre (Li *et al*., 2011), Imidazolium chloride immobilized SBA-15 (Parvin *et al*., 2012) and ammonium acetate (NH_4OAc)-basic alumina (Balalaie and Nemati, 2000). However, this employs hazardous benzene and requires prolonged heating with continuous water removal. The use of such bases/acids and solvents has led to environmental problems, i.e., the necessity to dispose of huge amounts of organic waste due to the formation of undesirable side products. Ionic liquid, recyclable catalysts (Ye *et al*., 2011), electrochemical (Feroci *et al*., 2007), microwave (Saha *et al*., 2008) and ultrasound (Li *et al*., 2004) activation methods have also been reported.

Recently microwave radiation, a non-conventional energy source, for the activation of reactions has gained

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the attention of chemists due to its unique advantages, such as shorter reaction times, cleaner reaction products, higher yields and better selectivities (Kappe, 2004; Lidstrom *et al.*, 2001; Varma, 1999). Moreover, the combination of MW activation and solvent free conditions leads to enhanced conversion rates, higher yields, easier workup and in general cleaner reactions, therefore, confirming the real advantages of this approach in the framework of green chemistry.

In continuation to earlier studies directed at the development of practical and efficient chemical processes (Bhuiyan *et al.*, 2012; 2011; Basu *et al.*, 2003), a sustainable Knoevenagel condensation protocol was reported using microwave irradiation (MWI) and ammonium acetate (NH$_4$OAc) catalysis under solvent-free conditions for the preparation of α-cyanoacrylates. The obtained compounds were screened for their antimicrobial activity.

Materials and Methods

Melting point was recorded with electro thermal melting point apparatus. Thin layer chromatography was performed on Kieselgel GF$_{254}$ and visualisation was accomplished by iodine vapour or uv flame. The infrared (IR) spectra were recorded by FTIR spectrophotometer (Model-8900, Shimadzu, Japan) using KBr matrix in the range 4000-200 cm^{-1}. ^{1}H-NMR (400 MHz and 500 MHz) and ^{13}C-NMR (100 MHz and 125 MHz) spectra were recorded on JEOL GS×400, GEOL JNM-AL 400 (400 MHz) and JEOL GS×400, GEOL JNM-AL 400 (100 MHz) spectrometer in CDCl$_3$, CD$_3$OD and DMSO-d$_6$ as solvent. Chemical shifts were reported in δ unit (ppm) with reference to TMS as an internal standard and *J* values are given in Hz. The carbon, hydrogen and nitrogen percentages in synthesised products were analysed according to the approved method ASTM D-5291 by employing Leco-CHNS-932 analyzer. All reactions were carried out in a commercially available LG microwave oven (MB - 3947C) having a maximum power output of 800 W operating at 2450 MHz.

Syntheses. *General procedure for the synthesis of* α-*cyanoacrylates.* To an equimolar mixture of aromatic aldehyde and ethyl cyanoacetate, catalytic amount of ammonium acetate was added and the reaction mixture irradiated under microwave condition at 160-320 watt for 20-60 sec. After complete conversion of the reaction (TLC; ethyl acetate: *n*-hexane; 1:5, v/v), the obtained solid mass was recrystallised from ethyl acetate and *n*-hexane solvent mixture.

Spectral data. *Ethyl 2-cyano-3-(2-methylphenyl)-acrylate (1).* Off-white crystals, IR (KBr)υ$_{max}$ (cm^{-1}): 3182-2981 (C-H), 2219.91 (s, C≡N), 1712.67 (s, C=O, ester), 1591.16 (s, C=C), 1112.85 (s, C-O str, ether). ^{1}H-NMR (400 MHz, CD$_3$OD): δ 8.62 (s, 1H, =CH), 8.05 (d, 1H, H-6', *J* = 7.80 Hz), 7.45 (m, 1H, H-3'), 7.33 (m, 2H, H-4', H-5'), 4.37 (q, 2H, OCH$_2$, *J* = 7.32 Hz), 2.44 (s, 3H, CH$_3$), 1.38 (t, 3H, OCH$_2$*CH$_3$*, *J* = 7.32 Hz). ^{13}C-NMR (100.40 MHz, CD$_3$OD): δ 163.50, 154.47, 141.04, 133.80, 132.08, 131.99, 129.39, 127.52, 116.17, 105.89, 63.71, 19.73, 14.42. DEPT - 90 (100.40 MHz, CD$_3$OD): δ 154.47, 133.81, 132.08, 129.40, 127.52. DEPT - 135 (100.40 MHz, CD$_3$OD): δ 154.47, 133.81, 132.08, 129.40, 127.52, 63.72 (CH$_2$), 19.73(CH$_3$), 14.42(CH$_3$). Analysis calculated for C$_{13}$H$_{13}$NO$_2$ (215.25): C, 72.54; H, 6.09; N, 6.51; found: C, 73.25; H, 5.68; N, 6.15.

Ethyl 2-cyano-3-(3-methyphenyl)-acrylate (2). Off-white crystals, IR (KBr)υ$_{max}$ (cm^{-1}): 3184, 2925 (C-H), 2217.99 (s, C≡N), 1726.17 (s, C=O, ester), 1606.59 (s, C=C), 1583.59 (s, C=C, Ph), 1178.43(s, C-O str.). 1H-NMR (400 MHz, CDCl$_3$): δ 8.23 (s, 1H, =CH), 7.82 (d, 1H, H-6' *J* = 7.32 Hz), 7.78 (s, 1H, H-2'), 7.41 (m, 2H, H-4', H-5'), 4.39 (q, 2H, OCH$_2$, *J* = 7.32 Hz), 2.42 (s, 3H, CH$_3$), 1.41 (t, 3H, OCH$_2$*CH$_3$*, *J* = 7.32 Hz). ^{13}C-NMR (100.40 MHz, CDCl$_3$): δ 162.53, 155.21, 139.06, 134.17, 131.63, 131.38, 129.12, 128.17, 115.51, 102.55, 62.63, 21.23, 14.11. DEPT - 135 (100.40 MHz, CDCl$_3$): δ 155.21, 134.17, 131.64, 129.11, 128.17, 62.64 (CH$_2$), 21.25 (CH$_3$), 14.12 (CH$_3$). Analysis calculated for C$_{13}$H$_{13}$NO$_2$ (215.25): C, 72.54; H, 6.09; N, 6.51; found: C, 73.14; H, 5.69; N, 5.39.

Ethyl 2-cyano-3-(4-hydroxyphenyl)-acrylate (3). Light yellow crystals, IR (KBr)υ$_{max}$ (cm^{-1}): 3257.55 (b, OH), 3161-2900 (C-H), 2231.49 (s, C≡N), 1731.96 (s, C=O, ester), 1587.31 (s, C=C), 1519.81 (s, C=C, Ph), 1089.71 (s, C-O str, ether). ^{1}H-NMR (400 MHz, CD$_3$OD): δ 8.20 (s, 1H, =CH), 7.96 (d, 2H, H-2', H-6', *J* = 9.16 Hz), 6.90 (d, 2H, H-3', H-5', *J* = 8.72 Hz), 4.33 (q, 2H, OCH$_2$, *J* = 7.32 Hz), 1.36 (t, 3H, OCH$_2$*CH$_3$*, *J* = 7.32 Hz). ^{13}C-NMR (100.40 MHz, CD$_3$OD): δ 164.51, 164.37, 155.89, 135.12, 133.64, 124.43, 117.32, 117.26, 116.84, 98.84, 63.30, 14.47. DEPT - 90 (100.40 MHz, CD$_3$OD): δ 155.90, 135.12, 117.26. DEPT - 135 (100.40 MHz, CD$_3$OD): δ 155.90, 136.12, 117.26, 63.30 (CH$_2$), 14.47 (CH$_3$). Analysis calculated for C$_{12}$H$_{11}$NO$_3$ (217.23): C, 66.35; H, 5.10; N, 6.45; found: C, 67.11; H, 4.94; N, 6.45.

Ethyl 2-cyano-3-(4-hydroxy-3-methoxyphenyl)-acrylate (4). Yellow crystals, IR (KBr) υ_{max} (cm^{-1}): 3375.20 (b, OH), 3128.32, 2931.60 (C-H), 2217.99 (s, C≡N), 1704.96 (s, C=O, ester), 1573.81 (s, C=C), 1508.23 (s, C=C, Ph), 1172.64 (s, C-O str, ether). ^{1}H-NMR (500 MHz, DMSO-d$_6$): δ 8.20 (s, 1H, =CH), 7.74 (s, ^{1}H, H-2'), 7.60 (d, 1H, H-6', J = 8.55 Hz), 6.94 (d, 1H, H-5', J = 8.00 Hz), 4.27 (q, 2H, -OCH$_2$, J = 6.90 Hz), 3.81 (s, 3H, OCH$_3$), 1.28 (t, 3H, OCH$_2$*CH$_3$*, J = 6.90 Hz). ^{13}C-NMR (100.40 MHz, CDCl$_3$): δ 162.65, 154.93, 152.78, 147.82, 127.20, 122.82, 116.65, 116.02, 114.05, 96.95, 61.94, 55.56, 14.07. DEPT - 135 (125 MHz, DMSO-d$_6$): δ 154.93, 127.20, 116.03, 114.04, 61.95 (CH$_2$), 55.576 (OCH$_3$), 14.07(CH$_3$). Analysis calculated for C$_{13}$H$_{13}$NO$_4$ (247.25): C, 63.15; H, 5.30; N, 5.66; found: C, 62.50; H, 3.75; N 5.29.

Ethyl 2-cyano-3-(2,4-dimethoxyphenyl)-acrylate (5). Orange crystals, IR (KBr) υ_{max} (cm^{-1}): 3110-2840 (C-H), 2214.13 (s, C≡N), 1714.60 (s, C=O, ester), 1610.45 (s, C=C), 1581.52 (s, C=C, Ph), 1126.35 (s, C-O str, ether). ^{1}H-NMR (500 MHz, CDCl$_3$): δ 8.70 (s, 1H, =CH), 8.40 (d, 1H, H-6', J = 8.60 Hz), 6.60 (d, 1H, H-5', J = 9.15 Hz), 6.44 (s, 1H, H-3'), 4.37 (q, 2H, OCH$_2$, J = 7.26 Hz), 3.89 (s, 6H, 2×OCH$_3$), 1.38 (t, 3H, OCH$_2$*CH$_3$*, J = 6.90 Hz). ^{13}C-NMR (125.00 MHz, CDCl$_3$): δ 165.63, 163.47, 161.32, 148.59, 131.00, 116.82, 113.92, 105.96, 98.01, 97.93, 62.10, 55.72, 55.63, 14.16. DEPT - 90 (125 MHz, CDCl$_3$): δ 148.58, 131.00, 105.96, 97.94. DEPT - 135 (100.40 MHz, CDCl$_3$): δ 148.59, 131.00, 105.96, 97.94, 62.10 (CH$_2$), 55.72 (OCH$_3$), 55.64 (OCH$_3$), 14.16 (CH$_3$). Analysis calculated for C$_{14}$H$_{15}$NO$_4$ (261.28): C, 64.36; H, 5.79; N, 5.36; found: C, 64.72; H, 5.85; N, 6.03.

Ethyl 2-cyano-3-(3-nitrophenyl)-acrylate (6). Off-white crystals, IR (KBr) υ_{max} (cm^{-1}): 3114-2870 (C-H), 2225.70 (s, C≡N), 1718.46 (s, C=O, ester),1606.59 (s, C=C), 1571.88 (s, C=C, Ph), 1529.45 (NO$_2$, sym. str.), 1473.51 (NO$_2$, asym. str.), 1207.36 (s, C-O str.). ^{1}H-NMR (400 MHz, CD$_3$OD): δ 8.91 (s, 1H, =CH), 8.47 (s, 1H, H-2'), 8.44 (d, 1H, H-4', J = 8.24 Hz), 8.38 (d, 1H, H-6', J = 8.24 Hz), 7.81 (t, 1H, H-5', J = 8.24 Hz), 4.40 (q, 2H, OCH$_2$, J = 7.32 Hz), 1.39 (t, 3H, OCH$_2$*CH$_3$*, J = 7.32 Hz). ^{13}C-NMR (100.40 MHz, DMSO-d$_6$): δ 163.18, 158.41, 146.87, 143.24, 141.29, 140.92, 137.51, 135.34, 125.46, 115.91, 73.06, 16.06. Analysis calculated for C$_{12}$H$_{10}$N$_2$O$_4$ (246.22): C, 58.54; H, 4.09; N, 25.99; found: C, 58.71; H, 3.58; N, 12.03.

Ethyl 2-cyano-3-(9-anthracenyl)-acrylate (7). Yellow crystals, IR (KBr) υ_{max} (cm^{-1}): 2981.74 (C-H), 2227.63 (s, C≡N), 1724.24 (s, C=O, ester), 1612.38 (s, C=C), 1060.78 (C-O). ^{1}H-NMR (500 MHz, CDCl$_3$): δ 9.32 (s, 1H, H-10'), 8.60 (s, 1H, =CH), 8.08 (d, 2H, H-1', H-8', J = 8.55 Hz), 7.97 (d, 2H, H-4', H-5', J = 8.60 Hz), 7.60 (d, 2H, H-2', H-7', J = 7.40 Hz), 7.56 (d, 2H, H-3', H-6', J = 8.05 Hz), 4.51 (q, 2H, OCH$_2$, J = 6.85 Hz), 1.49 (t, 3H, OCH$_2$*CH$_3$*, J = 6.90 Hz). ^{13}C-NMR (125 MHz, CDCl$_3$): δ 161.53, 155.42, 130.95, 130.83, 129.21, 128.95, 127.35, 125.71, 124.99, 124.54, 114.09, 112.77, 63.01, 14.17. DEPT - 90 (125 MHz, CDCl$_3$): δ 155.43, 130.83, 129.21, 127.35, 125.72, 124.54. DEPT - 135 (125 MHz, CDCl$_3$): δ 155.43, 130.83, 129.21, 127.35, 125.72, 124.54, 62.02 (CH$_2$), 14.18 (CH$_3$). Analysis calculated for C$_{20}$H$_{15}$NO$_2$ (301.35): C, 79.72; H, 5.02; N, 4.65; found: C, 79.38; H, 5.31; N, 5.16.

Ethyl 2-cyano-3-(4-N,N-dimethylaminophenyl)-acrylate (8). Yellow crystals, IR (KBr) υ_{max} (cm^{-1}): 3089.75 (=C-H), 2985.60 (C-H), 2208.34 (s, C≡N), 1704.96 (s, C=O, ester), 1612.38 (s, C=C), 1569.95 (s, C=C, Ph), 1168.78 (s, C-O str, ether). ^{1}H-NMR (400 MHz, CDCl$_3$): δ 8.08 (s, 1H, =CH), 7.94 (d, 2H, H-2', H-6', J = 9.16 Hz), 6.70 (d, 2H, H-3', H-5', J = 9.60 Hz), 4.34 (q, 2H, OCH$_2$, J = 7.32 Hz), 3.11 (s, 6H, 2×CH$_3$), 1.37 (t, 3H, OCH$_2$*CH$_3$*, J = 7.32 Hz). ^{13}C-NMR (100.40 MHz, CDCl$_3$): δ 164.27, 154.52, 153.48, 134.01, 119.28, 117.57, 111.41, 93.88, 61.84, 39.98, 14.24. Analysis calculated for C$_{14}$H$_{16}$N$_2$O$_2$ (244.30): C, 68.83; H, 6.60; N, 11.47 ; found : C, 69.43; H, 6.34; N, 11.27.

Ethyl 2-cyano-5-(4-N,N-dimethylaminophenyl)-penta-2,4-dienoate (9). Deep pink crystals, IR (KBr)υ_{max} (cm^{-1}): 3090-2905 (C-H), 2216.06 (s, C≡N), 1706.88 (s, C=O, ester), 1587.31 (s, C=C), 1548.73 (s, C=C, Ph), 1153.36 (C-O). ^{1}H-NMR (400 MHz, CDCl$_3$): δ 7.97 (d, 1H, H-3, J = 11.88 Hz), 7.49 (d, 2H, H-2', H-6', J = 9.12 Hz), 7.18 (d, 1H, H-5, J = 12.00 Hz), 7.11 (dd, 1H, H-4, J=11.88 Hz, 2.85Hz), 6.67 (d, 2H, H-3', H-5', J = 9.16 Hz), 4.31 (q, 2H, J = 7.36 Hz, OCH$_2$), 3.06 (s, 6H, 2×CH$_3$), 1.36 (t, 3H, J = 7.32 Hz, OCH$_2$*CH$_3$*). ^{13}C-NMR (100.40 MHz, CDCl$_3$): δ 163.19, 156.48, 152.23, 150.13, 130.68, 122.37, 117.94, 115.59, 111.65, 98.97, 61.62, 39.93, 14.08. DEPT - 90 (100.40 MHz, CD$_{13}$): δ 156.48, 150.14, 130.68, 117.94, 111.66. DEPT - 135 (100.40 MHz, CDCl$_3$): δ 156.48, 150.13, 130.68, 117.94, 111.66, 61.63 (CH$_2$), 39.93 (CH$_3$), 39.91 (CH$_3$), 14.09 (CH$_3$). Analysis calculated for C$_{16}$H$_{18}$N$_2$O$_2$ (270.33): C, 71.09; H, 6.71; N, 10.36; found: C, 71.46; H, 6.39; N, 11.25.

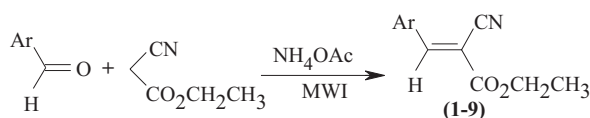**Table 1.** Antibacterial activity of the synthesised compounds (**1-9**)

Compounds	Zone of inhibition in mm(100 mg (dw)/ disc)				
	B. cereus	*S. aureus*	*V. cholerae*	*S. dysenteriae*	*S. typhi*
1	7	--	6.5	--	7
2	--	--	6	--	7.5
3	7	6	6	6	8
4	10	6	7	6.5	7
5	--	--	--	6.5	--
6	7	--	6	--	8
7	--	7	7	--	--
8	--	--	8	--	7.5
9	6.5	6.5	--	--	7.5
Ampicillin	20	12	17	30	24

-- = no inhibition; dw = dry weight

Antimicrobial screening. The synthesized compounds (**1-9**) were screened for antibacterial activity against five pathogenic organisms: *B. cereus* (BTCC 19), *S. aureus* (ATCC 6538), *V. cholerae, S. dysenteriae* (AE 14396) and *S. typhi* (AE 14612 (Table 1) and antifungal activity against two organisms: *A. flavus* and *S. cerevisiae* (Table 2). The disc diffusion method (Bauer *et al.,* 1966) and poisoned-food technique (Grover and Moore, 1962) were used for antibacterial and antifungal activities, respectively.

The tested compounds were dissolved in N, N-dimethyl formamide (DMF) to get a solution of 1 mg/mL. The inhibition zones were measured in

millimeters at the end of an incubation period of 48 h at (35±2)°C. DMF alone showed no inhibition. Nutrient agar (NA) and potato dextrose agar (PDA) were used as basal media to test the bacteria and fungi, respectively. Commercial antibacterial Ampicillin and antifungal Nystatin were also tested under similar conditions for comparison.

Scheme 1

Table 2. Antifungal activity of the synthesised compounds (**1-9**).

Compounds	% Inhibition of mycelial growth (100 μg(dw)/mL PDA)	
	A. flavus	*S. cerevisiae*
1	62	75*
2	71	80*
3	64	82*
4	71	87*
5	71	82*
6	62	85*
7	75*	90*
8	78*	85*
9	82*	87*
Nystatin	90	80

* = good inhibition; dw = dry weight

Results and Discussion

Various methods for the synthesis of α-cyanoacrylates have been developed and employed successfully in the light of green chemistry aspects. In the present work, nine α-cyanoacrylates derivatives were synthesised from several aromatic aldehydes and active methylene compound ethyl cyanoacetate in the presence of catalytic amount of NH_4OAc by modified Knoevenagel reaction using microwave irradiation, as indicated in Scheme 1 and Table 3. The corresponding reactions proceeded smoothly and in excellent yields (85-99%).
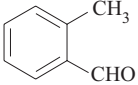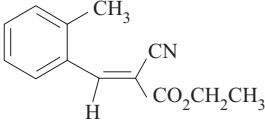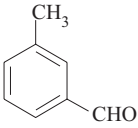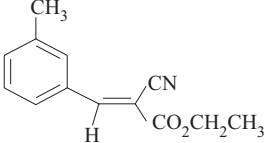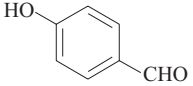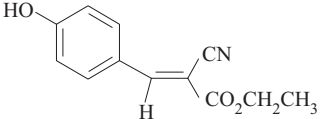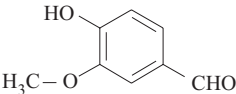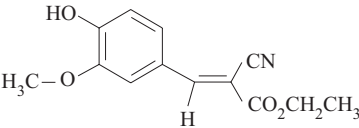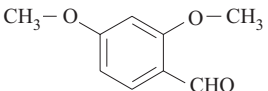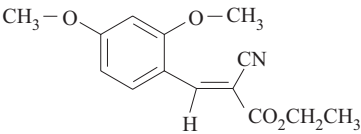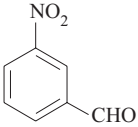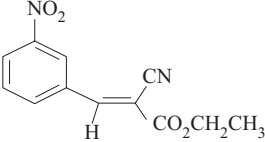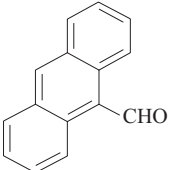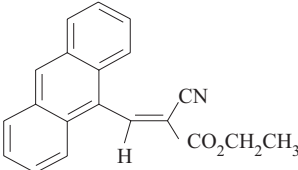
An important feature of this procedure is the survival of variety of functional groups such as nitro, chloro, amino and ether under the reaction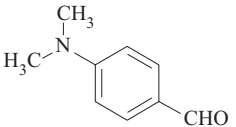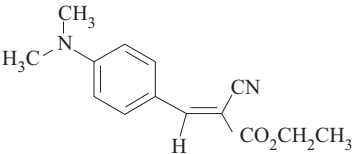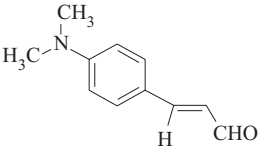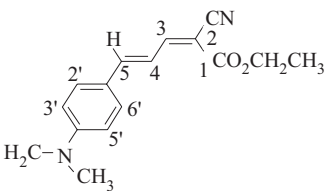 conditions. The structures of the products were established from their IR, ^{1}H NMR, ^{13}C NMR and elemental analyses. For example the IR spectrum of compound **9** displayed characteristic band absorption for C=O of ester functionality at 1706.88 cm^{-1}. The absorption band at

Table 3. Microwave assisted Knoevenagel reaction between various aldehydes and ethyl cyanoacetate

Compounds	Substrate	Product	Watt/ time (sec)	yield (%)	M.P. °C
1			320/60	76	55-56
2			320/30	82	85-86
3			160/30	98	166-167
4			160/20	99	110-111
5			160/40	97	140-141
6			320/60	98	134-135
7			160/40	97	174-175
8			320/50	94	121-122
9			160/40	98	181-182

2221.06 cm^{-1} was due to C=N stretch, while bands at 1587.31 cm^{-1}, 1548.73 cm^{-1} were assigned to the existence of C=C, aromatic ring and a band at 1153.36 cm^{-1} indicated the presence of C-O bond. The ^{1}H NMR spectrum of **9** exhibited two doublet signals resonated at δ 7.49 and at δ 6.77 with *J* value 9.12 Hz and 9.16 Hz were designated to four aromatic protons of H-2', H-6', H-3' and H-5'. A doublet signal at a lower field, δ 7.97 (*J* = 11.88 Hz) was attributed to H-3 of allylidene which was coupled with H-4 in a *trans*-relationship. Another doublet at δ 7.18 (*J* = 14.9 Hz) attributed to H-5 of the conjugated system which was coupled with H-4 in a *trans*-relationship. H-4 of the conjugated system appeared as a doublet of doublet centered at d 7.11 (*J* = 11.88 Hz, 2.85 Hz) coupled with H-3 and H-5. The ^{1}H NMR spectrum also displayed a two-proton quartet at δ 4.31 (*J* = 7.36 Hz) and a three proton triplet at δ 1.36 (*J* = 7.32 Hz) which were indicative for the presence of ester group (OCH$_2$CH$_3$) in the molecule. A six-proton singlet displayed at δ 3.06 attributed to –N(CH$_3$)$_2$ group. The ^{13}C–NMR spectrum of compound **9** showed the presence of thirteen signals attributed to sixteen carbons corresponding molecular formula C$_{16}$H$_{18}$N$_2$O$_2$. The spectrum displayed a downfield peak at δ 163.19 was assigned for C=O of ester functionality. The peaks at δ 115.59, 98.97, 61.62, 39.93, 14.08 were due to CN and =C<, OCH$_2$, –N(CH$_3$)$_2$ and CH$_3$ groups. The peaks at δ 156.48, 152.23, 150.13, 130.68, 122.37, 117.94, 111.6 were for the remaining carbons. The DEPT–90 spectrum of compound **9** showed peaks at δ 156.48, 150.14, 130.68, 117.94, 111.66 attributed to seven methine carbons (CH). Two methyl (CH$_3$) carbons appeared at δ 39.67 and 39.65. The DEPT-135 spectra of compound **9** displayed peaks at δ 156.48, 150.13, 130.68, 117.94, 111.66 attributed to seven methine carbons (CH). The-N(CH$_3$)$_2$ and CH$_3$ carbons appeared at δ 39.93, 39.91, 14.09. The OCH$_2$ carbon appeared at δ 61.63 for CH$_2$ as a negative value. The micro-analytical data of the compound **9** is also in good agreement with the assigned structure. Similarly the peaks in ^{1}H-NMR and ^{13}C-NMR spectra of the rest compounds were in accordance with the assigned structures.

Amongst the compounds **1-9** screened for antimicrobial activity, compound **4** showed the highest activity against *B. cereus*. Most of the compounds showed good to moderate antimicrobial activities and a few of them were unable to show inhibition for some pathogens. As far as antifungal activity is concerned, all compounds showed good to excellent activity against both of the fungi. All compounds except **1** and **2** exhibited even stronger activity than Nystatin against *S. cerevisiae.*

Conclusion

In this work, the synthesis of α-cyanoacrylates by microwave irradiation has been demonstrated using NH$_4$OAc under and solvent free condition. The advantages of this method are high yields, relatively short reaction times, low cost, simple experimental and isolation procedures, and in agreement with the green chemistry protocols. The activity data obtained during the study will be certainly useful to go for further research for drug designing and synthesising α-cyanoacrylates derivatives.

Acknowledgment

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