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(54) Title: CUCN-MEDIATED ONE POT PRODUCTION OF CINNAMONITRILE DERIVATIVES

(57) Abstract: The present invention discloses a cheaper and practical protocol for the construction of o-cyanocinnamionitrile and their structural analogues that proceeds with good yields in a single step using CuCN as the only reagent.

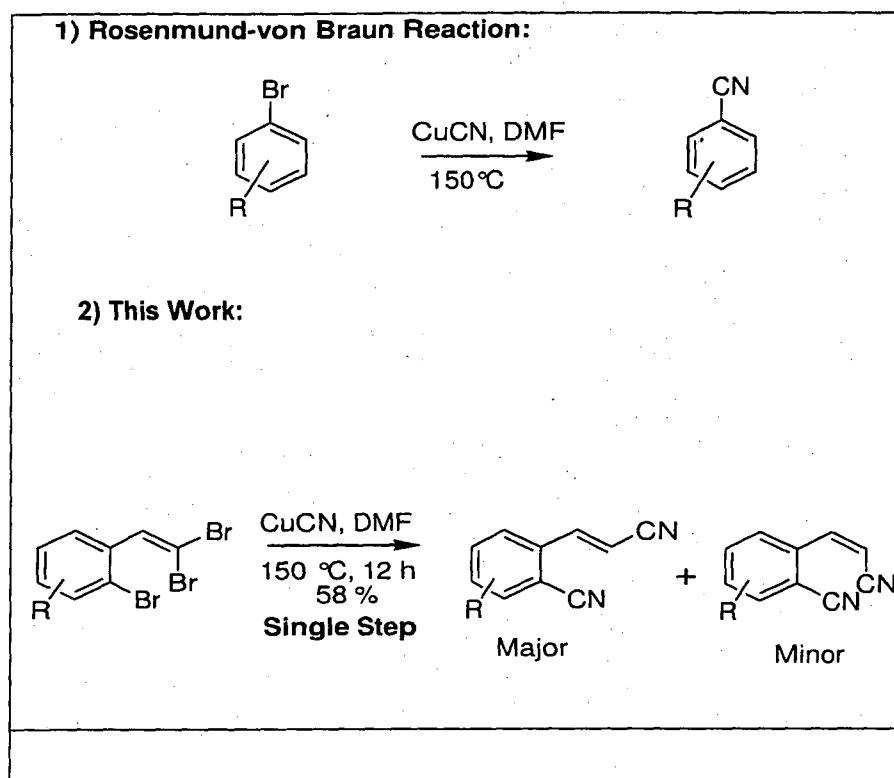


## CUCN - MEDIATED ONE POT PRODUCTION OF CINNAMONITRILE DERIVATIVES

### FIELD OF INVENTION

The present invention relates to a cheaper and practical protocol for the preparation of compounds of formula A, its isomers and their structural analogues in a one pot and single step via hydrocyanation reaction of compound of general formula I with good yields.

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### BACKGROUND OF INVENTION & DESCRIPTION OF PRIOR ART

Aryl nitriles can be prepared by the cyanation of aryl halides with an excess of copper(I) cyanide in a polar high-boiling solvent such as DMF, nitrobenzene, or pyridine at reflux temperature using Rosenmund-von Braun Reaction.

Alpha beta unsaturated nitriles are versatile reagents which have been used extensively in the synthesis of heterocycle compounds. Synthesis of cinnamonnitrile by treating benzaldehyde with acetonitrile in presence of alkali is disclosed in Organic Syntheses, Coll. Vol. 7, p.108 (1990); Vol. 62, p.179 (1984).

An article titled "Efficient One-Pot Synthesis of 2-Amino-4H-chromenes Catalyzed by Ferric Hydrogen Sulfate and Zr-Based Catalysts of FI" published in Synthesis and Reactivity in Inorganic, Metal-Organic, and Nano-Metal Chemistry, Volume 41, Issue 9, 2011, wherein, the preparation of  $\alpha$ -

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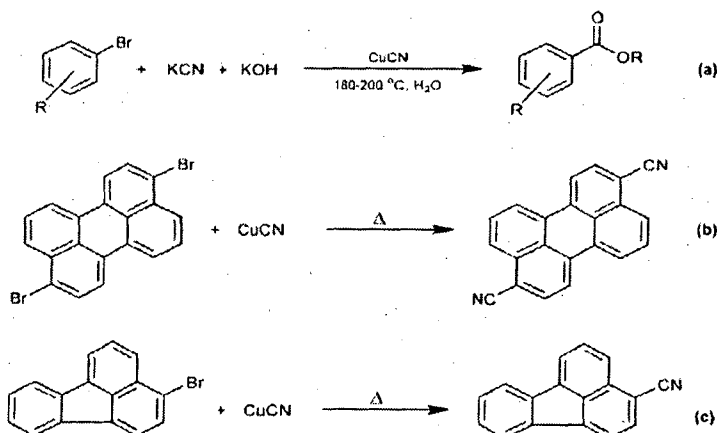
cyanocinnamitrile is carried by the condensation of aldehyde with malononitrile to afford  $\alpha$ -cyanocinnamitrile derivatives by Knoevenagel addition reaction.

Decarboxylation of E-3-phenyl-2-cyanopropenoic acid in dimethyl sulfoxide containing sodium bicarbonate, lithium chloride, and water in molar excess afforded, with high stereospecificity, Z-cinnamitrile is disclosed in an article titled "Stereochemistry of the dealkoxycarbonylation of methyl  $\alpha$ -cyanocinnamate and of the decarboxylation of the corresponding cyano acid: a facile stereoselective route to Z-cinnamitrile" Tetrahedron Letters, Volume 24, Issue 36, 1983, Pages 3835–3838.

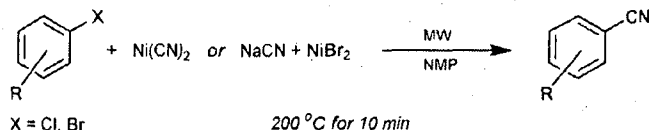
Article titled, "HYDROCYANATION OF ALKENES AND ALKYNES" by T. V. (BABU) RAJANBABU reports that Hydrogen cyanide itself is relatively unreactive, but in the presence of a catalyst HCN adds to carbonyl compounds, alkenes, and alkynes, offering a direct and economical way to such organonitrile intermediates.

In a scientific article titled, "The preparation of aryl nitriles" by DIANDRA M. RUDZINSKI, NICHOLAS E. LEADBEATER in *chimica oggi/Chemistry Today* - vol. 29 n. 4 July/August 2011, reports the process of CYANATION through Modern methodologies by using catalytic amounts of transition-metal complexes, together with less toxic cyanide sources making chemistry more efficient, applicable and safer.

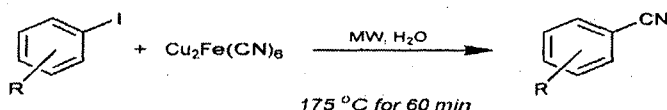
*Scheme 1. Historical perspective on the cyanation of aryl halides – (a) Rosenmund; (b) Pongrantz; (c) von Braun.*



Scheme 4. Nickel-mediated cyanation and tandem halide-exchange / cyanation approach to the conversion of aryl halides to nitriles.



Scheme 6. Use of  $\text{Cu}_2\text{Fe}(\text{CN})_6$  as both catalyst and cyanide source for cyanation of aryl halides.



Article titled, "Mechanistic Insights into the Hydrocyanation Reaction" by Laura Bini in page 121, reports the hydrocyanation of styrene in presence of  $\text{CuCN}$  giving 78% conversion and 88% selectivity with a ratio of 13:87 for linear and branched nitriles and a yield of 73-80%.

cinnamonnitrile and their esters have wide range of industrial applications for example in cosmetic industry.

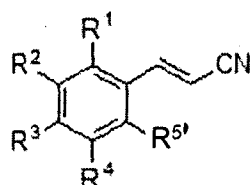
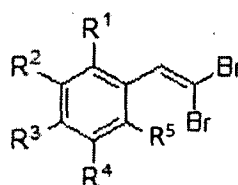
Although few inventions have been made in the synthesis of cinnamonnitrile they require multiple steps with consumption of large quantities of hazardous chemicals with less efficiency and narrow substrate scope. Therefore, there is a need in the art to provide an alternate and effective synthesis to provide a library of cinnamonnitrile. Further it would be desirable have a process of synthesis of cinnamonnitriles by a convenient single step one pot process. Specifically, it would be desirable to provide a simple process for the conversion of dibromovinyl benzenes to their corresponding cinnamonnitriles.

## OBJECTS OF INVENTION

The main object of the present invention is to provide an effective one pot synthesis, single step for the preparation of cinnamonnitrile derivatives via hydrocyanation reaction with good yields.

**SUMMARY OF INVENTION:**

In an embodiment of the present invention a one pot, single step process for the preparation of  
 5 compound of formula A and its isomers, starting from compounds of formula I,

**Formula A****Formula I**

10 Wherein,

$R^1$  is hydrogen;

$R^2$  is selected from H, OMe, OTs, OBn;

$R^3$  is selected from H, OMe, OTs, OBn,  $\text{NO}_2$ ;

$R^4$  is selected from H, OMe, F;

15  $R^5$  is selected from H,  $\text{NO}_2$ , BR;

$R^{5'}$  is selected from H,  $\text{NO}_2$ , CN;

$R^2$  and  $R^3$  can together be selected as  $-\text{O}-\text{CH}_2-\text{O}-$ ;

comprising the steps of reacting compound of formula I with CuCN in DMF, under reflux in presence  
 20 of  $\text{N}_2$  atmosphere to obtain the desired compound of formula A in the range of 50-90% yield.

In another embodiment of the present invention, the said compound of formula I and CuCN are in the  
 ratio of 1:2 to 1:3.

25 In yet another embodiment of the present invention, isomers of compound of formula A are trans and  
 cis isomers in the ratio of 3:1 to 10:1.

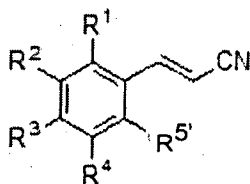
In yet another embodiment of the present invention, the reaction is carried out at a temperature ranging  
 from 140 to 160  $^\circ\text{C}$ .

In yet another embodiment of the present invention, the reaction is carried out for a time ranging from 10 to 15 hours.

### **DETAILED DESCRIPTION OF THE INVENTION:**

- 5 In accordance with the above, the instant invention provides one pot single step synthesis, of CuCN-mediated hydrocyanation reaction, for the preparation of cinnamitrile derivatives. The CuCN-mediated hydrocyanation reaction according to the invention essentially makes use of the conditions prescribed for Rosenmund-von Braun Reaction.
- 10 The process of the present invention is easier to adopt on industrial scale for preparation of library of cinnamitrile derivatives as it involves a one pot hydrocyanation reaction. The process of the instant invention is cost effective when compared to the existing methods as it involves CuCN, a very cheaper reagent, easy to maintain and perform at higher scales, showed remarkably broad substrate scope and good functional group tolerance and do not cause much effluent generation. The procedure tolerates a
- 15 series of functional groups, such as methoxyl, fluoro etc.

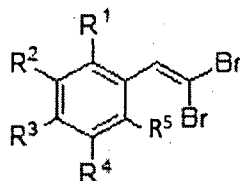
In an aspect of the invention, cinnamitrile derivative of formula (A) is represented as enlisted herein:



**Formula A**

- 20 Wherein,
- R<sup>1</sup> is hydrogen;
- R<sup>2</sup> is selected from H, OMe, OTs, OBn; (Ts = Tosyl, Bn = Benzyl)
- R<sup>3</sup> is selected from H, OMe, OTs, Obn, NO<sub>2</sub>;
- R<sup>4</sup> is selected from H, OMe, F;
- 25 R<sup>5'</sup> is selected from H, NO<sub>2</sub>, CN;
- R<sup>2</sup> and R<sup>3</sup> can together be selected as -O-CH<sub>2</sub>-O-;

In an aspect of the invention, the compound of Formula I is



**Formula I**

Wherein,

$R^1$  is hydrogen;

$R^2$  is selected from H, OMe, OTs, OBn;

10  $R^3$  is selected from H, OMe, OTs, OBn,  $NO_2$ ;

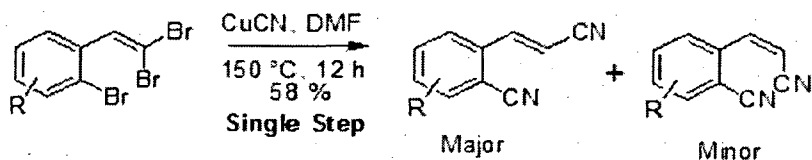
$R^4$  is selected from H, OMe, F;

$R^5$  is selected from H,  $NO_2$ , BR ;

$R^2$  and  $R^3$  can together be selected as  $-O-CH_2-O-$ ;

15 In a preferred embodiment, the invention discloses preparation of cinnamionitrile derivatives, which process comprises treating substituted 2,2-dibromovinyl benzene with CuCN in DMF at  $150^\circ C$  for 10-15 hrs to obtain substituted cinnamionitrile derivative in a single step. The bromo vinyl benzene and CuCN are used in the ratio of 1:2 to 1:3 in the process described herein. The reaction is shown in scheme below:

20



Wherein, R is selected from F, H, Br, OMe, OTs, OBn,  $NO_2$ ,  $-O-CH_2-O-$ .

Accordingly, in a preferred embodiment, a typical procedure is disclosed for the preparation of 3-(2-cyano-4,5-dimethoxyphenyl)acrylonitrile by refluxing a stirred solution of 1-bromo-2-(2,2-

5 dibromovinyl)-4,5-dimethoxybenzene or 1-bromo-2-ethynyl-4,5-dimethoxybenzene in DMF with the addition of CuCN under N<sub>2</sub> atmosphere for 12 h (monitored by TLC). The reaction mixture is cooled to room temperature followed by workup of the reaction mixture to obtain crude products which can be purified by column chromatography to get 3-(2-cyano-4,5-dimethoxyphenyl)acrylonitrile in 63 % yield.

The present invention discloses preparation of a library of compounds of cinnamionitrile derivatives by employing the process of the present invention. The reactants and the compounds obtained by the process of the invention is described herein below in tables 1 .

| Table 1  |                |                |                 |                |                 |                 |             |                        |
|--|----------------|----------------|-----------------|----------------|-----------------|-----------------|-------------|------------------------|
| <p style="text-align: center;">Single Step</p> |                |                |                 |                |                 |                 |             |                        |
| S.no   | Reactants      |                |                 |                |                 | Products        |             | Yield <sup>a</sup> (%) |
|  | R <sup>1</sup> | R <sup>2</sup> | R <sup>3</sup>  | R <sup>4</sup> | R <sup>5</sup>  | R <sup>5'</sup> | (trans/cis) |                        |
| 1  | H              | H              | H               | H              | H               | H               | 4/1         | 53                     |
| 2  | H              | H              | OMe             | H              | H               | H               | 3/1         | 52                     |
| 3  | H              | H              | NO <sub>2</sub> | H              | H               | H               | 4/1         | 86                     |
| 4  | H              | H              | H               | H              | NO <sub>2</sub> | NO <sub>2</sub> | 4/1         | 88                     |
| 5  | H              | H              | H               | H              | Br              | CN              | 10/1        | 56                     |
| 6  | H              | OMe            | H               | H              | Br              | CN              | 4/1         | 73                     |
| 7  | H              | OMe            | OMe             | H              | Br              | CN              | 3/1         | 82                     |
| 8  | H              | OMe            | H               | OMe            | Br              | CN              | 3/1         | 71                     |
| 9  | H              | OMe            | OMe             | OMe            | Br              | CN              | 4/1         | 73                     |
| 10   | H              | OBn            | OMe             | H              | Br              | CN              | 4/1         | 57                     |
| 11   | H              | OBn            | OBn             | H              | Br              | CN              | 4/1         | 71                     |
| 12   | H              | OTs            | OMe             | H              | Br              | CN              | 4/1         | 52                     |



|   |   |                        |   |   |    |    |     |    |
|---|---|------------------------|---|---|----|----|-----|----|
| 13  | H | H                      | H | F | Br | CN | 3/1 | 63 |
| 14  | H | -O-CH <sub>2</sub> -O- | H | H | Br | CN | 3/1 | 71 |
| <sup>a</sup> Combined isolated yield after column chromatographic purification. |   |                        |   |   |    |    |     |    |

## EXAMPLES

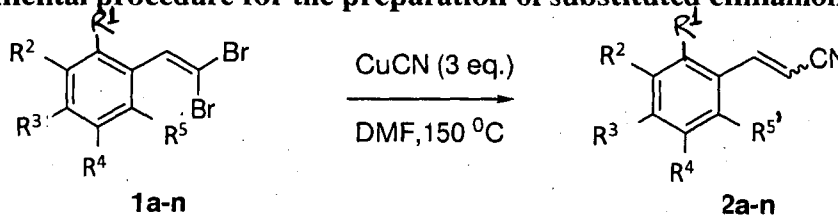
The following examples, which include preferred embodiments, will serve to illustrate the practice of this invention, it being understood that the particulars shown are by way of example and for purpose of illustrative discussion of preferred embodiments of the invention

### 1. General Information

Solvents were purified and dried by standard procedures before use; petroleum ether of boiling range 60–80 °C was used. Melting points are uncorrected. Infrared spectra were recorded on Shimadzu FTIR-8400 spectrometer. <sup>1</sup>H NMR and <sup>13</sup>C NMR were recorded on Bruker AV-200, AV-400 & AV-500 NMR spectrometers, respectively. Elemental analysis was carried on a Carlo Erba CHNS-O analyzer. Purification was done using column chromatography (230-400 mesh).

### 2. Experimental Section

A general experimental procedure for the preparation of substituted cinnamitrile (2a-n)



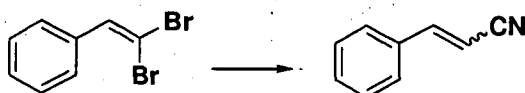
**Scheme 1: Synthesis of substituted cinnamitrile (2a-n)**

The dibromoolefines **1(a-n)** (1 mmol) was taken in dry DMF (10 mL) and CuCN (3 mmol) was added to it and the entire solution refluxed under N<sub>2</sub> for 12 h (monitored by TLC). The reaction mixture was then cooled to room temperature, and diluted with water (30 mL) and EtOAc (25 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organic extracts were washed with brine and dried over anhyd. Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced

pressure to give crude products which was purified by column chromatography [silica gel (230-400 mesh) and petroleum ether: EtOAc (7:3) as an eluent] to give substituted cinnamitrile (a-i) in 73-82% yield.

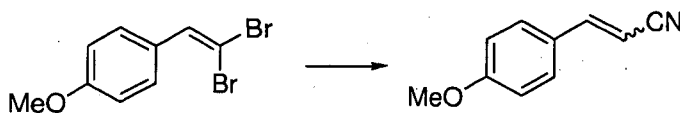
### 5 3. Experimental Data

#### Cinnamitrile (2a)



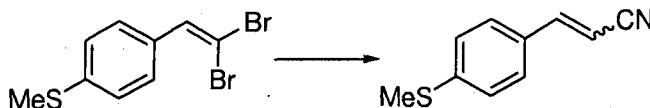
**Yield:** 72%; **IR** ( $\text{CHCl}_3$ ,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}}$  965, 1030, 1107, 1244, 1301, 1601, 1624, 2217;  **$^1\text{H}$  NMR** (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  5.44 (d,  $J = 12.2$  Hz, 0.23H) *Z*-isomer, 5.87 (d,  $J = 16.6$  Hz, 1H) *E*-isomer, 7.11 (d,  $J = 12.2$  Hz, 0.42H) *Z*-isomer, 7.40-7.47 (m, 7H), 7.80 (dd,  $J = 2.4, 3.6$  Hz, 0.5H), 7.87;  **$^{13}\text{C}$ -NMR** (50 MHz,  $\text{CDCl}_3$ ):  $\delta$  94.9, 96.3, 117.8, 127.2, 128.1, 128.7, 128.8, 128.9, 129.2, 130.7, 131.0, 133.4, 148.3, 150.2; **Analysis:**  $\text{C}_9\text{H}_7\text{N}$  requires C, 83.69; H, 5.46; N, 10.84; found: C, 83.49; H, 5.63; N, 10.24 %.

#### 3-(4-methoxyphenyl)acrylonitrile (2b)



**Yield:** 78%; **IR** ( $\text{CHCl}_3$ ,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}}$  985, 940, 1041, 1134, 1296, 1454, 1512, 1590, 2219;  **$^1\text{H}$  NMR** (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  3.84 (s, 3H), 3.85 (s, 3H), 5.28 (d,  $J = 12.2$ , 1H) *Z*-isomer, 5.70 (d,  $J = 16.5$  Hz, 0.82H) *E*-isomer, 6.87-7.05 (m, 5H), 7.26 (d,  $J = 3.0$ , 1H), 7.38 (d,  $J = 8.84$ , 2H), 7.78 (d,  $J = 8.84$ , 2H);  **$^{13}\text{C}$ -NMR** (50 MHz,  $\text{CDCl}_3$ ):  $\delta$  55.1, 55.2, 91.6, 93.1, 114.0, 114.3, 126.1, 126.3, 128.8, 130.7, 147.7, 149.6, 161.4, 161.8; **Analysis:**  $\text{C}_{10}\text{H}_9\text{NO}$  requires C, 75.45; H, 5.70; N, 8.80; found: C, 75.65; H, 5.47; N, 8.71 %.

#### 3-(4-(methylthio)phenyl)acrylonitrile (2c)



**Yield:** 74%; **IR** ( $\text{CHCl}_3$ ,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}}$  752, 992, 1090, 1215, 1279, 1297, 1520, 2219;  **$^1\text{H}$  NMR** (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.50 (s, 3H), 5.35 (d,  $J = 12.0$  Hz, 0.48H) *Z*-isomer, 5.80 (d,  $J = 16.6$  Hz, 1H) *E*-

isomer, 7.03 (d,  $J = 12.0$  Hz, 0.48H) *Z*-isomer, 7.18-7.36 (m, 6H), 7.72 (d,  $J = 8.4$  Hz, 1H);  $^{13}\text{C-NMR}$  (50 MHz,  $\text{CDCl}_3$ ):  $\delta$  14.6, 93.3, 94.7, 117.3, 118.0, 124.6, 125.3, 125.5, 127.4, 129.1, 129.6, 129.7, 142.9, 143.1, 147.5, 149.4; **Analysis:**  $\text{C}_{10}\text{H}_9\text{NS}$  requires C, 68.53 ; H, 5.18 ; N, 7.99, S, 18.3 found: C, 68.69 ; H, 5.18 ; N, 7.56%.

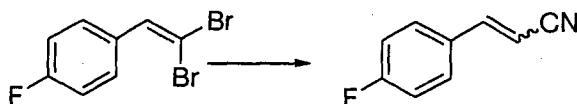
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### 3-(4-(trifluoromethyl)phenyl)acrylonitrile (2d)



**Yield:** 73%; **IR** ( $\text{CHCl}_3$ ,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}}$  816, 921, 1045, 1276, 1296, 2116;  $^1\text{H NMR}$  (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  5.60 (d,  $J = 12.1$  Hz, 0.82H) *Z*-isomer, 5.98 (d,  $J = 16.6$  Hz, 1H) *E*-isomer, 7.18 (d,  $J = 12.1$  Hz, 0.82H) *Z*-isomer, 7.43 (d,  $J = 16.6$  Hz, 1H) *E*-isomer, 7.57 (d,  $J = 8.8$  Hz 2H), 7.69 (t,  $J = 6.57$  Hz, 3H), 7.91 (d,  $J = 8.8$  Hz 2H);  $^{13}\text{C-NMR}$  (50 MHz,  $\text{CDCl}_3$ ):  $\delta$  97.9, 99.2, 116.4, 117.1, 102.8, 125.6, 125.7, 125.8, 125.9, 126.0, 126.1, 127.5, 129.0, 136.6, 146.8, 148.5; **Analysis:**  $\text{C}_{10}\text{H}_6\text{F}_3\text{N}$  requires C, 60.92 ; H, 3.07 ; F, 28.91; N, 7.01 found: C, 60.71 ; H, 3.11 ; N, 6.96%.

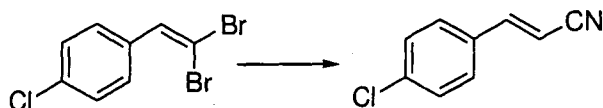
### 15 3-(4-fluorophenyl)acrylonitrile (2e)



**Yield:** 76%; **IR** ( $\text{CHCl}_3$ ,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}}$  814, 912, 1011, 1064, 1246, 1512, 2219;  $^1\text{H NMR}$  (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  5.44 (d,  $J = 12.2$  Hz, 1H), *Z*-isomer, 5.80 (d,  $J = 16.1$  Hz, 0.84H) *E*-isomer, 7.05-7.17 (m, 5), 7.36 (d,  $J = 16.1$  Hz, 0.84H) *E*-isomer, 7.41-7.48 (m, 2H), 7.79-7.86 (m, 2H);  $^{13}\text{C-NMR}$  (50 MHz,  $\text{CDCl}_3$ ):  $\delta$  97.5, 115.4, 117.0, 128.0, 130.8, 146.2, 162.1 **Analysis:**  $\text{C}_9\text{H}_6\text{FN}$  requires C, 73.46; H, 4.11; F, 12.91; N, 9.52; found: C, 73.62; H, 4.32; N, 9.42%.

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### 3-(4-chlorophenyl)acrylonitrile (2f)



**Yield:** 81%; Colorless oil; **IR** ( $\text{CHCl}_3$ ,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}}$  772, 915, 1052, 1124, 1206, 1512, 2121;  $^1\text{H NMR}$  (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  5.83 (d, 1H,  $J = 16.5$  Hz), 7.3(d,  $J = 16.5$  Hz, 1H), 7.38 (s, 4H;  $^{13}\text{C-NMR}$  (50

25

MHz,  $\text{CDCl}_3$ ):  $\delta$  97.1, 117.5, 128.4, 129.3, 131.9, 137.2, 148.8; **Analysis:**  $\text{C}_9\text{H}_6\text{ClN}$  requires C, 66.07; H, 3.70; Cl, 21.6; N, 8.56; found: C, 66.21; H, 6.62; N, 8.32%.

### 3-(2-nitrophenyl)acrylonitrile (2g)



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**Yield:** 88%; **IR** ( $\text{CHCl}_3$ ,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}}$  767, 1249, 1604, 1575, 1673, 2118;  **$^1\text{H}$  NMR** (200 MHz,  $\text{CDCl}_3$ ): **Z-isomer**  $\delta$  5.72 (d,  $J$  = 11.7 Hz, 1H), 7.61-7.90 (m, 4H), 8.22 (d,  $J$  = 8.0 Hz, 1H);  **$^{13}\text{C}$ -NMR** (50 MHz,  $\text{CDCl}_3$ ):  $\delta$  101.2, 115.7, 125.2, 129.5, 130.6, 130.9, 134.2, 146.3, 147.2; **E-isomer**;  $\delta$  5.85 (d,  $J$  = 16.4 Hz, 1H), 7.56-7.76 (m, 3H), 7.96 (d,  $J$  = 16.4 Hz, 1H), 8.13 (dd,  $J$  = 1.5, 8.09 Hz, 1H);  **$^{13}\text{C}$ -NMR** (50 MHz,  $\text{CDCl}_3$ ):  $\delta$  101.7, 116.7, 125.3, 128.6, 129.7, 131.2, 133.9, 146.4, 147.5; **Analysis:**  $\text{C}_9\text{H}_6\text{N}_2\text{O}_2$  requires C, 66.07; H, 3.47; N, 16.09; found: C, 66.03; H, 3.13; N, 16.89%.

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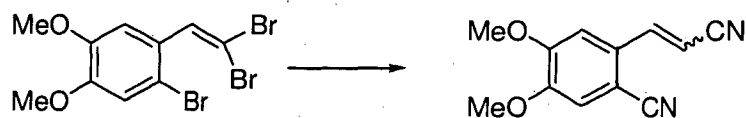
### 3-(4-nitrophenyl)acrylonitrile (2h)



**Yield:** 86%; **IR** ( $\text{CHCl}_3$ ,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}}$  736, 853, 1249, 1604, 1546, 1665, 2116;  **$^1\text{H}$  NMR** (200 MHz,  $\text{CDCl}_3$ ): **Z-isomer**  $\delta$  5.75 (d,  $J$  = 11.6 Hz, 1H), 7.32 (d,  $J$  = 11.6 Hz, 1H), 7.56 (d,  $J$  = 8.1 Hz, 1H), 8.14 (d,  $J$  = 8.1 Hz, 1H);  **$^{13}\text{C}$ -NMR** (50 MHz,  $\text{CDCl}_3$ ):  $\delta$  99.2, 117.0, 122.2, 127.3, 141.3, 146.1, 147.6, 134.2, 146.3, 147.2; **E-isomer**;  $\delta$  6.05 (d,  $J$  = 16.6 Hz, 1H), 7.47 (d,  $J$  = 16.6 Hz, 1H), 7.63 (d,  $J$  = 8.8 Hz, 2H), 8.28 (d,  $J$  = 8.8 Hz, 2H);  **$^{13}\text{C}$ -NMR** (50 MHz,  $\text{CDCl}_3$ ):  $\delta$  101.2, 116.7, 124.4, 128.1, 139.2, 147.6, 149.2; **Analysis:**  $\text{C}_9\text{H}_6\text{N}_2\text{O}_2$  requires C, 66.07; H, 3.47; N, 16.09; found: C, 66.012; H, 3.32; N, 16.32%.

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### 2-(2-cyanovinyl)-4,5-dimethoxybenzonitrile (2i)

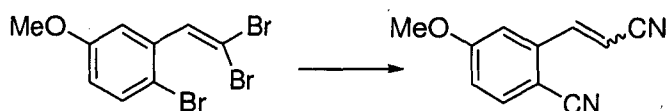


**Yield:** 82%; **IR** ( $\text{CHCl}_3$ ,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}}$  886, 927, 960, 1037, 1290, 1488, 1503, 2123;  **$^1\text{H}$  NMR** (200 MHz,  $\text{CDCl}_3$ ): **E-isomer**;  $\delta$  3.95 (s, 3H), 3.98 (s, 3H), 5.98 (d,  $J$  = 16.5 Hz, 1H), 7.01 (s, 1H), 7.09 (s,

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1H), 7.65 (d,  $J = 16.5$  Hz, 1H);  $^{13}\text{C-NMR}$  (50 MHz,  $\text{CDCl}_3$ ):  $\delta$  54.3, 93.7, 102.2, 106.7, 112.6, 115.1, 116.1, 128.2, 142.9, 149.2, 150.8;  $^1\text{H NMR}$  (200 MHz,  $\text{CDCl}_3$ ): **Z-isomer**;  $\delta$  3.96 (s, 3H), 4.02 (s, 3H), 5.60 (d,  $J = 12.1$  Hz, 1H), 7.10 (s, 1H), 7.46 (d,  $J = 12.1$  Hz, 1H), 7.99 (s, 1H);  $^{13}\text{C-NMR}$  (50 MHz,  $\text{CDCl}_3$ ):  $\delta$  56.3, 96.9, 106.0, 109.6, 114.1, 116.8, 130.3, 143.6, 150.9, 152.6; **Analysis**:  $\text{C}_{12}\text{H}_{10}\text{N}_2\text{O}_2$  requires C, 67.28; H, 4.71; N, 13.08; found: C, 67.79; H, 4.12; N, 13.46%.

### 2-(2-cyanovinyl)-4-methoxybenzonitrile (2j)



**Yield**: 73%; **IR** ( $\text{CHCl}_3$ ): 547, 709, 767, 833, 856, 1023, 1247, 1597, 2211  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$  (200 MHz,  $\text{CDCl}_3$ ): **Z-isomer**;  $\delta$  3.94 (s, 3H), 5.70 (d,  $J = 12.13$  Hz, 1H), 7.01 (dd,  $J = 2.53, 8.72$  Hz, 1H), 7.49 (d,  $J = 12.13$  Hz, 1H), 7.63 (d,  $J = 8.72$  Hz, 1H), 7.86 (d,  $J = 2.53$  Hz, 1H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  55.80, 99.94, 104.95, 112.23, 116.10, 116.83, 117.88, 134.57, 137.77, 144.00, 162.91;  $^1\text{H NMR}$  (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  3.91 (s, 3H), 6.07 (d,  $J = 16.54$  Hz, 1H), 7.00 (dd,  $J = 2.53, 8.59$  Hz, 1H), 7.09 (d,  $J = 2.53$  Hz, 1H), 7.62 (d,  $J = 16.54$  Hz, 1H), 7.64 (d, 8.59 Hz, 1H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  55.79, 101.60, 104.12, 111.95, 116.67, 116.86, 135.25, 137.77, 145.53, 162.94; **Analysis**:  $\text{C}_{11}\text{H}_8\text{N}_2\text{O}_1$  requires C 71.73, H 4.38, N 15.21, found C 70.18, H 4.16, N 14.97%.

### 6-(2-cyanovinyl)-2,3,4-trimethoxybenzonitrile (2k)



**Yield**: 71%; **IR** ( $\text{CHCl}_3$ ,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}}$  791, 845, 964, 1052, 1239, 1412, 1472, 1533, 1664, 2117;  $^1\text{H NMR}$  (200 MHz,  $\text{CDCl}_3$ ): **Z-isomer**;  $\delta$  3.93 (s, 3H), 4.00 (s, 3H), 4.07 (s, 3H), 5.64 (d,  $J = 12.2$ , 1H), 7.44 (d,  $J = 12.2$ , 1H), 7.71 (s, 1H);  $^{13}\text{C-NMR}$  (50 MHz,  $\text{CDCl}_3$ ):  $\delta$  56.4, 61.5, 61.8, 98.4, 101.1, 106.5, 114.1, 116.6, 132.0, 143.5, 143.7, 155.9, 157.3;  $^1\text{H NMR}$  (200 MHz,  $\text{CDCl}_3$ ): **E-isomer**;  $\delta$  3.91 (s, 3H), 3.96 (s, 3H), 4.06 (s, 3H), 6.03 (d,  $J = 16.5$ , 1H), 7.81 (s, 1H), 7.59 (d,  $J = 16.5$ , 1H);  $^{13}\text{C-NMR}$  (50 MHz,  $\text{CDCl}_3$ ): 56.3, 61.1, 61.7, 100.3, 104.6, 114.1, 116.9, 132.2, 143.6, 145.3, 155.8, 157.4; **Analysis**:  $\text{C}_{13}\text{H}_{12}\text{N}_2\text{O}_3$  requires C, 63.93; H, 4.95; N, 11.47; found: requires C, 63.71; H, 4.51;

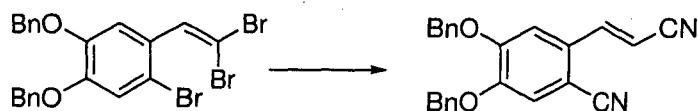
2-(2-cyanovinyl)-4,6-dimethoxybenzonitrile (2l)



5 **Yield:** 71%; **IR** ( $\text{CHCl}_3$ ,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}}$  791, 845, 964, 1052, 1215, 1239, 1240, 1412, 1472, 1533, 1664, 2970, 3332, 3451;  **$^1\text{H}$  NMR** (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  3.90 (s, 3H), 3.94 (s, 3H), 6.09 (d,  $J = 16.5$ , 1H), 6.52 (s, 1H), 6.64 (s, 1H), 7.61, (d,  $J = 16.5$ , 1H);  **$^{13}\text{C}$ -NMR** (50 MHz,  $\text{CDCl}_3$ ):  $\delta$  55.9, 56.3, 94.6, 100.1, 101.9, 103.2, 114.4, 116.7, 138.7, 145.8, 163.6, 164.2; **Analysis:**  $\text{C}_{12}\text{H}_{10}\text{N}_2\text{O}_2$  requires C, 67.28 ; H, 4.71 ; N, 13.08; found: requires C, 67.61 ; H, 4.42 ; N, 13.15.

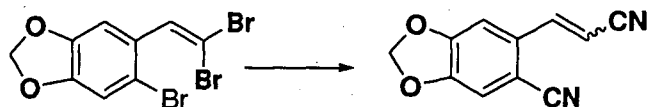
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4,5-bis(benzyloxy)-2-((E)-2-cyanovinyl)benzonitrile (2m)



**Yield:** 71%; **IR** ( $\text{CHCl}_3$ ,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}}$  752, 991, 1091, 1244, 1279, 1296, 1454, 1462, 1512, 1590, 2219;  **$^1\text{H}$  NMR** (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  5.21 (s, 2H), 5.29 (s, 2H), 5.54 (d,  $J = 12.2$ , 1H), 7.13 (s, 1H), 7.32-7.41 (m, 9H), 7.48, (d,  $J = 7.3$ , 2H), 8.02, (s, 1H);  **$^{13}\text{C}$ -NMR** (50 MHz,  $\text{CDCl}_3$ ):  $\delta$  71.0, 71.2, 97.0, 106.1, 111.7, 116.9, 127.2, 127.6, 128.4, 128.5, 128.7, 128.8 130.4, 135.5, 143.6, 150.5 152.4, ; **Analysis:**  $\text{C}_{24}\text{H}_{18}\text{N}_2\text{O}_2$  requires C, 68.67, ; H, 4.95 ; N, 7.65; found: requires C, 68.54 ; H, 4.85 ; N, 7.12..

20 6-(2-cyanovinyl)benzo[d][1,3]dioxole-5-carbonitrile (2n)



**Yield:** 71%; **IR** ( $\text{CHCl}_3$ ,  $\text{cm}^{-1}$ ):  $\nu_{\text{max}}$  791, 841, 962, 1034, 1245, 1412, 2217;  **$^1\text{H}$  NMR** (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  5.62 (d,  $J = 11.9$ , 1H), 6.17 (s, 2H), 7.10 (s, 1H), 7.45, (d,  $J = 11.9$ , 1H) 7.84, (s, 1H);  **$^{13}\text{C}$ -NMR** (50 MHz,  $\text{CDCl}_3$ ):  $\delta$  98.08, 103.1, 107.6, 11.8, 116.2, 116.5, 129.9, 132.4, 143.3, 149.7, 151.9; **Analysis:**  $\text{C}_{11}\text{H}_6\text{N}_2\text{O}_2$  requires C, 66.67 ; H, 3.05; N, 14.14; found: requires C, 66.61 ; H, 3.49; N,

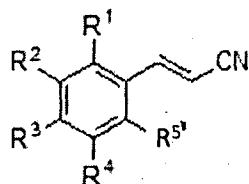
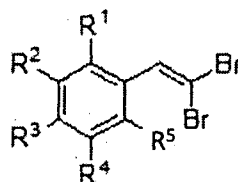
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**Advantages of Invention:**

1. One pot process
2. Cheaper, safe and efficient
3. O-cyanocinnamionitrile and their esters have wide range of industrial applications for example in cosmetic industry.
4. Broad substrate scope and good functional group tolerance
5. Less amount of effluent generate

**We claim:**

1. A one pot, single step process for the preparation of compound of general formula A and its isomers, starting from compounds of general formula I,

**Formula A****Formula 1**

Wherein,

$R^1$  is hydrogen;

$R^2$  is selected from H, OMe, OTs, OBn;

$R^3$  is selected from H, OMe, OTs, OBn,  $NO_2$ ;

$R^4$  is selected from H, OMe, F;

$R^5$  is selected from H,  $NO_2$ , Br;

$R^5$  is selected from H,  $NO_2$ , CN;

$R^2$  and  $R^3$  can together be selected as  $-O-CH_2-O-$ ;

- comprising the steps of reacting compound of formula I with CuCN in DMF, under reflux in presence of  $N_2$  atmosphere to obtain the desired compound of formula A in the range of 50-90% yield.

2. The process according to claim 1, wherein said compound of formula I and CuCN are in the ratio of 1:2 to 1:3.

3. The process according to claim 1, wherein said isomers of compound of formula A are trans and cis isomers in the ratio of 3:1 to 10:1.

4. The process according to claim 1, wherein the reaction is carried out at a temperature ranging from 140 to 160  $^{\circ}C$ .



5. The process according to claim 1, wherein the reaction is carried out for a time ranging from 10 to 15 hours.

6. The compound of formula A according to claim 1, as and when used in the preparation of cosmetic products.

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## INTERNATIONAL SEARCH REPORT

International application No  
PCT/IN2013/000137

|  |   |                       |
|--|---|-----------------------|
| <b>A. CLASSIFICATION OF SUBJECT MATTER</b><br>INV. C07D317/60 C07C303/30 C07C319/20 C07C253/14<br>ADD.   |   |                       |
| According to International Patent Classification (IPC) or to both national classification and IPC  |   |                       |
| <b>B. FIELDS SEARCHED</b><br>Minimum documentation searched (classification system followed by classification symbols)<br>C07D C07C  |   |                       |
| Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  |   |                       |
| Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)<br>EPO-Internal, WPI Data, BEILSTEIN Data, CHEM ABS Data  |   |                       |
| <b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>  |   |                       |
| Category*  | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
| X  | MILOS PROCHAZKA ET AL.: "Preparation of Unsaturated Nitriles", COLLECTION OF THE CZECHOSLOVAK CHEMICAL SOCIETY, vol. 48, 1983, pages 1765-1773, XP008163604, Czech Republic | 6                     |
| A  | page 1766, line 7 - page 1768, line 24; tables I,II<br><br>-----<br><br>-/--  | 1-5                   |
| <div style="display: flex; justify-content: space-between; align-items: center;"> <div> <input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C.         </div> <div> <input type="checkbox"/> See patent family annex.         </div> </div>  |   |                       |
| <div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>* Special categories of cited documents :</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</p> <p>"&amp;" document member of the same patent family</p> </div> </div> |   |                       |
| Date of the actual completion of the international search  | Date of mailing of the international search report  |                       |
| 15 July 2013   | 23/07/2013  |                       |
| Name and mailing address of the ISA/<br>European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040,<br>Fax: (+31-70) 340-3016   | Authorized officer<br><br>Zervas, Brigitte  |                       |

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/IN2013/000137

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|-----------|---|-----------------------|
| X         | YASUMASA SAKAKIBARA ET AL.: "The Cyanation of Vinyl Halides with Alkali Cyanides Catalyzed by Nickel(0)-Phosphine Complexes Generated In Situ: Synthetic and Stereochemical Aspects", BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, vol. 68, 1995, pages 3137-3143, XP008163605, Japan | 6                     |
| A         | the whole document -----  | 1-5                   |
| X         | LIAN-HUA LI ET AL: "An Environmentally Benign Procedure for the Synthesis of Aryl and Arylvinyl Nitriles Assisted by Microwave in Ionic Liquid", SYNLETT, vol. 2006, no. 13, 1 August 2006 (2006-08-01), pages 2094-2098, XP55071161, ISSN: 0936-5214, DOI: 10.1055/s-2006-947364   | 6                     |
| A         | table 3 -----   | 1-5                   |