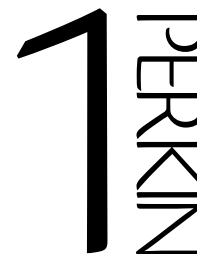


# Reactions of 2-[(2-arylimino-2-cyano-1,1-dimethylethyl)arylamino]-3-methylbut-2-enenitrile with copper(II) acetate: synthesis of 2-(2,3-dihydro-2,2-dimethyl-3-oxo-1*H*-indol-1-yl)-3-methylbut-2-enitriles



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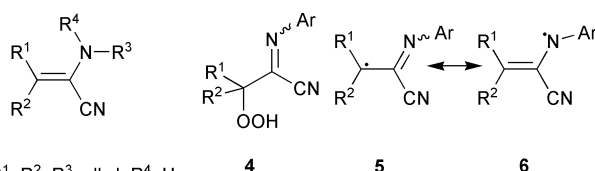
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Treatment of 2-[(2-arylimino-2-cyano-1,1-dimethylethyl)arylamino]-3-methylbut-2-enenitrile **15**, prepared by reactions of *N*-aryl  $\alpha$ -cyanoenamines **3** with  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  (2 equiv.) in the presence of pyridine (2 equiv.) in EtOH at reflux, and with  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  (1 equiv.) in HOAc at reflux gave 2-(2,3-dihydro-2,2-dimethyl-3-oxo-1*H*-indol-1-yl)-3-methylbut-2-enitriles **11** in moderate to good yields.

## Introduction

*N*-Alkyl- $\alpha$ -cyanoenamines **1** and *N*-methyl-*N*-phenyl- $\alpha$ -cyanoenamines **2** have received considerable attention as starting materials for the preparation of a variety of organic compounds.<sup>1</sup> Nevertheless, no radical reactions of **1** and **2** have been reported. Recently we found that, unlike  $\alpha$ -cyanoenamines **1** and **2**,<sup>2</sup> *N*-aryl  $\alpha$ -cyanoenamines **3** were slowly autoxidized to  $\alpha$ -hydroperoxy-*N*-arylimidoyl cyanides **4** in either crystalline or solution state in air.<sup>1</sup> The mechanism for the formation of hydroperoxides **4** is uncertain. A coupling between triplet oxygen and a radical **5** formed by oxidation of **3**<sup>3</sup> may be envisaged as a possible route leading to **4**. We were interested in the generation of **5** and **6** since the coupling product formed from **5** and **6** could be utilized as a new precursor for the preparation of 1,2-dihydroindol-3-one derivatives which are useful synthetic intermediates for the synthesis of biologically active compounds.<sup>4</sup>



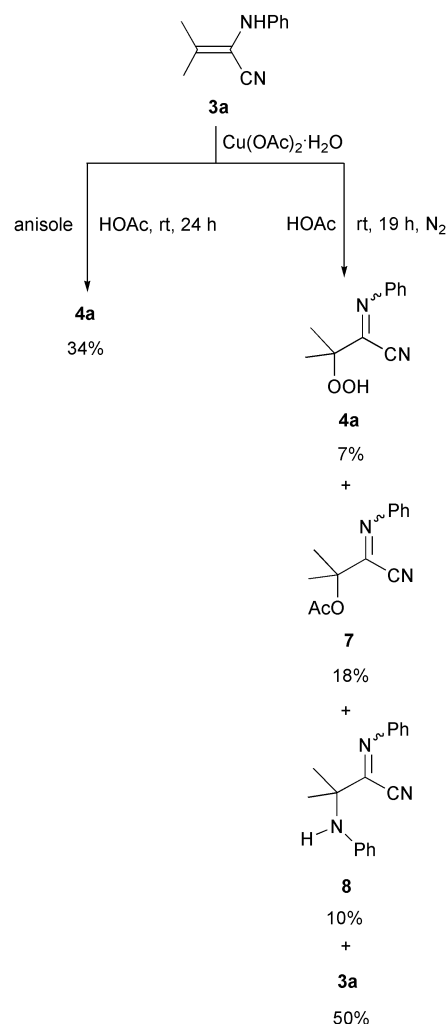
- 1, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>: alkyl; R<sup>4</sup>: H  
2, R<sup>1</sup>, R<sup>2</sup>: alkyl; R<sup>3</sup>: Me; R<sup>4</sup>: Ph  
3, R<sup>1</sup>, R<sup>2</sup>: alkyl; R<sup>3</sup>: H; R<sup>4</sup>: Ar

With this in mind, we examined the reactivity of **3** toward  $\text{Cu}(\text{II})$  acetate which is known as a good single electron oxidant<sup>5</sup> under various reaction conditions. The results are described herein.

## Results and discussion

### (i) In acetic acid at room temperature

Treatment of  $\alpha$ -cyanoenamine **3a** ( $\text{R}^1 = \text{R}^2 = \text{Me}$ ,  $\text{R}^3 = \text{H}$ ,  $\text{R}^4 = \text{Ph}$ ) with  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  (2 equiv.) in HOAc for 19 h at rt under a nitrogen atmosphere gave  $\alpha$ -hydroperoxyimidoenamine **4a** (7%),  $\alpha$ -acetoxyimidoenamine **7** (18%),  $\alpha$ -anilinoimidoenamine **8** (10%), along with unreacted **3a** (50%) (Scheme 1). In order to trap any cationic intermediate which might cause the formation of **7** and/or **8**, the same reaction was carried out in

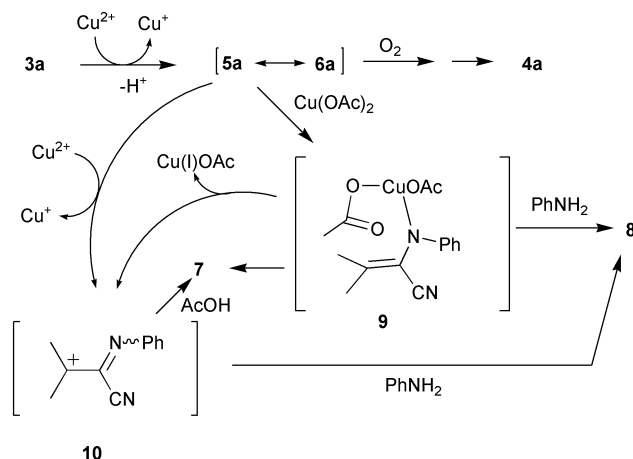


Scheme 1

the presence of anisole<sup>6</sup> in air. However, no anisole-derived product was detected. Instead, hydroperoxide **4a** (34%) which was the only identifiable product, was obtained, together with complex mixtures.

The formation of hydroperoxide **4a** in different yields under a nitrogen atmosphere and in air indicates the involvement of oxygen. A single electron transfer from **3a** by either self-oxidation (*vide infra*) or from  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ , followed by deprotonation would give radicals **5a** ( $\text{R}^1 = \text{R}^2 = \text{Me}$ ,  $\text{Ar} = \text{Ph}$ ) and **6a** ( $\text{R}^1 = \text{R}^2 = \text{Me}$ ,  $\text{Ar} = \text{Ph}$ ), which would react with oxygen to give **4a**.

The formation of **7** and **8** may be rationalized by assuming an intermediate **9** in which copper(II) acetate makes a complex on the nitrogen radical center of **5a** to give a Cu(III) intermediate **9**<sup>7</sup> (Scheme 2). As a result the C=C double bond may be acti-



Scheme 2

vated to give the acetoxy compound **7** via a pericyclic transition state. On the other hand the reaction of the intermediate **9** with aniline would give anilino compound **8**. Alternatively nucleophilic attack of acetic acid and aniline on a cation **10**,<sup>8</sup> generated via oxidation of **5a** and/or **6a** by copper(II) acetate might give **7** and/or **8**, respectively.

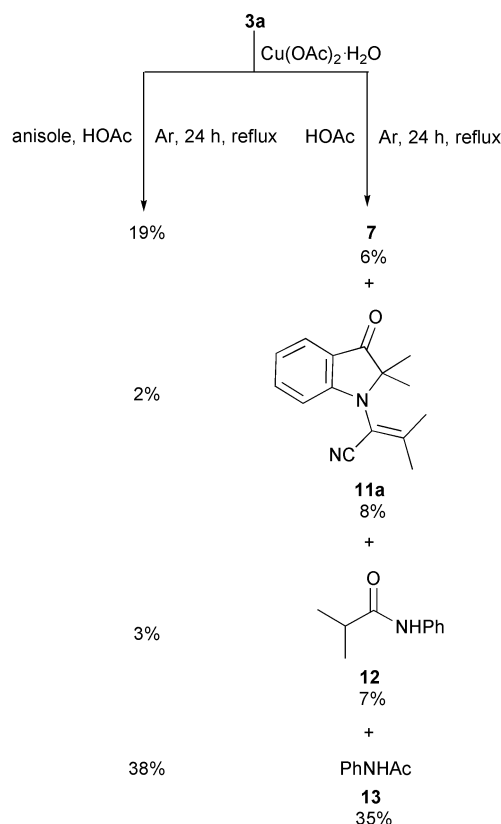
It is uncertain whether the intermediate cation **10** is directly formed from either **5a** or **6a**, or via Cu(III) intermediate **9**.

### (ii) In acetic acid at reflux

The foregoing reaction was carried out at reflux in expectation of a shorter reaction time. The reaction was allowed to proceed until no spot corresponding to **3a** was observed on TLC. Contrary to expectation, the reaction was not completed in a shorter time. From the reactions having no anisole as a cation trapping agent, were obtained **7** (6%), 2,3-dihydro-1*H*-indole derivative **11a** (8%), isobutyramide **12** (7%), acetanilide **13** (35%), and complex mixtures which were unidentifiable (Scheme 3). Similarly, **7** (19%), **11a** (2%), **12** (3%), **13** (38%), and unidentifiable complex mixtures were obtained from the reaction where anisole was added.

Amide **12** is envisaged to be formed by hydrolysis of **3a**, which is analogous to the formation of an amide by treatment of 2-alkylaminoalk-2-enitrile with anhydrous HCl in EtOH.<sup>9</sup> The formation of **13** may be explained by the reaction of aniline with  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ <sup>10</sup> at reflux. The structure of 1,2-dihydroindol-3-one **11a** was determined based on spectroscopic (<sup>1</sup>H and <sup>13</sup>C NMR, IR, MS) and analytical data. An examination of the structure **11a** suggested that the coupling of radicals **5a** and **6a**, followed by an intramolecular cyclization, was involved. From the reaction carried out in the presence of anisole under the same conditions were obtained the same products, **7**, **11a**, **12**, and **13**. However, no anisole-incorporating product was detected.

The formation of **11a**, albeit in low yield at reflux temperature may be due to an increase in the concentrations of **5a** and **6a** because it is expected that oxidation by  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  at an elevated temperature is more favorable than at rt as a result of

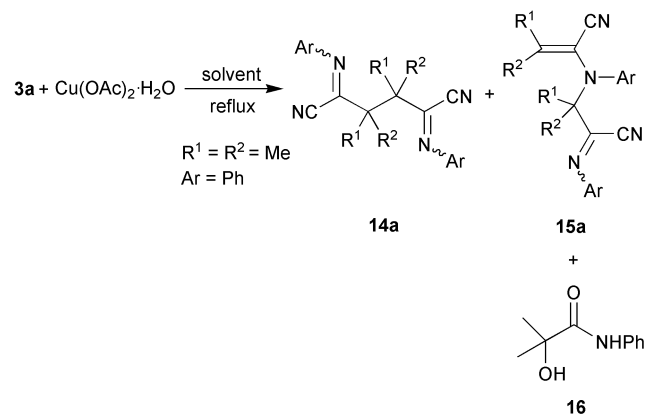


Scheme 3

an increase in the solubility of  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ .<sup>11</sup> Therefore, it was desirable to find better conditions giving rise to radicals **5a** and **6a** in order to obtain **11a** in a higher yield.

### (iii) Solvent effects

For higher concentrations of **5** and **6**, we chose non-acidic polar solvents such as absolute EtOH, DMF, and DMSO wherein  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  was more soluble than in HOAc. From the reaction of **3a** with  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  in such solvents were isolated the head-to-head dimer **14a**, head-to-tail dimer **15a**, and *N*-phenyl-2-hydroxy-2-methylpropionamide **16** (Scheme 4).



Scheme 4

The quantities of **3a** and  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ , solvent, temperature, reaction times, and yields of **14a**, **15a**, and **16** are summarized in Table 1.

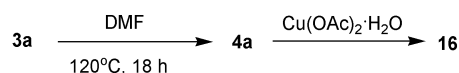
Table 1 shows that compound **16** is formed in DMSO and in wet or dried DMF. An independent experiment showed that *N*-phenyl-2-methylpropionamide was inert to  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  in DMF at 120 °C. However, Compound **3a** underwent self-oxidation in DMF at 120 °C to give **4a**<sup>1</sup> (Scheme 5), which was monitored by TLC and GC-MS. Addition of  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$

**Table 1** Reactions of **3a** with Cu(OAc)<sub>2</sub>·H<sub>2</sub>O in various solvents

Entry	3a/mmol	Cu(OAc) <sub>2</sub> ·H <sub>2</sub> O/mmol	Solvent	T/°C	t/h	Yield <sup>a</sup> (%)		
						14a	15a	16
1	1.05	2.10	EtOH	Reflux/Ar	48	36	25	0
2	1.08	2.16	DMF	120	24	41	15	27
3	0.77	1.69	Dried DMF	120/Ar	24	19	12	32
4	1.29	2.84	DMSO	120	24	37	0	28

<sup>a</sup> Isolated yields.**Table 2** Reactions of **3a** with different concentrations of Cu(OAc)<sub>2</sub>·H<sub>2</sub>O in EtOH

Entry	3a/mmol	Cu(OAc) <sub>2</sub> ·H <sub>2</sub> O/mmol	Additive	t/h	Yield <sup>a</sup> (%)		
					14a	15a	17a
1	1.05	2.10		48	36	25 <sup>b</sup>	
2	0.72	4.43		48	22	21	
3	0.99	1.98	Styrene	48	30	20	
4	0.78	1.72	Hex-1-ene	48	11	10	
5	3.31	6.62	Pyridine	48	44	34	7 <sup>c</sup>
6	5.01	15.03	Pyridine	96	26	30	20
7	1.47	3.23 <sup>d</sup>		48	27	22	

<sup>a</sup> Isolated yields. <sup>b</sup> Unreacted **3a** was recovered in 24% yield. <sup>c</sup> Unreacted **3a** was recovered in 13% yield. <sup>d</sup> Mn(OAc)<sub>3</sub> was used as an oxidant.**Scheme 5**

(2 equiv. based on **3a**) to the mixture produced by self-oxidation gave **16** in 47% yield.

Conversion of **4a** into **16** may be explained by assuming a complex formed by interaction between the imino nitrogen of **4a** and Cu(OAc)<sub>2</sub>·H<sub>2</sub>O acting as a Lewis acid,<sup>12</sup> followed by hydrolysis of the imidoyl cyanide complex to give an  $\alpha$ -hydroperoxyamide in which the O–O bond is readily cleaved by the action of Cu(OAc)<sub>2</sub>·H<sub>2</sub>O to give **16**. An analogous cleavage of the O–O bond has been reported.<sup>7</sup>

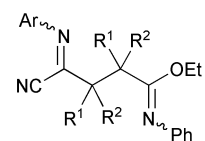
#### (iv) Concentrations of Cu(OAc)<sub>2</sub>·H<sub>2</sub>O

Since ethanol was found to be a better solvent than any of the other solvents tried for **15a**, dependence of the yield of **15a** with respect to the concentrations of Cu(OAc)<sub>2</sub> was examined in EtOH. The results are summarized in Table 2. When the concentration of Cu(OAc)<sub>2</sub>·H<sub>2</sub>O increased from 2 equiv. (entry 1) to 6 equiv. (entry 2), yields of both **14a** and **15a** decreased somewhat. Addition of either styrene (entry 3) or hex-1-ene (entry 4) to the solution of **3a** containing Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (2 equiv.), did not lead to the formation of a radical-incorporating product. Yields of **14a** and **15a** increased to 44% and 34%, respectively, when the reaction was carried out in the presence of pyridine (2 equiv.), which was reported to increase the oxidation potential of Cu(II)<sup>5a</sup> under the foregoing conditions. Interestingly, compound **17a**, which is envisaged to be formed by the substitution of one of the cyano groups of **14a** by an ethoxy group, was formed in 7% yield (entry 5). The yield of **17a** (20%) increased significantly at the expense of the yields of **14a** and **15a** when a higher concentration of Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (3 equiv.) and a longer reaction time (96 h) was allowed (entry 6). Use of Mn(OAc)<sub>3</sub><sup>13</sup> in place of Cu(OAc)<sub>2</sub>·H<sub>2</sub>O as an oxidant caused a decrease in the yields of **14a** and **15a** (entry 7). We chose the conditions represented by entry 5 for other reactions of cyanoenamines. Reaction times and yields of **14**, **15**, and **17** are summarized in Table 3.

Table 3 shows that the reactions of **3** bearing an electron-donating group on the Ar group, *i.e.*, 3-Me (24 h), 4-Me (22 h),

**Table 3** Reactions of **3** with Cu(OAc)<sub>2</sub>·H<sub>2</sub>O in the presence of pyridine

Compound	R <sup>1</sup>	R <sup>2</sup>	Ar	t/h	Yield <sup>a</sup> (%)		
					14	15	17
<b>3a</b>	Me	Me	Ph	48	a 44	a 34	a 7
<b>3b</b>	Me	Me	4-ClC <sub>6</sub> H <sub>4</sub>	60	b 21	b 34	b 24
<b>3c</b>	Me	Me	4-BrC <sub>6</sub> H <sub>4</sub>	48	c 24	c 35	c 18
<b>3d</b>	Me	Me	2-MeC <sub>6</sub> H <sub>4</sub>	24	d 34	d 8	
<b>3e</b>	Me	Me	3-MeC <sub>6</sub> H <sub>4</sub>	24	e 37	e 31	
<b>3f</b>	Me	Me	4-MeC <sub>6</sub> H <sub>4</sub>	22	f 37	f 33	
<b>3g</b>	Me	Me	4-MeOC <sub>6</sub> H <sub>4</sub>	12	g 15	g 0	
<b>3h</b> <sup>b</sup>	Me	Et	4-MeC <sub>6</sub> H <sub>4</sub>	22	h 25	h 17	
<b>3i</b>	–(CH <sub>2</sub> ) <sub>5</sub> –		Ph	48	i 20	i 29	
<b>3j</b>	Et	Et	Ph	48	j 0	j 41	

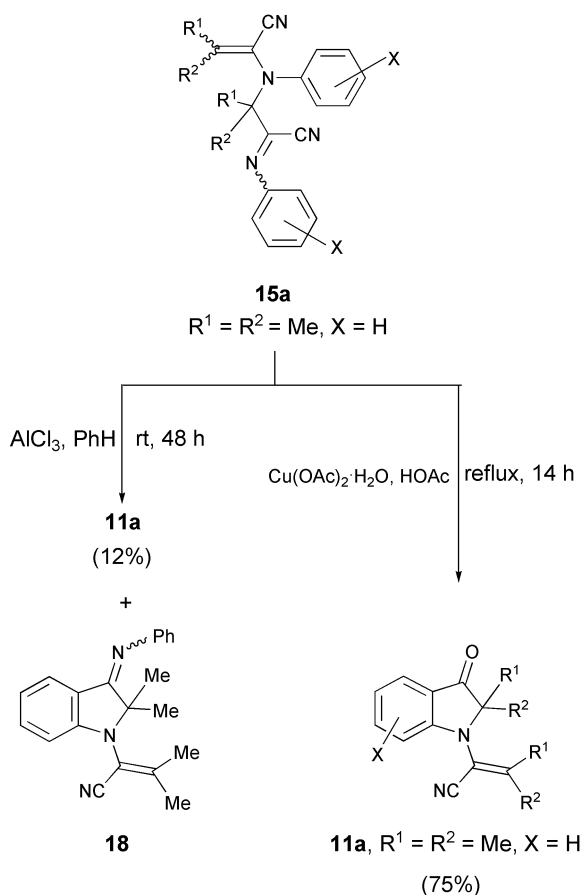
<sup>a</sup> Isolated yields. <sup>b</sup> A mixture of (*E*)- and (*Z*)-**3h** (1.2:1) was used.**17a**, Ar = Ph, R<sup>1</sup> = R<sup>2</sup> = Me

and 2-Me (24 h) have shorter reaction times compared with those with an electron-withdrawing group on the Ar, *i.e.*, 4-Cl (60 h), and 4-Br (48 h). Moreover, in the case of the Ar having an electron-withdrawing group, compounds **17b,c** were formed in comparable yields to those of **14b,c**, respectively. The result indicates that the yields of **17** increase with the reaction times. In addition, it is noteworthy that when R<sup>1</sup> = R<sup>2</sup> = Et, no head-to-head product **14j** is formed. This must be due to the severe steric hindrance arising from two ethyl groups of **5** (R<sup>1</sup> = R<sup>2</sup> = Et). In contrast, no head-to-tail product **15g** was detected. This might be due to the instability of radicals **5g** (R<sup>1</sup> = R<sup>2</sup> = Me, Ar = 4-MeOC<sub>6</sub>H<sub>4</sub>) and **6g** (R<sup>1</sup> = R<sup>2</sup> = Me, Ar = 4-MeOC<sub>6</sub>H<sub>4</sub>) and/or dimers **14g** and **15g**, which have an electron-donating group, in view of the relatively short reaction time (12 h) and a lower yield of **14g** compared with those of other head-to-head dimers.

Attempts to separate a mixture of stereoisomers **3h** (*E*:*Z* = 1.2:1) were unsuccessful. Their reaction afforded a mixture of diastereomers **14h** and **15h**, respectively, which were inseparable by column chromatography. However, the structures of diastereomeric mixtures of **14h** and **15h** together with the ratios of diastereomers **14h** and **15h**, were determined based on <sup>1</sup>H NMR and high resolution mass spectroscopy (*vide infra*).

#### (v) Cyclization of head-to-tail dimers **15**

Compound **11a** was obtained from the reaction of **3a** with Cu(OAc)<sub>2</sub>·H<sub>2</sub>O in HOAc at reflux under an argon atmosphere. In order to gain information about the mechanistic pathway, compounds **14a** and **15a** were subjected to the same reaction conditions. Interestingly, treatment of **14a** with Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (1.1 equiv.) in HOAc at reflux gave inseparable unknown mixtures, whereas compound **15a** under the same conditions as for **14a** afforded 2-(2,3-dihydro-2,2-dimethyl-3-oxo-1*H*-indol-1-yl)-3-methylbut-2-enitrile **11a** in 75% yield. The same reaction in the presence of AlCl<sub>3</sub> (2.0 equiv.) instead of Cu(OAc)<sub>2</sub>·H<sub>2</sub>O in benzene at rt afforded **11a** and imino compound **18** in 12% and 35% yields, respectively (Scheme 6).



Scheme 6

In order to ascertain the generality of the transformation of **15** into **11**, compound **15** was subjected to the conditions under which compound **11a** was obtained (Scheme 6). In contrast to the reactions of **14**, which gave rise to complex mixtures, reactions of compounds **15b–j** under the same conditions afforded 3-alkyl-2-(2,2-dialkyl-2,3-dihydro-3-oxo-1*H*-indol-1-yl)alk-2-enitriles **11b–j** in good yields except for **15j** (R<sup>1</sup> = R<sup>2</sup> = Et). Quantities of reactants, reaction times, and yields of **11** are summarized in Table 4.

The reactions of compound **15a** in the presence (1.1–1.8 equiv.) and in the absence of Cu(OAc)<sub>2</sub>·H<sub>2</sub>O gave **11a** in 75% and 56% yields, respectively. The higher yield of **11a** in

the presence of Cu(OAc)<sub>2</sub>·H<sub>2</sub>O indicates the importance of Cu(OAc)<sub>2</sub>·H<sub>2</sub>O as a Lewis acid catalyst. When the aryl group has a 3-Me group on it, regioisomers **11e(I)** and **11e(II)** were obtained in 14% and 58% yields, respectively. The predominant formation of **11e(II)** rather than **11e(I)** may be due to the lesser steric interaction in the course of the cyclization. When one of the R groups is an ethyl group (R<sup>2</sup> = Et), a longer reaction time was required than with R<sup>2</sup> = Me, presumably due to the steric hindrance. It took 48 h for the reaction of **15j** which has two ethyl groups. This indicates the significance of the steric hindrance.

To the best of our knowledge, this type of compound **11** has never been reported although several methods of synthesizing 1,2-dihydroindol-3-ones are known.<sup>14</sup> 1,2-Dihydroindol-3-ones are an important class of organic compound because not only have they been utilized as intermediates for the synthesis of various biologically active compounds such as indomethacin,<sup>15</sup> tryptamin,<sup>16</sup> ellipticine,<sup>17</sup> but also some natural products, *i.e.*, austamide<sup>18</sup> and brevianamide<sup>19</sup> consist of this skeleton. There have been numerous methods for the synthesis of 1,2-dihydroindol-3-ones which comprise mainly the cyclization of alkyl *o*-azidoaryl ketones under the basic conditions,<sup>20</sup> the reaction of 2-phenylindol-3-one with a Grignard reagent,<sup>21</sup> and MCPBA mediated oxidation of 1-substituted 3-formyl-1*H*-indoles.<sup>22</sup> In summary, it has been found that the title compound **8** undergoes an intramolecular cyclization, analogous to a Friedel–Craft acylation, in the presence of copper(II) acetate in HOAc at reflux to give 1,2-dihydro-2,2-dimethylindol-3-ones having an  $\alpha$ -cyanoisobutenyl group at N-1 of the indol-3-ones. It would appear worthwhile to explore further the synthetic utility of 1,2-dihydroindol-3-ones, and such research is currently in progress.

## Experimental

The <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded at 300 and 75 MHz, respectively, for samples in CDCl<sub>3</sub> solution containing tetramethylsilane as internal standard; *J*-values are given in Hz. IR spectra were recorded for KBr discs or thin-film samples on KBr plates. Mass spectra were obtained by electron impact at 70 eV, unless otherwise specified. Elemental analyses were determined by the National Center for Inter-University Research Facilities, Seoul National University. Column chromatography was performed using silica gel (Merck, 70–230 mesh ASTM). Mps were determined on a Fisher-Johns melting-point apparatus and are uncorrected.  $\alpha$ -Chloroalkylaldehydes<sup>23</sup> and  $\alpha$ -chloroaldimines<sup>24</sup> were prepared according to literature precedures.

### General procedure for the synthesis of 3-alkyl-2-arylaminoalk-2-enitriles **3**

To a solution of  $\alpha$ -chloroaldehyde (38–84 mmol) in CCl<sub>4</sub> (20 cm<sup>3</sup>) were added aniline derivatives (38–84 mmol) and potassium carbonate (23–91 mmol). The mixture was stirred for 12 h at rt and then heated for 1 h at reflux. The cooled reaction mixture was filtered to remove the solid which was washed with CH<sub>2</sub>Cl<sub>2</sub> (50 × 3 cm<sup>3</sup>). The filtrate was concentrated, followed by addition of CH<sub>3</sub>CN (120–150 cm<sup>3</sup>). Potassium cyanide (115–224 mmol) was added to the solution, which was heated for 8–13 h at reflux. The cooled reaction mixture was filtered and then washed with CH<sub>2</sub>Cl<sub>2</sub>. Removal of the solvent *in vacuo* gave a brown liquid, which was chromatographed on a silica gel column (2 × 20 cm) using a mixture of *n*-hexane and EtOAc (5:1) to give the title compound.

**3-Methyl-2-phenylaminobut-2-enitrile 3a.** 2-Chloro-2-methylpropionaldehyde (6.38 g, 59.3 mmol) was treated with aniline (5.52 g, 59.3 mmol) in the presence of K<sub>2</sub>CO<sub>3</sub> (9.84 g, 71.2 mmol) in CCl<sub>4</sub>, followed by addition of KCN (7.73 g, 118.6

**Table 4** Quantities of reactants, reaction times, and yields of **11**

Compound	R <sup>1</sup>	R <sup>2</sup>	X	mmol	Cu(OAc) <sub>2</sub> ·H <sub>2</sub> O/mmol	t/h	Compound	<b>11</b> Yield <sup>a</sup> (%)
<b>15a</b>	Me	Me	H	0.48	0.53	14	<b>a</b> (X = H)	75
<b>15a</b>	Me	Me	H	0.80	0	30	<b>a</b> (X = H)	56
<b>15c</b>	Me	Me	4-Br	0.17	0.20	28	<b>b</b> (X = 5-Br)	45
<b>15b</b>	Me	Me	4-Cl	0.36	0.65	14	<b>c</b> (X = 5-Cl)	86
<b>15d</b>	Me	Me	2-Me	0.19	0.23	14	<b>d</b> (X = 7-Me)	68
<b>15e</b>	Me	Me	3-Me	0.69	0.83	6	<b>e</b> ( <b>I</b> ) (X = 4-Me)	14
							<b>e</b> ( <b>II</b> ) (X = 6-Me)	58
<b>15f</b>	Me	Me	4-Me	0.38	0.46	4	<b>f</b> (X = 5-Me)	92
<b>15h</b>	Me	Et	4-Me	0.20	0.24	30	<b>h</b> (X = 5-Me)	60 <sup>b</sup>
<b>15j</b>	Et	Et	H	0.33	0.40	480	<b>j</b> (X = H)	15

<sup>a</sup> Isolated yields. <sup>b</sup> A mixture of (*E*)- and (*Z*)-stereoisomers.

mmol) in CH<sub>3</sub>CN (150 cm<sup>3</sup>). Work-up of the reaction mixture in accordance with the above general procedure gave **3a** (5.62 g, 55%).

**2-(4-Chlorophenylamino)-3-methylbut-2-enenitrile 3b.** 2-Chloro-2-methylpropionaldehyde (6.65 g, 61.8 mmol) was treated with 4-chloroaniline (7.89 g, 61.8 mmol) in the presence of K<sub>2</sub>CO<sub>3</sub> (10.26 g, 74.2 mmol) in CCl<sub>4</sub>, followed by addition of KCN (8.05 g, 123.6 mmol) in CH<sub>3</sub>CN (180 cm<sup>3</sup>). Work-up of the reaction mixture in accordance with the above general procedure gave **3b** (5.62 g, 50%).

**2-(4-Bromophenylamino)-3-methylbut-2-enenitrile 3c.** 2-Chloro-2-methylpropionaldehyde (8.37 g, 77.8 mmol) was treated with 4-bromoaniline (13.39 g, 77.8 mmol) in the presence of K<sub>2</sub>CO<sub>3</sub> (6.45 g, 46.7 mmol) in CCl<sub>4</sub>, followed by addition of KCN (15.20 g, 223.5 mmol) in CH<sub>3</sub>CN (230 cm<sup>3</sup>). Work-up of the reaction mixture in accordance with the above general procedure gave **3c** (8.21 g, 42%).

**3-Methyl-2-(*o*-tolylamino)but-2-enenitrile 3d.** 2-Chloro-2-methylpropionaldehyde (8.17 g, 76.0 mmol) was treated with *o*-toluidine (8.14 g, 76.0 mmol) in the presence of K<sub>2</sub>CO<sub>3</sub> (6.30 g, 45.6 mmol) in CCl<sub>4</sub>, followed by addition of KCN (9.90 g, 152.0 mmol) in CH<sub>3</sub>CN (230 cm<sup>3</sup>). Work-up of the reaction mixture in accordance with the above general procedure gave **3d** (8.06 g, 57%).

**3-Methyl-2-(*m*-tolylamino)but-2-enenitrile 3e.** 2-Chloro-2-methylpropionaldehyde (8.18 g, 76.1 mmol) was treated with *m*-toluidine (8.15 g, 76.1 mmol) in the presence of K<sub>2</sub>CO<sub>3</sub> (12.62 g, 91.3 mmol) in CCl<sub>4</sub>, followed by addition of KCN (9.90 g, 152.1 mmol) in CH<sub>3</sub>CN (230 cm<sup>3</sup>). Work-up of the reaction mixture in accordance with the above general procedure gave **3e** (7.51 g, 53%).

**3-Methyl-2-(*p*-tolylamino)but-2-enenitrile 3f.** 2-Chloro-2-methylpropionaldehyde (9.09 g, 84.5 mmol) was treated with *p*-toluidine (9.06 g, 84.5 mmol) in the presence of K<sub>2</sub>CO<sub>3</sub> (7.01 g, 50.7 mmol) in CCl<sub>4</sub>, followed by addition of KCN (11.01 g, 169.0 mmol) in CH<sub>3</sub>CN (250 cm<sup>3</sup>). Work-up of the reaction mixture in accordance with the above general procedure gave **3f** (9.13 g, 58%).

**2-(4-Methoxyphenylamino)-3-methylbut-2-enenitrile 3g.** 2-Chloro-2-methylpropionaldehyde (7.43 g, 69.1 mmol) was treated with *p*-anisidine (8.51 g, 69.1 mmol) in the presence of K<sub>2</sub>CO<sub>3</sub> (5.73 g, 41.5 mmol) in CCl<sub>4</sub>, followed by addition of KCN (13.49 g, 207.1 mmol) in CH<sub>3</sub>CN (210 cm<sup>3</sup>). Work-up of the reaction mixture in accordance with the above general procedure gave **3g** (7.26 g, 52%); liquid (Found: C, 71.2; H, 6.9; N, 13.9. C<sub>12</sub>H<sub>14</sub>N<sub>2</sub>O requires C, 71.3; H, 7.00; N 13.85%);  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 3352, 2910, 2224 and 1624;  $\delta_{\text{H}}$  1.87 (3H, s,

CH<sub>3</sub>), 2.11 (3H, s, CH<sub>3</sub>), 3.74 (3H, s, OCH<sub>3</sub>), 4.65 (1H, br s, NH), 6.67 (2H, d, *J* 8.9 Hz, ArH) and 6.83 (2H, d, *J* 8.9 Hz, ArH);  $\delta_{\text{C}}$  19.06, 21.99, 55.68, 110.00, 114.88, 116.19, 122.82, 137.58, 147.18 and 153.94; *m/z* 202 (M<sup>+</sup>, 91%), 187 (M<sup>+</sup> – CH<sub>3</sub>, 100).

**(*E*)- and (*Z*)-3-Methyl-2-(*p*-tolylamino)pent-2-enenitrile (*E*)- and (*Z*)-3h.** 2-Chloro-2-methylbutyraldehyde (4.98 g, 41.3 mmol) was treated with aniline (4.29 g, 40.0 mmol) in the presence of K<sub>2</sub>CO<sub>3</sub> (3.31 g, 24.0 mmol) in CCl<sub>4</sub>, followed by addition of KCN (8.07 g, 123.9 mmol) in CH<sub>3</sub>CN (120 cm<sup>3</sup>). Work-up of the reaction mixture in accordance with the above general procedure gave a mixture of (*E*)- and (*Z*)-**3h** (4.45 g, 56%); liquid (Found: C, 77.9; H, 8.1; N, 13.9. C<sub>13</sub>H<sub>16</sub>N<sub>2</sub> requires C, 78.0; H, 8.05; N 14.0%);  $\nu_{\max}$  (KBr)/cm<sup>-1</sup> 3352, 2960, 2920, 2208 and 1611; (*Z*)-isomer,  $\delta_{\text{H}}$  0.95 (3H, t, *J* 7.6 Hz, CH<sub>3</sub>), 2.05 (3H, d, *J* 1.2 Hz, CH<sub>3</sub>), 2.19 (3H, s, ArCH<sub>3</sub>), 2.26 (2H, q, *J* 7.6 Hz, CH<sub>2</sub>), 4.56 (1H, s, NH), 6.48–6.57 (2H, m, ArH) and 6.97 (2H, d, *J* 8.2 Hz, ArH); (*E*)-isomer, 1.10 (3H, t, *J* 7.5 Hz, CH<sub>3</sub>), 1.80 (3H, s, CH<sub>3</sub>), 2.19 (3H, s, ArCH<sub>3</sub>), 2.43 (2H, q, *J* 7.6 Hz, CH<sub>2</sub>), 4.56 (1H, s, NH), 6.48–6.57 (2H, m, ArH) and 6.97 (2H, d, *J* 8.2 Hz, ArH); *m/z* 200 (M<sup>+</sup>, 97%), 185 (M<sup>+</sup> – CH<sub>3</sub>, 100).

**2-Anilino-2-cyclohexylideneacetonitrile 3i.** 1-Chlorocyclohexanecarbaldehyde (7.94 g, 54.2 mmol) was treated with aniline (5.04 g, 54.2 mmol) in the presence of K<sub>2</sub>CO<sub>3</sub> (4.49 g, 32.5 mmol) in CCl<sub>4</sub>, followed by addition of KCN (10.58 g, 162.5 mmol) in CH<sub>3</sub>CN (160 cm<sup>3</sup>). Work-up of the reaction mixture in accordance with the above general procedure gave **3i** (6.52 g, 57%); mp 82–84 °C (from *n*-hexane–CH<sub>2</sub>Cl<sub>2</sub>) (Found: C, 79.3; H, 7.6; N, 13.1. C<sub>14</sub>H<sub>16</sub>N<sub>2</sub> requires C, 79.2; H, 7.6; N, 13.2%);  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 3352, 2976, 2208 and 1629;  $\delta_{\text{H}}$  0.85 (3H, t, *J* 7.6 Hz, CH<sub>3</sub>), 1.02 (3H, t, *J* 7.6 Hz, CH<sub>3</sub>), 2.15 (2H, q, *J* 7.6 Hz, CH<sub>2</sub>), 2.35 (2H, q, *J* 7.6 Hz, CH<sub>2</sub>), 4.68 (1H, s, NH), 6.53 (2H, d, ArH, *J* 7.5 Hz, ArH), 6.70 (1H, t, ArH, *J* 7.5 Hz, ArH) and 7.07 (2H, td, ArH, *J* 7.5, 0.9 Hz, ArH);  $\delta_{\text{C}}$  11.77, 12.71, 22.78, 26.15, 107.86, 114.10, 116.25, 119.59, 129.08, 143.95 and 160.37; *m/z* 200 (M<sup>+</sup>, 100%), 185 (M<sup>+</sup> – CH<sub>3</sub>, 95).

**2-Anilino-3-ethylpent-2-enenitrile 3j.** 2-Chloro-2-ethylbutyraldehyde (5.16 g, 38.3 mmol) was treated with aniline (3.57 g, 38.3 mmol) in the presence of K<sub>2</sub>CO<sub>3</sub> (3.18 g, 23.0 mmol) in CCl<sub>4</sub>, followed by addition of KCN (7.48 g, 114.9 mmol) in CH<sub>3</sub>CN (120 cm<sup>3</sup>). Work-up of the reaction mixture in accordance with the above general procedure gave **3j** (4.21 g, 54%); liquid (Found: C, 78.1; H, 8.1; N, 13.9. C<sub>13</sub>H<sub>16</sub>N<sub>2</sub> requires C, 78.0; H, 8.05; N, 14.0%);  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 3352, 2976, 2208 and 1629;  $\delta_{\text{H}}$  0.85 (3H, t, *J* 7.6 Hz, CH<sub>3</sub>), 1.02 (3H, t, *J* 7.6 Hz, CH<sub>3</sub>), 2.15 (2H, q, *J* 7.6 Hz, CH<sub>2</sub>), 2.35 (2H, q, *J* 7.6 Hz, CH<sub>2</sub>), 4.68 (1H, s, NH), 6.53 (2H, d, *J* 7.5 Hz, ArH), 6.70 (1H, t, *J* 7.5 Hz, ArH) and 7.07 (2H, td, *J* 7.5, 0.9 Hz, ArH);  $\delta_{\text{C}}$  11.77, 12.71, 22.78, 26.15, 107.86, 114.10, 116.25, 119.59, 129.08, 143.95 and 160.37; *m/z* 200 (M<sup>+</sup>, 100%), 185 (M<sup>+</sup> – CH<sub>3</sub>, 95).

## Reaction of **3a** with Cu(OAc)<sub>2</sub>

(i) **Under a nitrogen atmosphere at rt.** To a solution of **3a** (178 mg, 1.03 mmol) in HOAc (5 cm<sup>3</sup>) under a nitrogen atmosphere was added Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (453 mg, 2.27 mmol). The mixture was stirred for 19 h at rt, followed by addition of water (30 cm<sup>3</sup>) and CH<sub>2</sub>Cl<sub>2</sub> (30 cm<sup>3</sup>). The mixture was neutralized with aqueous Na<sub>2</sub>CO<sub>3</sub> and extracted with CH<sub>2</sub>Cl<sub>2</sub> (30 × 2 cm<sup>3</sup>). The combined extracts were dried over anhydrous MgSO<sub>4</sub>. Removal of the solvent *in vacuo* gave a brown liquid, which was chromatographed on a silica gel column (2 × 20 cm) using a mixture of *n*-hexane and EtOAc (10:1) to give 2-cyano-1,1-dimethyl-2-phenyliminoethyl acetate **7** (20 mg, 18%); liquid (Found: C, 67.9; H, 6.0; N, 12.1. C<sub>13</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub> requires C, 67.8; H, 6.1; N, 12.2%);  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 2990, 2940, 2219, 1742, 1638, 1591, 1483, 1371, 1250, 1147, 1081, 1018, 781 and 699;  $\delta_{\text{H}}$  1.64 (6H, s, 2 × CH<sub>3</sub>), 2.07 (3H, s, CH<sub>3</sub>) and 6.97–7.37 (5H, m, ArH);  $\delta_{\text{C}}$  21.82, 24.96, 81.39, 110.37, 120.27, 127.55, 129.63, 147.54, 148.79 and 170.92; *m/z* 230 (M<sup>+</sup>, 100%), 172 (58), 129 (75), 101 (42), 77 (72). Continuous elution with the same solvent mixture gave 3-anilino-3-methyl-2-phenyliminobutyronitrile **8** (12 mg, 10%); liquid (Found: C, 77.4; H, 6.4; N, 15.9. C<sub>17</sub>H<sub>17</sub>N<sub>3</sub> requires C, 77.5; H, 6.5; N, 16.0%);  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 2990, 2938, 2220, 1636, 1572, 1145 and 702;  $\delta_{\text{H}}$  1.69 (6H, s, 2 × CH<sub>3</sub>), 4.14 (1H, br s, NH), 6.69 (2H, d, *J* 7.8 Hz, ArH), 6.79 (1H, t, *J* 7.6 Hz, ArH), 6.68–7.08 (2H, m, ArH), 7.17 (2H, t, *J* 7.5 Hz, ArH), 7.25–7.33 (1H, m, ArH) and 7.41 (2H, t, *J* 7.4 Hz, ArH); *m/z* 263 (M<sup>+</sup>, 4%), 172 (3), 134 (100). Continuous elution with the same solvent mixture gave unreacted **3a** (87 mg, 50%) and 3-hydroperoxy-3-methyl-2-phenyliminobutyronitrile **4a** (14 mg, 7%); mp 53–55 °C (from *n*-hexane–CH<sub>2</sub>Cl<sub>2</sub>) (Found: C, 64.9; H, 6.1; N, 13.9. C<sub>11</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>: C, 64.7; H, 5.9; N 13.7%);  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 3250, 2990, 2224 and 1625;  $\delta_{\text{H}}$  1.63 (6H, s, 2 × CH<sub>3</sub>), 7.09 (2H, d, *J* 7.5 Hz, ArH), 7.32 (1H, t, *J* 7.4 Hz, ArH), 7.44 (2H, t, *J* 7.4 Hz, ArH) and 8.86 (1H, br s, OOH);  $\delta_{\text{C}}$  22.17, 84.96, 110.29, 120.05, 127.61, 129.26, 147.59 and 147.70.

(ii) **In the presence of anisole in air at rt.** To a solution of **3a** (342 mg, 2.00 mmol) in HOAc (10 cm<sup>3</sup>) was added anisole (238 mg, 2.20 mmol) and Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (453 mg, 2.27 mmol). The mixture was stirred for 24 h at rt. The mixture was worked up as described in (i). Chromatography of the reaction mixture using a mixture of *n*-hexane and EtOAc (5:1) gave **4a** (137 mg, 34%).

(iii) **Under a nitrogen atmosphere at reflux.** To a solution of **3a** (210 mg, 1.22 mmol) in HOAc (5 cm<sup>3</sup>) under a nitrogen atmosphere was added Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (465 mg, 2.33 mmol). The mixture was heated for 24 h at reflux and then worked up as before. Chromatography (2 × 20 cm) of the reaction mixture using a mixture of *n*-hexane and EtOAc (5:1) gave **7** (17 mg, 6%), unknown mixtures (40 mg), a mixture of *N*-phenylisobutyramide **12** and 2-(2,3-dihydro-2,2-dimethyl-3-oxo-1*H*-indol-1-yl)-3-methylbut-2-enitrile **11a** (45 mg). Elution with the same solvent mixture (2:1) gave acetanilide **13** (58 mg, 35%). Rechromatography (2 × 20 cm) of the mixture of **11a** and **12** using a mixture of *n*-hexane and CH<sub>2</sub>Cl<sub>2</sub> (2:1) gave **12** (14 mg, 7%) and **11a** (23 mg, 8%); mp 60–62 °C (from *n*-hexane–CH<sub>2</sub>Cl<sub>2</sub>) (Found: C, 75.0; H, 6.7; N, 11.7. C<sub>15</sub>H<sub>16</sub>N<sub>2</sub>O requires C, 75.0; H, 6.7; N, 11.7%);  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 2210, 1707 and 1611;  $\delta_{\text{H}}$  1.22 (3H, s, CH<sub>3</sub>), 1.40 (3H, s, CH<sub>3</sub>), 1.82 (3H, s, CH<sub>3</sub>), 2.22 (3H, s, CH<sub>3</sub>), 6.56 (1H, d, *J* 8.2 Hz, ArH), 6.82 (1H, t, *J* 7.4 Hz, ArH), 7.44 (1H, t, *J* 7.2 Hz, ArH) and 7.61 (1H, d, *J* 7.6 Hz, ArH);  $\delta_{\text{C}}$  20.54, 22.10, 22.54, 22.56, 69, 89, 105.91, 110.23, 116.44, 119.35, 119.70, 125.29, 137.61, 156.85, 159.99 and 202.74; *m/z* 240 (M<sup>+</sup>).

(iv) **In the presence of anisole under a nitrogen atmosphere at reflux.** To a solution of **3a** (200 mg, 1.16 mmol) in HOAc

(5 cm<sup>3</sup>) under a nitrogen atmosphere was added anisole (275 mg, 2.55 mmol) and Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (463 mg, 2.55 mmol). The mixture was heated for 24 h at reflux and then worked up as before. Chromatography of the reaction mixture using a mixture of *n*-hexane and EtOAc (5:1) gave **7** (51 mg, 19%), unknown mixtures (32 mg), and a mixture of **11a** and **12** (14 mg). Elution with the same solvent mixture (2:1) gave **13** (59 mg, 38%). Rechromatography (2 × 20 cm) of the mixture of **11a** and **12** using a mixture of *n*-hexane and EtOAc (2:1) gave **12** (7 mg, 3%) and **11a** (5 mg, 2%).

## Reaction of **3a** with Cu(OAc)<sub>2</sub>·H<sub>2</sub>O in different solvents

(i) **In EtOH.** To a solution of **3a** (180 mg, 1.05 mmol) in EtOH (5 cm<sup>3</sup>) was added Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (381 mg, 2.10 mmol) under an argon atmosphere. The mixture was heated for 48 h at reflux, followed by work-up as before. Chromatography (2 × 20 cm) of the reaction mixture using a mixture of *n*-hexane and EtOAc (10:1) as the eluent gave 3,3,4,4-tetramethyl-2,5-bis(phenylimino)adiponitrile **14a** (47 mg, 36%), 2-(2-cyano-*N*-phenyl-2-phenylimino-1,1-dimethylethylamino)-3-methylbut-2-enitrile **15a** (33 mg, 25%), and unreacted **3a** (43 mg, 24%). **14a**: mp 110–112 °C (from MeOH–H<sub>2</sub>O) (Found: C, 77.0; H 6.4; N, 16.2. C<sub>22</sub>H<sub>22</sub>N<sub>4</sub> requires C, 77.2; H, 6.50; N, 16.4%);  $\nu_{\max}$  (KBr)/cm<sup>-1</sup> 2211 and 1616;  $\delta_{\text{H}}$  1.49(12H, s, 4 × CH<sub>3</sub>) and 6.92–7.34 (10H, m, 2 × ArH);  $\delta_{\text{C}}$  23.38, 48.60, 111.60, 120.09, 127.46, 129.68, 149.13 and 149.99; *m/z* 342 (M<sup>+</sup>, 47%), 341 (22), 327 (13), 250 (32), 213 (55), 172 (77), 171 (100). **15a**: liquid (Found: C, 77.1; H, 6.4; N, 16.3. C<sub>22</sub>H<sub>22</sub>N<sub>4</sub> requires C, 77.2; H, 6.5; N, 16.4%);  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 2207, 1632 and 1592;  $\delta_{\text{H}}$  1.68 (6H, s, 2 × CH<sub>3</sub>), 2.05 (3H, s, CH<sub>3</sub>), 2.12 (3H, s, CH<sub>3</sub>) and 6.89–7.35 (10H, m, 2 × ArH);  $\delta_{\text{C}}$  22.85, 22.68, 23.91, 65.75, 111.93, 112.44, 118.57, 119.93, 122.12, 123.81, 126.30, 127.60, 129.75, 129.85, 145.19, 148.75, 150.33 and 158.77; *m/z* 342 (M<sup>+</sup>, 30%), 341 (26), 327 (9), 250 (11), 213 (14), 172 (41), 171 (51), 155 (30), 144 (53), 77 (100).

(ii) **In DMF.** To a solution of **3a** (186 mg, 1.08 mmol) in DMF (10 cm<sup>3</sup>) was added Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (381 mg, 2.16 mmol) at rt. The mixture was heated for 24 h at 120 °C. Water (50 cm<sup>3</sup>) was added to the cooled reaction mixture, which was then extracted with CH<sub>2</sub>Cl<sub>2</sub> (50 cm<sup>3</sup> × 3) and EtOAc (50 cm<sup>3</sup>) in a series. The combined organic layer was dried and worked up as usual. Chromatography (2 × 20 cm) of the residue using a mixture of *n*-hexane and EtOAc (10:1) gave **14a** (74 mg, 41%) and **15a** (26 mg, 15%). Subsequent elution with the same solvent mixture (3:1) gave 2-hydroxy-2-methyl-*N*-phenylpropionamide **16** (52 mg, 27%); liquid (Found: C, 67.1; H, 7.1; N, 7.7. C<sub>10</sub>H<sub>13</sub>NO<sub>2</sub> requires C, 67.0; H, 7.3; N, 7.8%);  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 3263, 2974, 1653, 1441, 1185 and 1152;  $\delta_{\text{H}}$  1.47 (6H, s, 2 × CH<sub>3</sub>), 2.73 (1H, br s, OH), 7.04 (1H, t, *J* 7.4 Hz, ArH), 7.25 (2H, t, *J* 7.6 Hz, ArH), 7.49 (2H, d, *J* 7.6 Hz, ArH) and 8.67 (1H, br s, NH); *m/z* 179 (M<sup>+</sup>, 29%), 121 (45), 93 (100). The same reaction of **3a** (133 mg, 0.77 mmol) with Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (34 mg, 1.69 mmol) in dried DMF under an argon atmosphere gave **14a** (34 mg, 19%), **15a** (21 mg, 12%), and **16** (62 mg, 32%).

(iii) **In DMSO.** From the reaction of **3a** (222 mg, 1.29 mmol) with Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (516 mg, 2.84 mmol) in DMSO (10 cm<sup>3</sup>) at 120 °C were obtained **14a** (83 mg, 37%) and **15a** (64 mg, 28%).

## Reaction of **4a** with Cu(OAc)<sub>2</sub>·H<sub>2</sub>O

A solution of **3a** (186 mg, 1.05 mmol) in DMF (10 cm<sup>3</sup>) was heated for 24 h at 120 °C by which time **3a** was completely converted into 3-hydroperoxy-3-methyl-2-phenyliminobutyronitrile **4a**. Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (500 mg, 2.60 mmol) was added to the mixture, which was then stirred for 18 h at 120 °C. Work-up of the reaction mixture as described in (ii) gave **16** (101 mg, 47%).

### General procedure for the reactions of **3** with $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ in the presence of pyridine

To a solution of **3** (1.72–5.36 mmol) in absolute EtOH (15–52 cm<sup>3</sup>) was added  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  (6.62–10.34 mmol) and pyridine (6.62–10.34 mmol). The mixture was heated for an appropriate time at reflux. Water (50 cm<sup>3</sup>) was added to the cooled reaction mixture, which was then extracted with  $\text{CH}_2\text{Cl}_2$  (50 cm<sup>3</sup>) and dimethyl ether (50 cm<sup>3</sup> × 3). The combined organic layers were dried ( $\text{MgSO}_4$ ). Removal of the solvent gave a residue, which was chromatographed on silica gel (2 × 20 cm) using a mixture of *n*-hexane and EtOAc (10:1) to give **14**, **15**, and **17**.

**Reaction of 3a.** Reaction of **3a** (570 mg, 3.31 mmol) with  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  (1.02 g, 6.62 mmol) in the presence of pyridine (523 mg, 6.62 mmol) in EtOH (30 cm<sup>3</sup>) for 48 h gave **14a** (217 mg, 44%), **15a** (164 mg, 34%), 4-cyano-2,2,3,3-tetramethyl-*N*-phenyl-4-phenyliminobutyrimidic acid ethyl ester **17a** (41 mg, 7%), and unreacted **3a** (75 mg, 13%).

**17a:** sticky solid (Found: C, 76.2; H, 7.4; N, 11.7.  $\text{C}_{23}\text{H}_{27}\text{N}_3\text{O}$  requires C, 76.4; H, 7.5; N, 11.6%);  $\nu_{\text{max}}$  (KBr)/cm<sup>-1</sup> 1637 and 1581;  $\delta_{\text{H}}$  0.52 (3H, t, *J* 7.1 Hz,  $\text{OCH}_2\text{CH}_3$ ), 1.20 (6H, s, 2 ×  $\text{CH}_3$ ), 1.29 (6H, s, 2 ×  $\text{CH}_3$ ), 3.57 (2H, q, *J* 7.1 Hz,  $\text{OCH}_2\text{CH}_3$ ), 6.53 (2H, d, *J* 7.6 Hz, ArH), 6.80 (2H, d, *J* 7.1 Hz, ArH) and 6.85–6.98 (2H, m, ArH), 7.05–7.21 (m, 4H, ArH);  $\delta_{\text{C}}$  12.94, 21.05, 22.29, 46.99, 47.39, 62.90, 118.23, 123.07, 127.96, 128.20, 148.51, 150.50, 157.58, 161.54 and 164.04.

**Reaction of 2-(4-chlorophenylamino)-3-methylbut-2-enitrile 3b.** The reaction of **3b** (971 mg, 4.70 mmol) with  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  (1.88 g, 10.34 mmol) in the presence of pyridine (818 mg, 10.34 mmol) in EtOH (50 cm<sup>3</sup>) for 60 h gave 2,5-bis(4-chlorophenylimino)-3,3,4,4-tetramethyladiponitrile **14b** (201 mg, 21%), 2-[*N*-(4-chlorophenyl)-2-(4-chlorophenylimino)-2-cyano-1,1-dimethylethylamino]-3-methylbut-2-enitrile **15b** (331 mg, 34%), and *N*-(4-chlorophenyl)-4-(4-chlorophenylimino)-4-cyano-2,2,3,3-tetramethylbutyrimidic acid ethyl ester **17b** (237 mg, 24%).

**14b:** mp 187–188 °C (from *n*-hexane) (Found: C, 64.3; H, 5.0; N, 13.5.  $\text{C}_{22}\text{H}_{20}\text{Cl}_2\text{N}_4$  requires C, 64.2; H, 4.90; N, 13.6%);  $\nu_{\text{max}}$  (KBr)/cm<sup>-1</sup> 2213 and 1617;  $\delta_{\text{H}}$  1.54 (12H, s, 4 ×  $\text{CH}_3$ ), 6.94 (4H, d, *J* 6.7 Hz, 2 × ArH) and 7.36 (4H, d, *J* 6.7 Hz, 2 × ArH);  $\delta_{\text{C}}$  22.82, 48.31, 110.93, 121.14, 129.44, 132.82, 146.84 and 150.12.

**15b:** mp 74–75 °C (from *n*-hexane– $\text{CH}_2\text{Cl}_2$ ) (Found: C, 64.3; H, 5.15; N, 13.7.  $\text{C}_{22}\text{H}_{20}\text{Cl}_2\text{N}_4$  requires C, 64.2; H, 4.9; N, 13.6%);  $\delta_{\text{H}}$  1.65 (6H, s, 2 ×  $\text{CH}_3$ ), 2.02 (3H, s, Ar $\text{CH}_3$ ), 2.11 (3H, s,  $\text{CH}_3$ ), 6.87 (2H, d, *J* 7.8 Hz, ArH), 6.90 (2H, d, *J* 8.6 Hz, ArH), 7.18 (2H, d, *J* 8.6 Hz, ArH) and 7.20 (1H, d, *J* 7.8 Hz, ArH);  $\delta_{\text{C}}$  20.36, 22.23, 23.42, 65.44, 111.17, 111.63, 117.72, 121.06, 122.81, 128.78, 129.40, 129.50, 133.09, 143.22, 146.32, 149.78 and 158.78.

**17b:** mp 88–89 °C (from *n*-hexane–EtOAc (10:1)) (Found: C, 66.5; H, 5.9; N, 10.2.  $\text{C}_{23}\text{H}_{25}\text{N}_3\text{Cl}_2\text{O}$  requires C, 66.7; H, 6.1; N, 10.1%);  $\nu_{\text{max}}$  (KBr)/cm<sup>-1</sup> 1637 and 1581;  $\delta_{\text{H}}$  0.69 (3H, t, *J* 7.1 Hz,  $\text{OCH}_2\text{CH}_3$ ), 1.25 (6H, s, 2 ×  $\text{CH}_3$ ), 1.33 (6H, s, 2 ×  $\text{CH}_3$ ), 3.69 (2H, q, *J* 7.1 Hz,  $\text{OCH}_2\text{CH}_3$ ), 6.55 (2H, d, *J* 8.6 Hz, ArH), 6.79 (2H, d, *J* 8.6 Hz, ArH) and 7.20 (1H, d, *J* 8.6 Hz, ArH);  $\delta_{\text{C}}$  12.94, 21.05, 22.29, 46.99, 47.39, 62.90, 118.23, 123.07, 127.96, 128.20, 148.51, 150.50, 157.58, 161.54 and 164.04.

**Reaction of 2-(4-bromophenylamino)-3-methylbut-2-enitrile 3c.** The reaction of **3c** (432 mg, 1.72 mmol) with  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  (687 mg, 3.78 mmol) in the presence of pyridine (299 mg, 3.78 mmol) for 48 h in EtOH gave 2,5-bis(4-bromophenylimino)-3,3,4,4-tetramethyladiponitrile **14c** (100 mg, 24%), 2-[*N*-(4-bromophenyl)-2-(4-bromophenylimino)-2-cyano-1,1-dimethylethylamino]-3-methylbut-2-enitrile **15c** (149 mg, 35%), and

*N*-(4-bromophenyl)-4-(4-bromophenylimino)-4-cyano-2,2,3,3-tetramethylbutyrimidic acid ethyl ester **17c** (81 mg, 18%).

**14c:** mp 193–194 °C (from *n*-hexane) (Found: C, 53.0; H, 4.3; N, 11.0.  $\text{C}_{22}\text{H}_{20}\text{Br}_2\text{N}_4$  requires C, 52.8; H, 4.0; N, 11.2%);  $\nu_{\text{max}}$  (KBr)/cm<sup>-1</sup> 2213 and 1617;  $\delta_{\text{H}}$  1.47 (12H, s, 4 ×  $\text{CH}_3$ ), 6.80 (4H, d, *J* 8.7 Hz, 2 × ArH) and 7.44 (4H, d, *J* 8.7 Hz, 2 × ArH);  $\delta_{\text{C}}$  22.83, 48.33, 110.90, 120.74, 121.40, 132.41, 147.34 and 150.15.

**15c:** mp 132–133 °C (from *n*-hexane– $\text{CH}_2\text{Cl}_2$ ) (Found: C, 52.8; H, 4.0; N, 11.0.  $\text{C}_{22}\text{H}_{20}\text{Br}_2\text{N}_4$  requires C, 52.8; H, 4.0; N, 11.2%);  $\nu_{\text{max}}$  (neat)/cm<sup>-1</sup> 2200 and 1626;  $\delta_{\text{H}}$  1.66 (6H, s, 2 ×  $\text{CH}_3$ ), 2.03 (3H, s, Ar $\text{CH}_3$ ), 2.13 (3H, s,  $\text{CH}_3$ ), 6.81 (2H, d, *J* 8.7 Hz, ArH), 6.84 (2H, d, *J* 9.1 Hz, ArH), 7.32 (2H, d, *J* 9.1 Hz, ArH) and 7.49 (1H, d, *J* 8.7 Hz, ArH);  $\delta_{\text{C}}$  20.33, 22.22, 23.38, 65.39, 111.07, 111.33, 116.07, 117.58, 120.96, 121.29, 122.59, 131.81, 132.43, 143.64, 146.74, 149.84 and 158.94.

**17c:** sticky solid (Found: C, 53.1; H, 4.7; N, 7.9.  $\text{C}_{23}\text{H}_{25}\text{N}_3\text{Br}_2\text{O}$  requires C, 53.2; H, 4.85; N, 8.1%);  $\nu_{\text{max}}$  (KBr)/cm<sup>-1</sup> 1626 and 1584;  $\delta_{\text{H}}$  0.72 (3H, t, *J* 7.1 Hz,  $\text{OCH}_2\text{CH}_3$ ), 1.26 (6H, s, 2 ×  $\text{CH}_3$ ), 1.35 (6H, s, 2 ×  $\text{CH}_3$ ), 3.71 (2H, q, *J* 7.1 Hz,  $\text{OCH}_2\text{CH}_3$ ), 6.56 (2H, d, *J* 8.6 Hz, ArH), 6.81 (2H, d, *J* 8.6 Hz, ArH) and 7.18 (1H, d, *J* 8.6 Hz, ArH).

**Reaction of 3-methyl-2-(*o*-tolylamino)but-2-enitrile 3d.** The reaction of **3d** (947 mg, 5.30 mmol) with  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  (2.03 g, 11.2 mmol) in the presence of pyridine (876 mg, 11.2 mmol) in EtOH (50 cm<sup>3</sup>) for 24 h gave 3,3,4,4-tetramethyl-2,5-bis(*o*-tolylimino)adiponitrile **14d** (324 mg, 34%) and 2-[2-cyano-1,1-dimethyl-*N*-(*o*-tolyl)-2-(*o*-tolylimino)ethylamino]-3-methylbut-2-enitrile **15d** (72 mg, 8%).

**14d:** mp 132–133 °C (from *n*-hexane–EtOAc) (Found: C, 77.6; H 6.8; N, 15.2.  $\text{C}_{24}\text{H}_{26}\text{N}_4$  requires C, 77.8; H, 7.1; N, 15.1%);  $\nu_{\text{max}}$  (KBr)/cm<sup>-1</sup> 2200 and 1603;  $\delta_{\text{H}}$  1.51 (12H, s, 4 ×  $\text{CH}_3$ ), 2.10 (6H, s, 2 × Ar $\text{CH}_3$ ), 6.72–6.78 (2H, m, 2 × ArH) and 7.02–7.18 (6H, m, 2 × ArH);  $\delta_{\text{C}}$  17.85, 23.04, 48.21, 111.15, 117.75, 125.79, 126.62, 127.06, 129.49, 130.56, 147.45 and 149.15; *m/z* 370 ( $\text{M}^+$ , 26%), 355 ( $\text{M}^+ - \text{Me}$ , 44), 185 (100).

**15d:** sticky solid (Found: C, 77.6; H, 7.0; N, 15.0.  $\text{C}_{24}\text{H}_{26}\text{N}_4$  requires C, 77.8; H, 7.1; N, 15.1%);  $\nu_{\text{max}}$  (neat)/cm<sup>-1</sup> 2912 and 1622;  $\delta_{\text{H}}$  1.67 (6H, s, 2 ×  $\text{CH}_3$ ), 1.94 (3H, s, Ar $\text{CH}_3$ ), 2.00 (3H, s, Ar $\text{CH}_3$ ), 2.03 (3H, s,  $\text{CH}_3$ ), 2.36 (3H, s,  $\text{CH}_3$ ), 6.57–6.64 (1H, m, ArH), 7.01–7.17 (6H, m, ArH) and 7.47–7.54 (1H, m, ArH);  $\delta_{\text{C}}$  17.51, 20.42, 21.62, 23.04, 24.82, 67.34, 11.13, 114.22, 117.40, 118.76, 126.27, 126.51, 126.58, 127.07, 129.35, 129.90, 130.51, 132.04, 137.39, 143.22, 146.92, 147.19 and 154.35; *m/z* 370 ( $\text{M}^+$ , 31%), 355 ( $\text{M}^+ - \text{CH}_3$ , 60), 185 (100).

**Reaction of 3-methyl-2-(*m*-tolylamino)but-2-enitrile 3e.** The reaction of **3e** (998 mg, 5.36 mmol) with  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  (2.14 g, 11.8 mmol) in the presence of pyridine (933 mg, 11.8 mmol) in EtOH (50 cm<sup>3</sup>) for 24 h gave 3,3,4,4-tetramethyl-2,5-bis(*m*-tolylimino)adiponitrile **14e** (371 mg, 37%) and 2-[2-cyano-1,1-dimethyl-*N*-(*m*-tolyl)-2-(*m*-tolylimino)ethylamino]-3-methylbut-2-enitrile **15e** (310 mg, 31%).

**14e:** mp 62–64 °C (from *n*-hexane) (Found: C, 77.85; H 6.8; N, 15.3.  $\text{C}_{24}\text{H}_{26}\text{N}_4$  requires C, 77.8; H, 7.1; N, 15.1%);  $\nu_{\text{max}}$  (KBr)/cm<sup>-1</sup> 2216 and 1599;  $\delta_{\text{H}}$  1.45 (12H, s, 4 ×  $\text{CH}_3$ ), 2.23 (6H, s, 2 × Ar $\text{CH}_3$ ), 6.67–6.76 (4H, m, 2 × ArH), 6.95 (2H, d, *J* 7.7 Hz, 2 × ArH) and 7.16 (2H, t, *J* 8.0 Hz, 2 × ArH);  $\delta_{\text{C}}$  21.21, 22.83, 48.01, 111.07, 116.45, 120.22, 127.64, 128.94, 138.99, 148.61 and 149.15.

**15e:** mp 74–75 °C (from *n*-hexane– $\text{CH}_2\text{Cl}_2$ ) (Found: C, 77.7; H 7.3; N, 15.25.  $\text{C}_{24}\text{H}_{26}\text{N}_4$  requires C, 77.8; H, 7.1; N, 15.1%);  $\nu_{\text{max}}$  (neat)/cm<sup>-1</sup> 2209 and 1633;  $\delta_{\text{H}}$  1.64 (6H, s, 2 ×  $\text{CH}_3$ ), 2.02 (3H, s, Ar $\text{CH}_3$ ), 2.09 (3H, s, Ar $\text{CH}_3$ ), 2.23 (3H, s,  $\text{CH}_3$ ), 2.28 (3H, s,  $\text{CH}_3$ ), 6.64–6.73 (2H, m, ArH), 6.75–6.84 (3H, m, ArH), 6.95–7.02 (1H, m, ArH), 7.04–7.12 (1H, m, ArH) and 7.16–7.24 (1H, m, ArH);  $\delta_{\text{C}}$  20.29, 21.26, 21.67, 22.11, 23.27, 65.14, 111.41, 111.94, 116.11, 118.10, 118.79,

119.92, 122.27, 124.12, 127.70, 129.03, 129.08, 138.98, 139.13, 144.67, 148.37, 149.77 and 158.0.

**Reaction of 3-methyl-2-(*p*-tolylamino)but-2-enenitrile 3f.** The reaction of **3f** (998 mg, 5.30 mmol) with  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  (2.12 g, 11.7 mmol) in the presence of pyridine (922 mg, 11.7 mmol) in EtOH (50 cm<sup>3</sup>) for 22 h gave 3,3,4,4-tetramethyl-2,5-bis(*p*-tolylimino)adiponitrile **14f** (360 mg, 37%), 2-[2-cyano-1,1-dimethyl-*N*-(*p*-tolyl)-2-(*p*-tolylimino)ethylamino]-3-methylbut-2-enenitrile **15f** (325 mg, 33%).

**14f:** mp 116–117 °C (from *n*-hexane) (Found: C, 78.0; H, 7.15; N, 15.0.  $\text{C}_{24}\text{H}_{26}\text{N}_4$  requires C, 77.8; H, 7.1; N, 15.1%);  $\nu_{\text{max}}$  (KBr)/cm<sup>-1</sup> 2208 and 1604;  $\delta_{\text{H}}$  1.42 (12H, s, 4 × CH<sub>3</sub>), 2.21 (6H, s, 2 × ArCH<sub>3</sub>), 6.84 (4H, d, *J* 7.8 Hz, 2 × ArH) and 7.06 (4H, d, *J* 7.8 Hz, 2 × ArH);  $\delta_{\text{C}}$  20.92, 22.73, 47.97, 111.27, 119.75, 129.61, 136.89, 146.00 and 148.51.

**15f:** mp 74–75 °C (from *n*-hexane–CH<sub>2</sub>Cl<sub>2</sub>) (Found: C, 77.7; H 7.3; N, 15.25.  $\text{C}_{24}\text{H}_{26}\text{N}_4$  requires C, 77.8; H, 7.1; N, 15.1%);  $\nu_{\text{max}}$  (neat)/cm<sup>-1</sup> 2209 and 1633;  $\delta_{\text{H}}$  1.64 (6H, s, 2 × CH<sub>3</sub>), 2.02 (3H, s, ArCH<sub>3</sub>), 2.09 (3H, s, ArCH<sub>3</sub>), 2.23 (3H, s, CH<sub>3</sub>), 2.28 (3H, s, CH<sub>3</sub>), 6.64–6.73 (2H, m, ArH), 6.75–6.84 (3H, m, ArH), 6.95–7.02 (1H, m, ArH), 7.04–7.12 (1H, m, ArH) and 7.16–7.24 (1H, m, ArH);  $\delta_{\text{C}}$  20.29, 21.26, 21.67, 22.11, 23.27, 65.14, 111.41, 111.94, 116.11, 118.10, 118.79, 119.92, 122.27, 124.12, 127.70, 129.03, 129.08, 138.98, 139.13, 144.67, 148.37, 149.77 and 158.0.

**Reaction of 2-(4-methoxyphenylamino)-3-methylbut-2-enenitrile 3g.** The reaction of **3g** (889 mg, 4.40 mmol) with  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  (1.60 g, 8.80 mmol) in the presence of pyridine (696 mg, 8.80 mmol) in EtOH (44 cm<sup>3</sup>) for 12 h gave 2,5-bis-(4-methoxyphenylimino)-3,3,4,4-tetramethyladiponitrile **14g** (127 mg, 15%); mp 140–142 °C (from *n*-hexane) (Found: C, 71.4; H 6.4; N, 13.8.  $\text{C}_{24}\text{H}_{26}\text{N}_4\text{O}_2$  requires C, 71.6; H, 6.5; N, 13.9%);  $\nu_{\text{max}}$  (KBr)/cm<sup>-1</sup> 2206 and 1608;  $\delta_{\text{H}}$  1.45 (12H, s, 4 × CH<sub>3</sub>), 3.73 (6H, s, 2 × CH<sub>3</sub>O), 6.83 (4H, d, *J* 8.9 Hz, 2 × ArH) and 7.02 (4H, d, *J* 8.9 Hz, 2 × ArH);  $\delta_{\text{C}}$  22.83, 48.20, 55.40, 111.80, 114.26, 122.15, 141.32, 146.95 and 158.98.

**Reaction of (*E*)- and (*Z*)-3-methyl-2-(*p*-tolylamino)pent-2-enenitrile (*E*)- and (*Z*)-3h.** The reaction of a mixture of (*E*)- and (*Z*)-**3h** (757 mg, 3.78 mmol) with  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  (1.51 g, 8.32 mmol) in the presence of pyridine (658 mg, 8.32 mmol) in EtOH (38 cm<sup>3</sup>) for 22 h gave a diastereomeric mixture of 3,4-diethyl-3,4-dimethyl-2,5-bis(*p*-tolylimino)adiponitrile **14h** (191 mg, 25%) and a diastereomeric mixture of 2-[1-[cyano-(*p*-tolylimino)methyl]-1-methyl-*N*-(*p*-tolyl)propylamino]-3-methylpent-2-enenitrile **15h** (132 mg, 17%).

**14h:** sticky solid;  $\delta_{\text{H}}$  0.80–0.92 (6H, m, 2 × CH<sub>3</sub>), 1.36–1.44 (6H, m, 2 × CH<sub>3</sub>), 1.63–1.87 (2H, m, CH<sub>2</sub>), 2.27 (6H, s, 2 × ArCH<sub>3</sub>), 2.24–2.42 (2H, m, CH<sub>2</sub>), 6.81–6.92 (4H, m, 2 × ArH), 7.05–7.16 (4H, m, 2 × ArH).

**15h:** sticky solid;  $\delta_{\text{H}}$  0.80–0.91 (4.5H, m, CH<sub>3</sub>), 1.05 (1.5H, t, *J* 7.5 Hz, CH<sub>3</sub>), 1.57–1.63 (3H, m, CH<sub>3</sub>), 1.97–2.03 (3H, m, CH<sub>3</sub>), 2.04 (2H, q, *J* 7.5 Hz, CH<sub>2</sub>), 2.22 (3H, s, ArCH<sub>3</sub>), 2.29 (3H, s, ArCH<sub>3</sub>), 2.39 (1H, qd, *J* 7.6, 2.0 Hz, CH<sub>2</sub>), 2.56 (1H, d, *J* 7.6 Hz, CH<sub>2</sub>), 6.77–6.83 (2H, m, ArH), 6.94–7.10 (4H, m, ArH) and 7.10–7.16 (2H, m, ArH); *m/z* 398 (M<sup>+</sup>, 10%), 369 (M<sup>+</sup> – CH<sub>2</sub>CH<sub>3</sub>, 5), 342 (9), 292 (11), 255 (100). *m/z* HRMS (EI) Calc. for  $\text{C}_{26}\text{H}_{30}\text{N}_4$ : [M + H]; 398.2470. Found: *m/z*, 398.2472.

**Reaction of 1,1'-cyclohexylidene-1-phenylaminoacetonitrile 3i.** The reaction of **3i** (998 mg, 4.70 mmol) with  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  (1.88 g, 10.3 mmol) in the presence of pyridine (818 mg, 10.3 mmol) in EtOH (50 cm<sup>3</sup>) for 48 h gave {1'-[cyano(phenylimino)methyl]bicyclohexan-1-yl}phenyliminoacetonitrile **14i** (198 mg, 20%) and {1-[cyano(phenylimino)methyl]-*N*-phenylcyclohexylamino}cyclohexylidenacetonitrile **15i** (312 mg, 31%).

**14i:** mp 224–225 °C (from *n*-hexane–EtOAc) (Found: C, 79.7; H 7.2; N, 13.3.  $\text{C}_{28}\text{H}_{30}\text{N}_4$  requires C, 79.6; H, 7.2; N, 13.3%);

$\nu_{\text{max}}$  (KBr)/cm<sup>-1</sup> 2200 and 1621;  $\delta_{\text{H}}$  1.14–1.41 (6H, m, 3 × CH<sub>2</sub>), 1.56–1.81 (10H, m, 5 × CH<sub>2</sub>), 2.44 (4H, d, *J* 12.3 Hz, 2 × CH<sub>2</sub>), 6.93 (4H, d, *J* 7.9 Hz, 2 × ArH), 7.17 (2H, t, *J* 7.9 Hz, 2 × ArH) and 7.30 (4H, t, *J* 7.9 Hz, 2 × ArH);  $\delta_{\text{C}}$  22.88, 25.46, 29.51, 53.47, 111.66, 119.62, 126.94, 129.18, 147.88 and 149.16.

**15i:** sticky solid (Found: C, 79.4; H, 7.1; N, 13.3.  $\text{C}_{28}\text{H}_{30}\text{N}_4$  requires C, 79.6; H, 7.2; N, 13.3%);  $\nu_{\text{max}}$  (neat)/cm<sup>-1</sup> 2208 and 1626;  $\delta_{\text{H}}$  1.15–1.86 (12H, m, 4 × CH<sub>3</sub>), 1.88–2.10 (2H, m, CH<sub>3</sub>), 2.39–2.53 (4H, m, CH<sub>3</sub>), 2.53–2.68 (2H, m, CH<sub>3</sub>), 6.80 (2H, d, *J* 7.5 Hz, ArH) and 7.04–7.41 (8H, m, 2 × ArH);  $\delta_{\text{C}}$  23.12, 25.08, 25.79, 26.87, 27.65, 29.92, 32.13, 32.82, 66.83, 109.70, 111.19, 118.85, 119.20, 119.52, 125.84, 126.84, 127.87, 129.03, 129.09, 144.79, 146.14, 148.54 and 163.74.

**Reaction of 3-ethyl-2-phenylaminopent-2-enenitrile 3j.** The reaction of **3j** (1.06 g, 5.24 mmol) with  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  (2.09 g, 11.5 mmol) in the presence of pyridine (912 mg, 11.5 mmol) in EtOH (52 cm<sup>3</sup>) for 48 h gave 2-[1-[cyano(phenylimino)methyl]-1-ethyl-*N*-phenylpropylamino]-3-ethylpent-2-enenitrile **15j** (434 mg, 41%); sticky solid (Found: C, 78.5; H, 7.5; N, 14.0.  $\text{C}_{26}\text{H}_{30}\text{N}_4$  requires C, 78.35; H, 7.6; N, 14.1%);  $\nu_{\text{max}}$  (neat)/cm<sup>-1</sup> 2209 and 1633;  $\delta_{\text{H}}$  0.67 (3H, t, *J* 7.5 Hz, CH<sub>3</sub>), 0.98 (6H, t, *J* 7.5 Hz, 2 × CH<sub>3</sub>), 1.11 (3H, t, *J* 7.5 Hz, CH<sub>3</sub>), 2.10 (2H, sextet, *J* 7.3 Hz, CH<sub>2</sub>), 2.29–2.52 (6H, m, 3 × CH<sub>2</sub>), 6.95–7.12 (3H, m, ArH), 7.13–7.34 (5H, m, ArH) and 7.36–7.51 (2H, m, ArH);  $\delta_{\text{C}}$  8.27, 10.36, 12.39, 23.83, 24.86, 25.93, 70.09, 111.56, 113.13, 119.40, 119.58, 123.88, 124.39, 127.07, 128.92, 129.34, 146.62, 148.60, 149.29 and 166.39; *m/z* 398 (M<sup>+</sup>, 14%), 369 (M<sup>+</sup> – CH<sub>2</sub>CH<sub>3</sub>, 14), 342 (29), 306 (15), 269 (100). *m/z* HRMS (EI) Calc. for  $\text{C}_{26}\text{H}_{30}\text{N}_4$ : [M + H]; 398.2470. Found: *m/z*, 398.2472.

#### Reaction of 15a with AlCl<sub>3</sub>

To a solution of **15a** (89 mg, 0.26 mmol) in benzene (3 cm<sup>3</sup>) was added anhydrous AlCl<sub>3</sub> (69 mg, 0.52 mmol). The mixture was stirred for 48 h at rt. Water (30 cm<sup>3</sup>) was added into the mixture and then the mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (30 cm<sup>3</sup> × 2). The combined extract was dried (MgSO<sub>4</sub>). Removal of the solvent, followed by chromatography (2 × 20 cm) of the residue using a mixture of *n*-hexane and EtOAc (5:1) gave 2-(2,3-dihydro-2,2-dimethyl-3-phenylimino-1*H*-indol-1-yl)-3-methylbut-2-enenitrile **18** (29 mg, 35%) and **11a** (7 mg, 12%).

**18:** sticky solid (Found: C, 81.0; H, 6.9; N, 13.1.  $\text{C}_{21}\text{H}_{21}\text{N}_3$  requires C, 80.0; H, 6.7; N, 13.3%);  $\nu_{\text{max}}$  (neat)/cm<sup>-1</sup> 2209, 1660 and 1598;  $\delta_{\text{H}}$  1.39 (3H, s, CH<sub>3</sub>), 1.56 (3H, s, CH<sub>3</sub>), 1.87 (3H, s, CH<sub>3</sub>), 2.22 (3H, s, CH<sub>3</sub>), 6.56 (1H, t, *J* 8.2 Hz, ArH), 6.82 (1H, d, *J* 7.6 Hz, ArH), 7.44 (1H, t, *J* 8.2 Hz, 3 × ArH), 7.61 (1H, d, *J* 7.6 Hz, ArH); *m/z* 315 (M<sup>+</sup>, 36%), 300 (29), 235 (100).

#### General procedure for the synthesis of 1,2-dihydroindol-3-ones 11

A mixture of compound **15** and  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  in HOAc (3 cm<sup>3</sup>) was heated for an appropriate length of time at reflux. The reaction mixture was cooled to rt, followed by addition of water (50 cm<sup>3</sup>), and CH<sub>2</sub>Cl<sub>2</sub> (30 cm<sup>3</sup>), and then neutralized with aqueous Na<sub>2</sub>CO<sub>3</sub>. The mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (30 cm<sup>3</sup> × 2). The combined extract was dried (MgSO<sub>4</sub>). Evaporation of the solvent gave a brown liquid, which was chromatographed on a silica gel column (2 × 20 cm<sup>3</sup>) using a mixture of *n*-hexane and EtOAc (5:1) as the eluent.

**2-(2,3-Dihydro-2,2-dimethyl-3-oxo-1*H*-indol-1-yl)-3-methylbut-2-enenitrile 11a.** The reaction of **15a** (164 mg, 0.48 mmol) with  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  (96 mg, 0.53 mmol) in HOAc (10 cm<sup>3</sup>) for 14 h gave **11a** (86 mg, 75%). From the reaction of **15a** (273 mg, 0.80 mmol) in HOAc (20 cm<sup>3</sup>) for 30 h was obtained **11a** (108 mg, 56%).

**2-(5-Chloro-2,3-dihydro-2,2-dimethyl-3-oxo-1*H*-indol-1-yl)-3-methylbut-2-enenitrile 11b.** The reaction of **15b** (149 mg, 0.36 mmol) with  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  (78 mg, 0.43 mmol) in HOAc



(8 cm<sup>3</sup>) for 96 h gave **11b** (85 mg, 86%); mp 91–92 °C (from *n*-hexane–CH<sub>2</sub>Cl<sub>2</sub>) (Found: C, 65.4; H 5.6; N, 10.1. C<sub>15</sub>H<sub>15</sub>ClN<sub>2</sub>O requires C, 65.6; H, 5.6; N, 10.1%);  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 2960, 2209, 1717 and 1607;  $\delta_{\text{H}}$  1.22 (3H, s, CH<sub>3</sub>), 1.39 (3H, s, CH<sub>3</sub>), 1.81 (3H, s, CH<sub>3</sub>), 2.22 (3H, s, CH<sub>3</sub>), 6.53 (1H, dd, *J* 8.7, 2.2 Hz, ArH), 7.39 (1H, d, *J* 8.7 Hz, ArH) and 7.57 (1H, d, *J* 2.2 Hz, ArH);  $\delta_{\text{C}}$  20.49, 22.01, 22.45, 22.53, 70.59, 105.49, 111.45, 116.10, 120.37, 124.52, 125.00, 137.38, 155.14, 160.38 and 201.41; *m/z* 276 (M<sup>+</sup> + 2, 29%), 274 (M<sup>+</sup>, 89), 259 (44), 231 (100), 152 (51).

**2-(5-Bromo-2,3-dihydro-2,2-dimethyl-3-oxo-1H-indol-1-yl)-3-methylbut-2-enitrile 11c.** The reaction of **15c** (85 mg, 0.17 mmol) with Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (36 mg, 0.20 mmol) in HOAc (4 cm<sup>3</sup>) for 28 h gave **15c** (30 mg, 35%) and **11c** (15 mg, 45%); sticky solid (Found: C, 56.6; H, 4.9; N, 9.0. C<sub>15</sub>H<sub>15</sub>BrN<sub>2</sub>O requires C, 56.4; H, 4.7; N, 8.8%);  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 2990, 2208 and 1698;  $\delta_{\text{H}}$  1.29 (3H, s, CH<sub>3</sub>), 1.47 (3H, s, CH<sub>3</sub>), 1.88 (3H, s, CH<sub>3</sub>), 2.29 (3H, s, CH<sub>3</sub>), 6.55 (1H, d, *J* 8.7 Hz, ArH), 7.60 (1H, dd, *J* 8.7, 2.1 Hz, ArH) and 7.81 (1H, d, *J* 2.1 Hz, ArH);  $\delta_{\text{C}}$  20.55, 22.01, 22.51, 22.61, 70.49, 105.41, 111.85, 111.92, 116.12, 120.93, 127.72, 140.03, 155.45, 160.46 and 201.27; *m/z* 320 (M<sup>+</sup> + 2, 97%), 318 (M<sup>+</sup>, 100), 305 (M<sup>+</sup> + 2 – CH<sub>3</sub>, 44), 303 (M<sup>+</sup> – CH<sub>3</sub>, 45), 277 (81), 275 (83).

**2-(2,3-Dihydro-3-oxo-2,2,7-trimethyl-1H-indol-1-yl)-3-methylbut-2-enitrile 11d.** The reaction of **15d** (70 mg, 0.19 mmol) with Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (42 mg, 0.23 mmol) in HOAc (2 cm<sup>3</sup>) for 18 h gave **11d** (32 mg, 68%); sticky solid;  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 2208, 1698 and 1613;  $\delta_{\text{H}}$  1.20 (3H, s, CH<sub>3</sub>), 1.37 (3H, s, CH<sub>3</sub>), 1.86 (3H, s, CH<sub>3</sub>), 2.16 (3H, s, CH<sub>3</sub>), 2.17 (3H, s, CH<sub>3</sub>), 6.79 (1H, t, *J* 7.5 Hz, ArH), 7.24 (1H, d, *J* 7.2 Hz, ArH) and 7.61 (1H, d, *J* 7.5 Hz, ArH);  $\delta_{\text{C}}$  18.21, 20.77, 22.22, 22.62, 22.74, 70.15, 109.65, 117.04, 120.47, 120.89, 122.45, 123.00, 140.77, 155.94, 157.18 and 203.35; *m/z* 254 (M<sup>+</sup>, 98%), 239 (73), 211 (100), 198 (21). *m/z* HRMS (EI) Calc. for C<sub>16</sub>H<sub>18</sub>N<sub>2</sub>O: [M + H]; 254.1419. Found: *m/z*, 254.1407.

**2-(2,3-Dihydro-3-oxo-2,2,4-trimethyl-1H-indol-1-yl)-3-methylbut-2-enitrile 11e(I) and 2-(2,3-dihydro-3-oxo-2,2,6-trimethyl-1H-indol-1-yl)-3-methylbut-2-enitrile 11e(II).** The reaction of **15e** (254 mg, 0.69 mmol) with Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (151 mg, 0.83 mmol) in HOAc (14 cm<sup>3</sup>) for 6 h gave **11e(I)** (26 mg, 14%); mp 84–86 °C (from *n*-hexane–CH<sub>2</sub>Cl<sub>2</sub>) (Found: C, 75.7; H 7.0; N, 11.0. C<sub>16</sub>H<sub>18</sub>N<sub>2</sub>O requires C, 75.6; H, 7.1; N, 11.0%);  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 2209, 1699 and 1598;  $\delta_{\text{H}}$  1.19 (3H, s, CH<sub>3</sub>), 1.38 (3H, s, CH<sub>3</sub>), 1.80 (3H, s, CH<sub>3</sub>), 2.20 (3H, s, CH<sub>3</sub>), 2.53 (3H, s, CH<sub>3</sub>), 6.36 (1H, d, *J* 8.1 Hz, ArH), 6.58 (1H, d, *J* 7.4 Hz, ArH) and 7.29 (1H, t, *J* 7.8 Hz, ArH);  $\delta_{\text{C}}$  18.31, 20.48, 22.29, 22.47, 22.68, 69.54, 106.13, 107.40, 116.49, 117.33, 121.27, 136.78, 140.82, 157.35, 159.69 and 203.32; *m/z* 254 (M<sup>+</sup>, 98%), 239 (100), 211 (84), 132 (25); and **11e(II)** mp 81–82 °C (from *n*-hexane–CH<sub>2</sub>Cl<sub>2</sub>) (Found: C, 75.3; H 7.35; N, 11.1. C<sub>16</sub>H<sub>18</sub>N<sub>2</sub>O requires C, 75.6; H, 7.1; N, 11.0%);  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 2208, 1704 and 1613;  $\delta_{\text{H}}$  1.19 (3H, s, CH<sub>3</sub>), 1.37 (3H, s, CH<sub>3</sub>), 1.81 (3H, s, CH<sub>3</sub>), 2.21 (3H, s, CH<sub>3</sub>), 2.30 (3H, s, CH<sub>3</sub>), 6.35 (1H, s, ArH), 6.65 (1H, d, *J* 7.9 Hz, ArH) and 7.49 (1H, d, *J* 7.9 Hz, ArH);  $\delta_{\text{C}}$  20.35, 22.03, 22.41 (3 overlapped peaks), 69.99, 105.75, 110.15, 116.34, 116.97, 121.29, 124.79, 149.32, 157.20, 159.99 and 201.86; *m/z* 254 (M<sup>+</sup>, 100%), 239 (75), 211 (84), 174 (20), 132 (30).

**2-(2,3-Dihydro-3-oxo-2,2,5-trimethyl-1H-indol-1-yl)-3-methylbut-2-enitrile 11f.** The reaction of **15f** (142 mg, 0.38 mmol) with Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (84 mg, 0.46 mmol) in HOAc (8 cm<sup>3</sup>) for 4 h gave **11f** (90 mg, 92%); mp 96–97 °C (from *n*-hexane–CH<sub>2</sub>Cl<sub>2</sub>) (Found: C, 75.6; H 7.4; N, 11.1. C<sub>16</sub>H<sub>18</sub>N<sub>2</sub>O requires C, 75.6; H, 7.1; N, 11.0%);  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 2200, 1698 and 1613;  $\delta_{\text{H}}$  1.19 (3H, s, CH<sub>3</sub>), 1.36 (3H, s, CH<sub>3</sub>), 1.80 (3H, s, CH<sub>3</sub>), 2.19 (3H, s, CH<sub>3</sub>), 2.23 (3H, s, CH<sub>3</sub>), 6.49 (1H, d, *J* 8.3 Hz, ArH), 7.27 (1H,

d, *J* 8.3 Hz, ArH) and 7.39 (1H, s, ArH);  $\delta_{\text{C}}$  13.99, 20.29, 21.32, 22.07, 22.32, 69.96, 106.02, 110.11, 116.34, 119.25, 124.45, 129.11, 138.76, 155.16, 159.55 and 202.57; *m/z* 254 (M<sup>+</sup>, 100%), 239 (57), 211 (98), 132 (43).

**2-(2,3-Dihydro-2,5-dimethyl-2-ethyl-3-oxo-1H-indol-1-yl)-3-methylpent-2-enitrile 11h.** The reaction of **15h** (81 mg, 0.20 mmol) with Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (44 mg, 0.24 mmol) in HOAc (1 cm<sup>3</sup>) for 480 h gave **11h** (35 mg, 60%); sticky solid;  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 2968, 2208, 1692 and 1606;  $\delta_{\text{H}}$  0.77–0.83 (3H, m), 1.02 (2H, m), 1.23–1.44 (4H, m), 1.45 (2H, m), 1.75 (1H, m), 1.97 (1H, m), 2.27–2.34 (5H, m), 2.61 (1H, m), 6.47–6.64 (1H, m, ArH), 7.31–7.39 (1H, m, ArH) and 7.47 (1H, m, ArH); *m/z* of isomer-1 282 (M<sup>+</sup>, 50%), 267 (M<sup>+</sup> – CH<sub>3</sub>, 10), 253 (M<sup>+</sup> – CH<sub>2</sub>CH<sub>3</sub>, 100); *m/z* of isomer-2 282 (M<sup>+</sup>, 53%), 267 (M<sup>+</sup> – CH<sub>3</sub>, 10), 253 (M<sup>+</sup> – CH<sub>2</sub>CH<sub>3</sub>, 100). *m/z* HRMS (EI) Calc. for C<sub>18</sub>H<sub>22</sub>N<sub>2</sub>O: [M + H]; 282.1732. Found: *m/z*, 282.1743.

**2-(2,2-Diethyl-2,3-dihydro-3-oxo-1H-indol-1-yl)-3-ethylpent-2-enitrile 11j.** The reaction of **15j** (133 mg, 0.33 mmol) with Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (77 mg, 0.40 mmol) in HOAc (4 cm<sup>3</sup>) for 480 h gave **11j** (15 mg, 15%); sticky solid (Found: C, 77.2; H 8.3; N, 9.6. C<sub>19</sub>H<sub>24</sub>N<sub>2</sub>O requires C, 77.0; H, 8.2; N, 9.45%);  $\nu_{\max}$  (neat)/cm<sup>-1</sup> 2968, 2200, 1698 and 1606;  $\delta_{\text{H}}$  0.71 (3H, t, *J* 7.4 Hz, CH<sub>3</sub>), 0.78 (3H, t, *J* 7.4 Hz, CH<sub>3</sub>), 0.96 (3H, t, *J* 7.5 Hz, CH<sub>3</sub>), 1.20 (3H, t, *J* 7.5 Hz, CH<sub>3</sub>), 1.56 (1H, q, *J* 7.5 Hz, CH<sub>2</sub>), 1.71 (1H, q, *J* 7.5 Hz, CH<sub>2</sub>), 1.89 (1H, q, *J* 7.5 Hz, CH<sub>2</sub>), 2.01 (1H, q, *J* 7.5 Hz, CH<sub>2</sub>), 2.16 (2H, q, *J* 7.5 Hz, CH<sub>2</sub>), 2.58 (2H, octet, *J* 7.5 Hz, CH<sub>2</sub>), 6.49 (1H, d, *J* 8.3 Hz, ArH), 6.79 (1H, t, *J* 7.5 Hz, ArH), 7.42 (1H, t, *J* 8.3 Hz, ArH), 7.58 (1H, d, *J* 7.9 Hz, ArH); *m/z* 296 (M<sup>+</sup>, 22%), 267 (100).

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