

## Reaction of $\omega$ -Vinylalkylamines with Isatin

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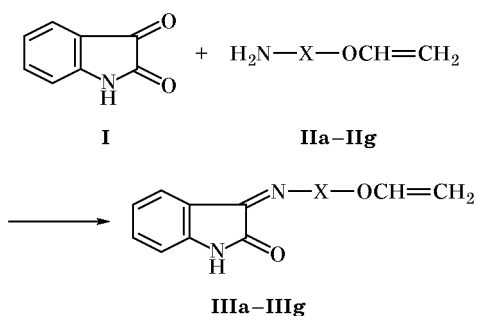
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**Abstract**—3-( $\omega$ -Vinylalkylimino)-2,3-dihydroindol-2-ones and 3-(vinylalkoxyphenylimino)-2,3-dihydroindol-2-ones were synthesized in 34–93% yield by reactions of  $\omega$ -aminoalkyl and aminophenyl vinyl ethers with isatin.

Isatin and its derivatives exhibit versatile biological activity and are widely used in the synthesis of various compounds for technical applications [1]. The present study was aimed at obtaining isatin derivatives having a reactive vinyl group. A combination of the latter with the isatin skeleton was expected to give rise to compounds which may be promising as monomers and intermediate products in organic synthesis [2]. The condensation of isatin (**I**) with vinyl ethers **IIa–IIg** derived from amino alcohols was carried out in methanol at an isatin-to-amine molar ratio of 1:1.1 (Scheme 1).

Scheme 1.



**II, III, X** =  $(\text{CH}_2)_2$  (**a**),  $(\text{CH}_2)_3$  (**b**),  $(\text{CH}_2)_4$  (**c**),  $\text{CH}_2\text{CHMe}$  (**d**),  $\text{CH}_2\text{CH}(\text{OH})\text{CH}_2\text{OCH}_2\text{CH}_2$  (**e**), 1,2- $\text{C}_6\text{H}_4$  (**f**), 1,4- $\text{C}_6\text{H}_4$  (**g**).

Vinyl ethers **IIa–IIc**, **IIf**, and **IIg** derived, respectively, from 2-aminoethanol, 3-amino-1-propanol, 4-amino-1-butanol, *o*-aminophenol, and *p*-aminophenol readily reacted with isatin (**I**) on mixing the reactants at room temperature. As a result, the corresponding 3-imino-2,3-dihydroindol-2-ones **IIIa–IIIc**,

**IIIe**, and **IIIg** were obtained in 50–94% yield. 2-Aminopropyl vinyl ether (**IIe**) and 1-amino-3-[2-(vinylalkoxy)ethoxy]propan-2-ol (**IIe**) showed a considerably weaker reactivity. In these cases, the reaction mixture was heated for 3.5–4 h under reflux to obtain condensation products **IIIe** and **IIIe** in 34–40% yield. No condensation occurred in the reaction of isatin (**I**) with vinyl ethers derived from 2-amino-2-methyl-1-propanol and 2-amino-1-butanol even on prolonged heating of the reactant mixture in the presence of 2 equiv of the amine. Presumably, this is explained by steric shielding of the amino group in the vinyl ether.

Compounds **IIIa–IIIg** were isolated as colored finely crystalline substances. Their color changed from bright yellow (**IIIa–IIIc**) to orange (**IIIe, IIIg**) and red-brown (**IIIe** and **IIIe**). The products are readily soluble in DMF and DMSO, sparingly soluble in ethanol, and insoluble in water, benzene, and chloroform. Their yields, melting points, and elemental analyses are given in Table 1, and Tables 2 and 3 contain, respectively, the IR and  $^1\text{H}$  NMR spectra of **IIIa–IIIg**.

In the  $^1\text{H}$  NMR spectra of all compounds **IIIa–IIIg** we observed a doublet of doublets at  $\delta$  6.38–6.57 ppm which belongs to the vinyl proton nearest to the oxygen atom. In addition, compounds **IIIe** and **IIIg** showed in the spectra doublets of doublets at 4.47–4.73 and 4.36–4.49 ppm from *trans* and *cis* protons of the  $\text{H}_2\text{C}=\text{C}$  fragment. The corresponding protons in the spectra of **IIIa–IIIe** appear as doublets of doublets at  $\delta$  4.17–4.27 and 3.98–4.02 ppm. However, these signals are completely or partially overlapped by those of the substituent at the imino nitrogen atom. The coupling constants for the vinyl protons are as

**Table 1.** Yields, melting points, and elemental analyses of 3-( $\omega$ -vinyloxyalkylamino)-2,3-dihydroindol-2-ones and 3-(vinyloxyphenylamino)-2,3-dihydroindol-2-ones **IIIa–IIIg**

Comp. no.	Yield, %	mp, °C	Found, %			Formula	Calculated, %		
			C	H	N		C	H	N
<b>IIIa</b>	67	162–164	67.09	5.75	12.40	C <sub>12</sub> H <sub>12</sub> N <sub>2</sub> O <sub>2</sub>	66.65	5.59	12.96
<b>IIIb</b>	59	112–114	67.82	6.09	11.98	C <sub>13</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub>	67.81	6.13	12.17
<b>IIIc</b>	56	106–108	68.84	6.78	11.51	C <sub>14</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub>	68.83	6.60	11.47
<b>III d</b>	40	127–128	67.51	6.45	11.85	C <sub>13</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub>	67.81	6.13	12.17
<b>IIIe</b>	34	129–130	62.29	6.09	9.37	C <sub>15</sub> H <sub>18</sub> N <sub>2</sub> O <sub>4</sub>	62.06	6.25	9.65
<b>III f</b>	50	141–143	72.56	4.69	10.43	C <sub>16</sub> H <sub>12</sub> N <sub>2</sub> O <sub>2</sub>	72.72	4.58	10.60
<b>III g</b>	94	220–222	72.47	4.73	10.66	C <sub>16</sub> H <sub>12</sub> N <sub>2</sub> O <sub>2</sub>	72.72	4.58	10.60

**Table 2.** IR spectra of compounds **IIIa–IIIg**

Comp. no.	$\nu$ , cm <sup>-1</sup>
<b>IIIa</b>	490, 575, 605, 640, 660, 700, 725, 740, 760, 800, 815, 820, 870, 915, 975, 990, 1015, 1030, 1060, 1105, 1155, 1195, 1205, 1260, 1285, 1320, 1335, 1350, 1380, 1395, 1465, 1585, 1605, 1645, 1700, 1720, 1730, 1885, 1925, 1965, 2320–2370, 2880, 2905, 2930, 3200–3250
<b>IIIb</b>	490, 510, 580, 600, 650, 740, 765, 780, 800, 820, 860, 870, 890, 915, 930, 960, 990, 1025, 1085, 1100, 1150, 1205, 1255, 1285, 1320, 1335, 1385, 1465, 1520, 1610, 1655, 1710, 1740, 1785, 1900, 1945, 2320–2375, 2870, 2955, 3050, 3070–3085, 3140, 3190, 3420–3450
<b>IIIc</b>	465, 485, 515, 585, 600, 645, 660, 730, 740, 790, 825, 860, 875, 920, 930, 960, 980, 990, 1020, 1030, 1075, 1095, 1100, 1150, 1180, 1205, 1260, 1285, 1335, 1380, 1400, 1470, 1620, 1655, 1715, 1740, 1900, 1940, 2355, 2615, 2660–2690, 2795, 2870, 2880, 2940, 2960, 2985, 3075, 3110, 3155, 3390
<b>III d</b>	480, 640, 665, 740, 810, 970, 1010, 1090, 1185, 1320, 1370, 1465, 1475, 1615, 1640, 1650, 1715, 1730, 2920, 2970, 3380–3440
<b>IIIe</b>	490, 520, 560, 595, 640, 670, 750, 820, 875, 940, 970, 1020, 1040, 1090, 1120, 1170, 1195, 1245, 1320, 1395, 1465, 1480, 1505, 1575, 1615, 1635, 1700, 1715, 2320–2360, 2865, 2910–2930, 3260, 3350–3410
<b>III f</b>	480, 500, 530, 530, 570, 590, 630, 650, 670, 700, 720, 735, 740, 755, 790, 840, 875, 935, 950, 955, 980, 1040, 1085, 1100, 1140, 1190, 1210, 1240, 1260, 1285, 1305, 1330, 1380, 1440, 1455, 1475, 1515, 1530, 1550, 1570, 1585, 1600, 1610, 1635, 1695, 1725, 1915, 1940, 2315–2350, 2975, 3015, 3045, 3105, 3200, 3220–3255
<b>III g</b>	485, 520, 545, 565, 625, 655, 690, 720, 730, 740, 785, 825, 840, 880, 945, 960, 985, 1000, 1085, 1100, 1135, 1155, 1185, 1200, 1240, 1275, 1285, 1300, 1325, 1375, 1405, 1450, 1485, 1585, 1600, 1630, 1710, 1725, 1730, 2315–2360, 3050, 3075, 3100, 3160, 3220–3255, 3420–3440

follows:  $^2J = 1.6\text{--}2.2$ ,  $^3J_{cis} = 6.3\text{--}6.9$ ,  $^3J_{trans} = 13.1\text{--}14.3$  Hz.

The  $^1\text{H}$  NMR spectra of compounds **III f** and **III g** contain a complex multiplet in the region  $\delta$  6.7–7.7 ppm, which corresponds to protons of the dihydroindole fragment and aromatic protons. Compounds **IIIa–IIIe** show in the same region of the spectrum

a simpler pattern: a doublet at  $\delta \sim 7.7$  ppm, a triplet at  $\delta \sim 7.4$  ppm, and a two-proton multiplet at  $\delta \sim 7.1$  ppm.

For compound **IIIa** we also recorded two-dimensional NOESY spectrum (400 MHz). On the basis of this spectrum we assigned the doublet at  $\delta$  7.75 ppm to 4-H, triplets at  $\delta$  7.43 and 7.05 ppm to 6-H and 5-H, respectively, and doublet at  $\delta$  6.91 ppm to 7-H.

**Table 3.**  $^1\text{H}$  NMR spectra of compounds **IIIa–IIIg**

Comp. no.	Chemical shifts $\delta$ , ppm ( $J$ , Hz)
<b>IIIa</b>	4.00 d.d (1H, <i>cis</i> -HC=CO), 4.15 m (4H, NCH <sub>2</sub> CH <sub>2</sub> O), 4.24 d.d (1H, <i>trans</i> -HC=CO), 6.56 d.d (1H, OCH=C), 6.95–7.03 m (2H, 7-H, 5-H), 7.43 t (1H, 6-H), 7.74 d (1H, 4-H), 10.78 br.s (1H, NH)
<b>IIIa<sup>a</sup></b>	4.02 d.d (1H, <i>cis</i> -HC=CO, $^2J = 1.79$ , $^3J_{cis} = 6.85$ ), 4.12 t (2H, NCH <sub>2</sub> , $^3J = 5.15$ ), 4.18 t (2H, OCH <sub>2</sub> ), 4.27 d.d (1H, <i>trans</i> -HC=CO, $^3J_{trans} = 14.32$ ), 6.57 d.d (1H, OCH=C), 6.91 d (1H, 7-H, $^3J = 7.74$ ), 7.05 t (1H, 5-H, $^3J = 7.63$ ), 7.43 t (1H, 6-H, $^3J = 7.70$ ), 7.75 d (1H, 4-H, $^3J = 7.64$ ), 10.82 s (1H, NH)
<b>IIIb</b>	2.09 m (2H, CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> ), 3.81–4.08 m (5H, <i>cis</i> -HC=CO, NCH <sub>2</sub> , OCH <sub>2</sub> ), 4.26 d.d (1H, <i>trans</i> -HC=CO), 6.52 d.d (1H, OCH=C), 6.88–7.02 m (2H, 7-H, 5-H), 7.43 t (1H, 6-H), 7.73 d (1H, 4-H), 10.80 s (1H, NH)
<b>IIIc</b>	1.82 m (4H, CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> ), 3.74–4.25 m (6H, NCH <sub>2</sub> , OCH <sub>2</sub> , OC=CH <sub>2</sub> ), 6.50 d.d (1H, OCH=C), 6.94–7.01 m (2H, 7-H, 5-H), 7.42 t (1H, 6-H), 7.73 d (1H, 4-H), 10.75 s (1H, NH)
<b>III<sup>d</sup></b>	1.15 m (3H, CH <sub>3</sub> ), 3.76–4.25 m (5H, NCH <sub>2</sub> CHO, OC=CH <sub>2</sub> ), 6.45 d.d (1H, OCH=C), 6.92–7.02 m (2H, 7-H, 5-H), 7.41 t (1H, 6-H), 7.75 d (1H, 4-H), 10.29 s (1H, NH)
<b>IIIe</b>	3.98–4.26 m (12H, NCH <sub>2</sub> , OCH <sub>2</sub> CH <sub>2</sub> O, CHCH <sub>2</sub> O, OH, OC=CH <sub>2</sub> ), 6.39 d.d (1H, OCH=C), 6.95–7.07 m (2H, 7-H, 5-H), 7.31 t (1H, 6-H), 7.77 d (1H, 4-H), 10.75 s (1H, NH)
<b>III<sup>f</sup></b>	4.36 d.d (1H, <i>cis</i> -HC=CO), 4.47 d.d (1H, <i>trans</i> -HC=CO), 6.38 d.d (1H, OCH=C), 6.75–7.67 m (8H, NC <sub>6</sub> H <sub>4</sub> O, C <sub>6</sub> H <sub>4</sub> ), 11.01 s (1H, NH)
<b>III<sup>g</sup></b>	4.49 d.d (1H, <i>cis</i> -HC=CO), 4.73 d.d (1H, <i>trans</i> -HC=CO), 6.57 d.d (1H, OCH=C), 6.70–7.61 m (8H, NC <sub>6</sub> H <sub>4</sub> O, C <sub>6</sub> H <sub>4</sub> ), 10.94 s (1H, NH)

<sup>a</sup> The spectrum was recorded on a Bruker DPX-400 instrument at 400.13 MHz.

The  $^1\text{H}$  NMR spectra of compounds **IIIa–IIIe** indicate that they exist as a single stereoisomer. By analogy with published data [3], we believe that this isomer has *E* configuration. No *Z* isomer was detected by  $^1\text{H}$  NMR spectroscopy.

### EXPERIMENTAL

The  $^1\text{H}$  NMR spectra were recorded at 30°C on a Jeol FX-90Q spectrometer (90 MHz) using DMSO-*d*<sub>6</sub> as solvent and HMDS as internal reference. The  $^1\text{H}$  NMR spectrum of **IIIa** was also obtained on a Bruker DPX-400 instrument (400.13 MHz) in DMSO-*d*<sub>6</sub> with HMDS as internal reference. The IR spectra were measured on a Specord 75IR spectrophotometer from samples pelleted with KBr.

**3-( $\omega$ -Vinyloxyalkylimino)-2,3-dihydroindol-2-ones IIIa–IIIe and 3-(vinyloxyphenylimino)-2,3-dihydroindol-2-ones III<sup>f</sup> and III<sup>g</sup>.** A solution of 0.11 mol of vinyloxyalkylamine **IIa–IIc**, **II<sup>f</sup>**, or **II<sup>g</sup>** in 50 ml of ethanol was added with stirring at a temperature not exceeding 20°C to a suspension of 14.71 g (0.1 mol) of isatin (**I**) in 100 ml of ethanol. The mixture spontaneously warmed up to 30–40°C

and was stirred for 2–4 h. It was then left to stand for 16 h at room temperature, and crystals of **IIIa–IIIc**, **III<sup>f</sup>**, or **III<sup>g</sup>** were filtered off and recrystallized from ethanol.

In the reaction of isatin (**I**) with amines **II<sup>d</sup>** and **II<sup>e</sup>**, a mixture of 14.71 g (0.1 mol) of isatin, 0.11 mol of amine **II<sup>d</sup>** or **II<sup>e</sup>**, and 150 ml of ethanol was heated under reflux for 4 h. The mixture was cooled and poured into 200 ml of cold water. The product was filtered off and recrystallized from ethanol.

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