

SHORT  
COMMUNICATIONS

## Synthesis of New Aromatic Isatin Derivatives

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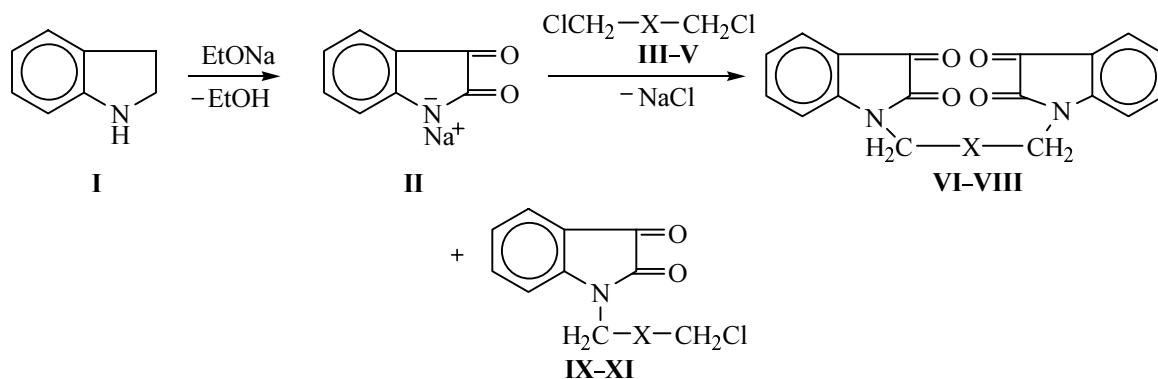
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While continuing our studies in the field of isatin chemistry [1–4], we have synthesized new isatin derivatives containing a fatty–aromatic fragment attached to the pyrrole nitrogen atom. For this purpose, isatin (**I**) was converted into sodium salt **II** which was treated with bis(chloromethyl)dimethylbenzenes **III–V** at a molar ratio of 2 : 1 in DMF. As a result, the corresponding bis(2,3-dioxindol-1-ylmethyl)dimethylbenzenes **VI–VIII** and 1-chloromethyl(dimethyl)benzylindole-2,3-diones **IX–XI** were isolated (Scheme 1). Compound **VIII** was brought

into reaction with morpholine to obtain 1-(4-morpholinomethyl-2,5-dimethylbenzyl)indole-2,3-dione (**XII**) (Scheme 2).

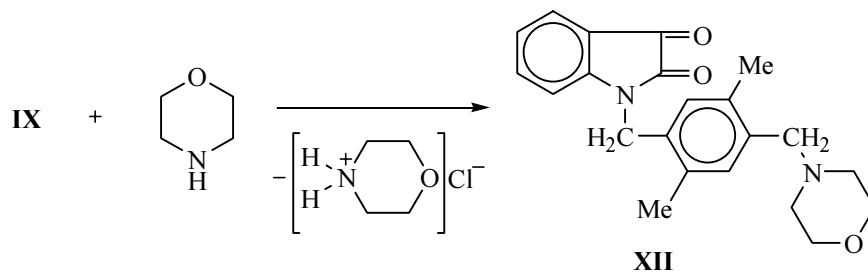
**Substituted dimethylbenzenes VI–XII (general procedure).** A solution of 1 g (4.9 mmol) of bis(chloromethyl)dimethylbenzene **III–V** in 10 ml of anhydrous DMF was added dropwise under stirring to a solution of 1.66 g (9.8 mmol) isatin sodium salt **II** in 10 ml of anhydrous DMF. The mixture was stirred for 24 h at room temperature, and the precipitate was filtered off,

Scheme 1.



**III, VI, IX, X**, X = 2,5-Me<sub>2</sub>C<sub>6</sub>H<sub>2</sub>-1,4; **IV, VII, X**, X = 2,4-Me<sub>2</sub>C<sub>6</sub>H<sub>2</sub>-1,5; **V, VIII, XI**, X = 4,5-Me<sub>2</sub>C<sub>6</sub>H<sub>2</sub>-1,2.

Scheme 2.



washed with water, and recrystallized from water to obtain compounds **VI–VIII**. The filtrate was evaporated under reduced pressure, and the precipitate was washed with water and dried in air. We thus isolated products **IX–VII**.

**1,4-Bis(2,3-dioxindol-1-ylmethyl)-2,5-dimethylbenzene (VI)**. Yield 43%, orange substance, mp 351–353°C,  $R_f$  0.52. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1600 ( $\text{C}=\text{C}_{\text{arom}}$ ); 1670, 1730 ( $\text{C}=\text{O}$ ).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 2.25 s (6H,  $\text{CH}_3$ ), 4.81 s (4H,  $\text{CH}_2\text{N}$ ), 6.79 d (2H, benzene), 7.4 m (8H, indole). Found, %: C 73.09; H 5.00; N 6.31.  $\text{C}_{26}\text{H}_{20}\text{N}_2\text{O}_4$ . Calculated, %: C 73.58; H 4.72; N 6.60. Thiosemicarbazone: light orange crystals, mp 310°C.

**1,5-Bis(2,3-dioxindol-1-ylmethyl)-2,4-dimethylbenzene (VII)**. Yield 40%, orange substance, mp 220–225°C,  $R_f$  0.56. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1610 ( $\text{C}=\text{C}_{\text{arom}}$ ); 1675, 1720 ( $\text{C}=\text{O}$ ).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 2.25 s (6H,  $\text{CH}_3$ ), 4.83 s (4H,  $\text{CH}_2\text{N}$ ), 6.83 d (2H, benzene), 7.45 m (8H, indole). Found, %: C 73.36; H 4.51; N 6.50.  $\text{C}_{26}\text{H}_{20}\text{N}_2\text{O}_4$ . Calculated, %: C 73.58; H 4.72; N 6.60. Thiosemicarbazone: light orange crystals, mp 285–290°C.

**1,2-Bis(2,3-dioxindol-1-ylmethyl)-4,5-dimethylbenzene (VIII)**. In the synthesis of compound **VIII**, the reaction mixture was stirred for 0.5 h and was treated as described above. Yield 54%, orange substance, mp 293°C,  $R_f$  0.52. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1610 ( $\text{C}=\text{C}_{\text{arom}}$ ), 1720 br.s ( $\text{C}=\text{O}$ ).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 2.26 s (6H,  $\text{CH}_3$ ), 4.8 s (4H,  $\text{CH}_2\text{N}$ ), 6.84 d (2H, benzene), 7.43 m (8H, indole). Found, %: C 73.27; H 4.51; N 6.38.  $\text{C}_{26}\text{H}_{20}\text{N}_2\text{O}_4$ . Calculated, %: C 73.58; H 4.72; N 6.60. Thiosemicarbazone: orange crystals, mp 225–227°C.

**1-(4-Chloromethyl-2,5-dimethylbenzyl)indole-2,3-dione (IX)**. Yield 43%, red–orange substance, mp 190°C,  $R_f$  0.52. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1600 ( $\text{C}=\text{C}_{\text{arom}}$ ); 1670, 1730 ( $\text{C}=\text{O}$ ).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 2.25 s (6H,  $\text{CH}_3$ ), 4.5 s (2H,  $\text{CH}_2\text{Cl}$ ), 4.8 s (2H,  $\text{CH}_2\text{N}$ ), 6.81 d (2H, benzene), 7.5 m (4H, indole). Found, %: C 68.71; H 5.00; N 4.08.  $\text{C}_{18}\text{H}_{16}\text{ClNO}_2$ . Calculated, %: C 68.89; H 5.10; N 4.46. Thiosemicarbazone: yellow–orange crystals, mp 173–175°C.

**1-(5-Chloromethyl-2,4-dimethylbenzyl)indole-2,3-dione (X)**. Yield 30%, red–orange substance, mp 185–187°C,  $R_f$  0.57. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1610 ( $\text{C}=\text{C}_{\text{arom}}$ ); 1675, 1720 ( $\text{C}=\text{O}$ ).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 2.26 s (6H,  $\text{CH}_3$ ), 4.51 s (2H,  $\text{CH}_2\text{Cl}$ ), 4.85 s (2H,  $\text{CH}_2\text{N}$ ),

6.81 d (2H, benzene), 7.52 m (4H, indole). Found, %: C 68.59; H 4.97; N 4.12.  $\text{C}_{18}\text{H}_{16}\text{ClNO}_2$ . Calculated, %: C 68.89; H 5.10; N 4.46. Thiosemicarbazone: brown crystals, mp 200°C.

**1-(2-Chloromethyl-4,5-dimethylbenzyl)indole-2,3-dione (XI)**. Yield 24%, red–orange substance, mp 280–285°C,  $R_f$  0.54. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1590 ( $\text{C}=\text{C}_{\text{arom}}$ ), 1720 s, br ( $\text{C}=\text{O}$ ).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 2.25 s (6H,  $\text{CH}_3$ ), 4.53 s (2H,  $\text{CH}_2\text{Cl}$ ), 4.83 c (2H,  $\text{CH}_2\text{N}$ ), 6.82 d (2H, benzene), 7.53 m (4H, indole). Found, %: C 68.71; H 4.89; N 4.00.  $\text{C}_{18}\text{H}_{16}\text{ClNO}_2$ . Calculated, %: C 68.89; H 5.10; N 4.46. Thiosemicarbazone: dark yellow crystals, mp 190°C.

**1-(4-Morpholinomethyl-2,5-dimethylbenzyl)indole-2,3-dione (XII)**. A solution of 0.25 g (2.87 mmol) of morpholine in 2 ml of anhydrous DMF was added dropwise under stirring to a solution of 0.3 g (0.96 mmol) of compound **IX** in 2 ml of anhydrous DMF, and the mixture was stirred for 24 h at room temperature. The precipitate was filtered off and washed with water. Yield 85%, mp 105°C (decomp.). Found, %: C 72.38; H 6.34; N 7.83.  $\text{C}_{18}\text{H}_{16}\text{NO}_2$ . Calculated, %: C 72.51; H 6.64; N 7.69. Thiosemicarbazone: yellow crystals, mp 173°C.

The IR spectra were recorded on a Specord 75IR spectrometer from samples dispersed in mineral oil. The  $^1\text{H}$  NMR spectra were measured on a Varian Mercury-300 instrument (300 MHz) from solutions in  $\text{DMSO}-d_6$  at 30°C using HMDS as internal reference. The purity of the products was monitored by TLC on Silufol UV-254 plates using chloroform–acetone–hexane (1.0:0.4:0.3 for **VI–VIII** and 1.0:0.2:1.6 for **IX–XI**) as eluent; spots were visualized by treatment with iodine vapor.

## REFERENCES

- Mesropyan, E.G., Martirosyan, E.V., Ambartsumyan, G.B., Galoyan, L.A., and Avetisyan, A.A., *Arm. Khim. Zh.*, 1989, vol. 42, p. 264.
- Mesropyan, E.G., Ambartsumyan, G.B., Avetisyan, A.A., Sarkisyan, M.G., and Amaspyan, G.S., *Russ. J. Org. Chem.*, 2001, vol. 37, p. 1476.
- Mesropyan, E.G., Ambartsumyan, G.B., Avetisyan, A.A., and Sarkisyan, M.G., *Russ. J. Org. Chem.*, 2003, vol. 39, p. 1130.
- Mesropyan, E.G., Avetisyan, A.A., Galstyan, A.S., and Sargsyan, M.G., *Uch. Zap. Erevan. Gos. Univ.*, 2003, no. 3, p. 93.