Monatshefte für Chemie 124, 319–321 (1993)

Monatshefte für Chemie
Chemical Monthly

Printed in Austria

Short Communication

Synthesis of Indolo Phenothiazin-6-one Derivatives

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Summary. 5*H*-Indolo[3,2-a]-6*H*-phenothiazin-6-one and its regioisomer 1*H*-Indolo[2,3-a]-6*H*-phenothiazin-6-one were prepared by the condensation of 2-aminobenzenethiol with carbazole-1, 4-dione or with isomeric mixture of bromo-carbazole-1,4-diones.

Keywords. 5*H*-Indolo[3,2,-a]-6*H*-phenothiazin-6-one, 1*H*-Indolo[2,3-a]-6*H*-phenothiazin-6-one.

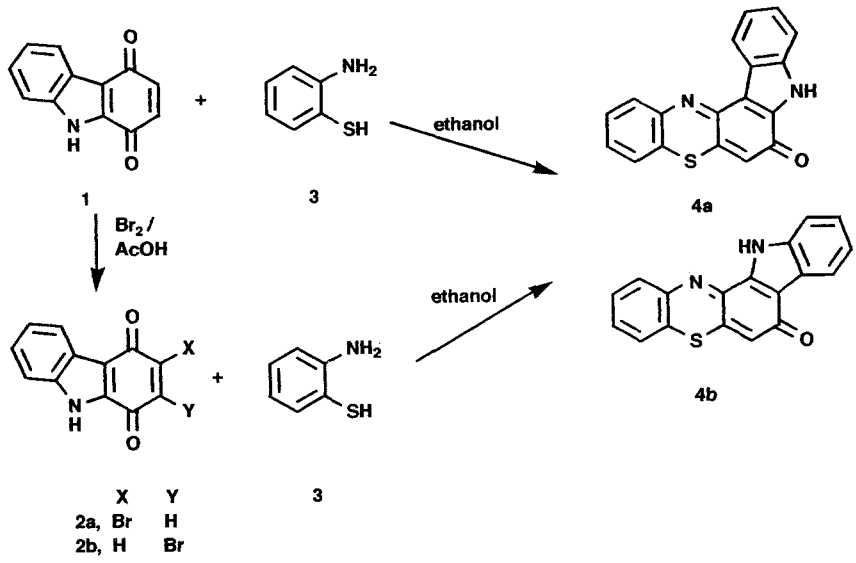
Synthese von Indolo-Phenothiazin-6-on-Derivaten (Kurze Mitteilung)

Zusammenfassung. 5*H*-Indolo[3,2-a]-6*H*-phenothiazin-6-on und sein Regioisomer 1*H*-Indolo[2,3-a]-6*H*-phenothiazin-6-on wurden mittels Kondensation von 2-Aminobenzolthiol mit Carbazol-1,4-dion oder mit einer isomeren Mischung von Bromcarbazol-1,4-dionen hergestellt.

Iminoquinones are widely used in medical practice and in the dye industry. Some phenoxazine and phenothiazine derivatives containing stable iminoquinone system have been studied for biological and pharmaceutical activities and to obtain useful pigments [1–3]. In previous communications, we have described the preparation of some derivatives of the phenothiazine ring system [4–6].

In this paper we report the synthesis of 5*H*-Indolo[3,2-a]-6*H*-phenothiazin-6-one (**4a**) and 1*H*-Indolo[2,3-a]-6*H*-phenothiazin-6-one (**4b**). Bromination of carbazole 1,4-dione (**1**) [7, 8] in acetic acid followed by addition of sodium acetate afforded the regioisomeric mixture of **2a** and **2b**. However, they could not be separated by silica gel column chromatography, their ratio **2a**:**2b** = 4:1 was determined by the appearance of two signals at δ 12.86 and δ 13.06 for NH in a ratio of 4:1.

2-Aminobenzenethiol **3** and **1** or the regioisomeric mixture of **2a** and **2b** were stirred in ethanol at room temperature for 2 h to afford condensation products **4a** and **4b**, which were readily separated by silica gel column chromatography. Their structures were determined by the characteristic chemical shift of NH at δ 12.85 for **4a** and δ 12.7 for **4b**: in **4a** NH is near to the carbonyl oxygen and therefore it is expected slightly downfield [6]. It is worth noting that the isolated yields of 76% for **4a** and 19% for **4b** agree with the anticipated ratio of **2a** and **2b** (4:1), as calculated earlier on the basis of the intensities of NH signals in the ^{1}H-NMR spectra for **2a** and **2b**.



Experimental Part

Melting points were determined on a Yanagimoto micromelting apparatus and are uncorrected. The infrared spectra were recorded on a Jasco A-102 spectrometer. The ^{1}H-NMR spectra were measured on a Varian Gemini-200 spectrometer using tetramethyl silane as internal reference. Mass spectra were obtained with a Hitachi M-200 spectrometer.

Bromination of Carbazole-1,4-dione (**1**)

Quinone **1** (50 mg, 0.252 mmol) was dissolved in acetic acid (1 ml) and the solution was protected from light. Bromine (48 mg, 1.2 eq) was added to it. The mixture was stirred in the dark for 4 h, then a stream of argon was passed for 1 h in order to sweep out excess of bromine. Sodium acetate (80 mg, 3.87 eq) was added, and the mixture stirred over night. Then it was poured into cold water, and extracted with chloroform, washed with 10% sodium bicarbonate solution and water. Solvent was evaporated and the residue was recrystallized from chloroform, m.p. 263–265 °C. IR (KBr): 3200 (NH), 1610 (C=O) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 13.06.12.86 (br, 1:4, NH), 8.19 (m, 1 H, aromatic-H), 7.39 (m, 3 H, aromatic-H), 7.16 (s, 1 H, vinylic-H). MS calcd. for $C_{12}H_6NO_2Br$: 276.08; found *m/z* 276.01 (M^+). Yield 85%.

General Method of Condensation of **1** *or* **2a**, **2b** *with 2-Aminobenzenethiol* (**3**)

To a suspension of (0.18 mmol) of **1** or **2a**, **2b** in 7 ml of ethanol, (0.21 mmol) of **3** was added, and the mixture was stirred at room temperature for 2 h. The resulting solid was filtered and separated by column chromatography with silica gel using hexane: ethyl acetate (8:2) as eluent.

4a: M.p. 298 °C. IR (KBr) 3300 (NH, 1615 (C=O), 1515 (C=N) cm^{-1}. ^{1}H-NMR (*DMSO-d_6*): δ 12.85 (br, 1 H, NH), 8. 82 (m, 1 H, aromatic-H), 8.21 (m, 1 H, aromatic-H), 7.84 (m, 1 H, aromatic-H), 7.65 (m 2 H, aromatic-H), 7.4 (m, 3 H, aromatic-H), 6.65 (s, 1 H, vinylic-H). MS calcd. for $C_{18}H_{10}N_2SO$:302.1; found *m/z* 302.1 (M^+). Yield 76%.

4b: M.p. 292 °C. IR (KBr) 3300 (NH), 1615 (C=O), 1515 (C=N) cm^{-1}. ^{1}H-NMR (*DMSO-d_6*): δ12.7 (br, 1 H, NH), 8.82 (m, 1 H, aromatic-H), 8.21 (m, 1 H, aromatic-H), 7.79 (m, 1 H, aromatic-H), 7.62 (m, 2 H, aromatic-H), 7.4 (m, 3 H, aromatic-H, 6.65 (s, 1 H, vinylic-H). MS calcd. for $C_{18}H_{10}N_2SO$: 302.1; found *m/z* 302.1 (M^+). Yield 19%.

References

[1] Agarwal N. L., Schafer W. J. (1980) J. Org. Chem. **45**: 2155
[2] Bird C. W., Latif M. (1980) Tetrahedron **36**: 529
[3] Terdic M. (1971) Liebigs Ann. Chem. **746**: 200
[4] Kang W. B., Nanya S., Takashi S., Ueno Y. (1989) Monatsh. Chem. **120**: 311
[5] Hasegawa K., Sakakibara M., Ishida T., Ueno Y. (1990) Bull. Chem. Soc. Jpn. **63**: 1467
[6] Sakakibara M., Nagai W., Hasegawa K., Ueno Y. (1991) Pharmazie **46**: 28
[7] Blackhall A., Thomson R. H. (1954) J. Chem. Soc. 3916
[8] Parrick J., Yahya A. (1990) J. Chem. Research(s) 1

Received March 23, 1992. Accepted September 2, 1992