

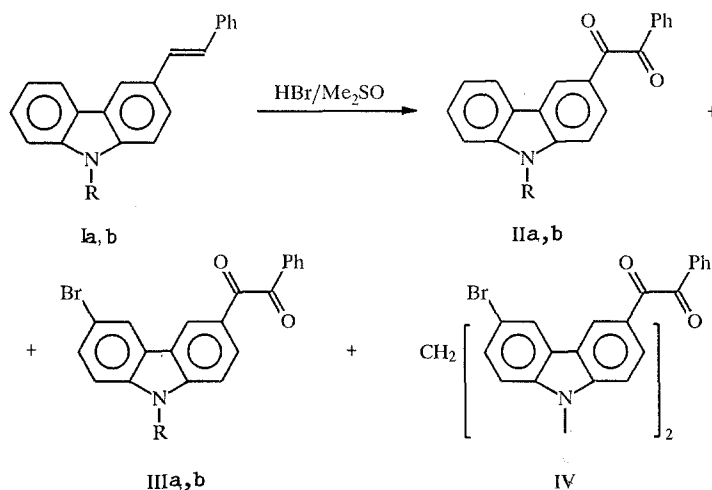
# OXIDATION, BROMINATION, AND METHYLENATION OF CARBAZOLE AND (E)-3-(2-PHENYLETHENYL)CARBAZOLE WITH HBr/DMSO

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*It is shown that oxidation of (E)-3-(2-phenylethenyl)-9-methylcarbazole with HBr/DMSO leads to the formation of 1-(6-bromo-9-methylcarbazol-3-yl)-2-phenylethane-1,2-dione. In the case of (E)-3-(2-phenylethenyl)carbazole, methylenation occurs with formation of 9,9'-bis[3-(2-phenylethane-1,2-dionyl)-6-bromocarbazolyl]methane in addition to oxidation of the double bond and bromination of the phenyl ring. This reagent can also be successfully used for the preparative bromination and methylenation of certain carbazoles.*

It was recently shown that an HBr/DMSO mixture is a unique reagent in terms of its mildness and selectivity for the direct oxidation of stilbenes, vicinal dibromides, diols, and other compounds to 1,2-diketones [1-3]. In the present study we have examined for the first time the preparative potential of this reagent for the oxidation of a heterocyclic compound — (E)-3-(2-phenylethenyl)carbazole (Ia) and its 9-methyl derivative (Ib).

The heating of styrylcarbazole Ib with HBr in DMSO at 60°C for 49 h resulted in oxidation of the olefinic bond to a 1,2-diketone group under much milder conditions than in the oxidation of the stilbene (120°C, 18 h) [1, 3]. However, it transpired that an oxidation, 1-(6-bromo-9-methylcarbazol-3-yl)-2-phenylethane-1,2-dione (IIIb) was formed in 52% yield rather than 1-(9-methylcarbazol-3-yl)-2-phenylethane-1,2-dione (IIb).



I-III a R=H, b R=Me

It follows from the results of a previous study [3] that the high activity of styrylcarbazole Ib toward oxidation by HBr/DMSO relative to stilbene is governed by the well-defined electron-donating properties of the 3-carbazolyl substituents ( $\pi$ -rich heterocycle [4]) relative to a benzene ring. The  $\pi$ -abundance of carbazole is also responsible for the bromination of the

carbazole ring during the oxidation of compound Ib. It follows from the data on the mechanism of the oxidation of stilbenes with HBr/DMSO that the first stage of oxidation is generation of electrophilic bromine followed by addition to the C=C bond [3]. The known tendency of carbazole to undergo electrophilic substitution reactions [4] because of its  $\pi$ -rich nature is responsible for the observed effect of bromination together with oxidation. At the same time, the rates of bromination and oxidation are approximately equal, since neither (E)-[3-(2-phenylethenyl)-6-bromo-9-methyl]carbazole nor 1-(9-methylcarbazol-3-yl)-2-phenylethane-1,2-dione (IIb) occur to any appreciable extent among the reaction products of compound Ib.

The reaction with styrylcarbazole Ia is more complex. In this case the composition of the products is strongly dependent on temperature. Thus, at 60°C for 36 h, i.e., under the same conditions as for compound Ib, an inseparable mixture of the two products IIa and IIIa is formed with an overall yield of 50%. The structure of products IIa and IIIa and their relative proportions were determined from the PMR spectroscopic data. In the region of the resonance absorption of the H-4 and H-5 protons of the carbazole ring of compounds IIa, a doublet signal occurs at 8.47 ppm due to the H-5 proton and there is a singlet at 8.94 ppm due to the H-4 proton. The signals due to the H-4 and H-5 protons of compound IIIa appear as singlets at 9.03 and 8.80 ppm, respectively.

The NH group of compounds IIa and IIIa gives rise to a signal at 12.18 ppm in the PMR spectrum (DMSO- $d_6$ ). The integral relationship of the signals at 8.47, 8.80, 8.94, and 9.03 ppm demonstrates that the mixture contains approximately equal quantities of compounds IIa and IIIa. In the IR spectrum of products IIa and IIIa there is an intense absorption band due to the 1,2-diketone group at 1680  $\text{cm}^{-1}$  and an absorption due to the NH group at 3335  $\text{cm}^{-1}$ .

On increasing the temperature of reaction of styrylcarbazole Ia to 80°C, pure compound IIIa is formed after 36 h in 47% yield. A further increase in temperature of the reaction of compound Ia to 120°C results again in the formation of a mixture of products, one of whose components is compound IIIa. The PMR spectrum of this mixture displays singlet signals at 9.1 and 8.83 ppm, which is an indication of substitution of the carbazole ring at the 3- and 6-positions. In addition, a signal corresponding to a methylene group appears at 6.06 ppm in the spectrum. The intensity of the signals from the free NH group in the PMR and IR spectra of the mixture is substantially reduced compared to compound IIIa. The remaining characteristic absorption bands in the IR spectrum of the product mixture match the spectra of compounds IIa and IIIa. Since the carbazole rings of the products of this reaction are substituted at the 3- and 6-positions, we can relate the presence of a methylene group to the formation of 9,9'-bis[3-(2-phenylethane-1,2-dionyl)-6-bromocarbazolyl]methane (IV), which we did not isolate in a pure state, in addition to compound IIIa.

Bis(carbazolyl)methane derivatives are obtained by reaction of certain carbazole derivatives with formaldehyde in acid media [5]. Dimethyl sulfoxide is also known to undergo partial decomposition to formaldehyde at elevated temperatures [6]. On the basis of these findings, the formation of compound IV may be readily attributed to the reaction of compound IIIa with formaldehyde that is generated from DMSO during oxidation.

In order to confirm the arguments put forward here for the bromination and methylenation of styrylcarbazoles Ia, b during their oxidation with HBr/DMSO and also to study the preparative potential of this system in the synthesis of carbazole derivatives, we have investigated the reaction of 9-methylcarbazole (V) and carbazole (VI) with HBr and DMSO.

9-Methylcarbazole V was brominated with HBr in DMSO at 120°C for 4.5 h to form 3,6-dibromo-9-methylcarbazole (VII) with a preparative yield of 79%.

Carbazole VI reacted with HBr/DMSO under the same conditions to form 9,9'-bis(3,6-dibromocarbazolyl)methane (VIII), which was identified by comparison with an authentic sample obtained by a known method from 3,6-dibromocarbazole and paraformaldehyde in acetic acid [5].

When carbazole was reacted under milder conditions (80°C) for 10 h, 3,6-dibromocarbazole (IX) was formed.

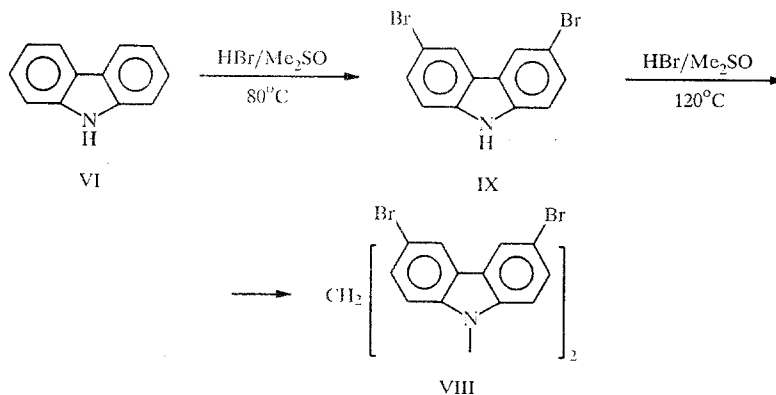


TABLE 1. Properties of Synthesized Compounds

Compound	Empirical formula	Mp, °C	Reaction conditions		IR spectrum, $\nu$ , $\text{cm}^{-1}$	PMR spectrum, $\delta$ , ppm (J, Hz)	Yield, % (method)
			T, °C	time, h			
Ia	C <sub>20</sub> H <sub>15</sub> N	156...158	130...140	8	980(C=C); 3348(NH)	—	57
Ib	C <sub>21</sub> H <sub>17</sub> N	137...139	130...140	8	980(C=C)	—	66
IIIa	C <sub>20</sub> H <sub>12</sub> BrNO <sub>2</sub>	172...173	60	36	650(C-Br); 1680(C=O) 3350(NH)	7,76...7,92 (6H, m, H-1, H-7, H-8, 3-H groups in C <sub>6</sub> H <sub>5</sub> ); 8,17 (3H, d, 6,7, H-2, 2H groups in C <sub>6</sub> H <sub>5</sub> ); 8,77 (1H, s, H-5); 9,03 (1H, s H-4); 12,24 (1H, s NH)	47
IIIb	C <sub>21</sub> H <sub>14</sub> BrNO <sub>2</sub>	157...160	60	48	650 (C-Br); 1680(C=O)	4,10 (3H, s, CH <sub>3</sub> ), 7,48...8,10 (6H, m, H-1, H-7, H-8, 3 H groups in C <sub>6</sub> H <sub>5</sub> ); 8,18 (3H, d, 7,6, H-2, 2H groups in C <sub>6</sub> H <sub>5</sub> ); 8,83 (1H, s, H-5); 9,07 (1H, s, H-4)	52
VII	C <sub>13</sub> H <sub>9</sub> Br <sub>2</sub> N	152...153	120	4,5	620,820 (C-Br)	4,63 (3H, s, CH <sub>3</sub> ); 7,79 (4H, s H-1, H-2, H-7, H-8); 8,65 (2H, s, H-4, H-5)	79
VIII	C <sub>25</sub> H <sub>14</sub> Br <sub>4</sub> N <sub>2</sub>	320...321	120(A) 120(B)	7(A) 10(B)	620 (C-Br)	—	77(A), 52(B)
IX	C <sub>12</sub> H <sub>7</sub> Br <sub>2</sub> N	211...212**	80	10	620,680 (C-Br) 3420 (NH)	—	67

\*Compounds Ia, b were crystallized from butyl acetate, IIIa, b from ethanol, VII from benzene, and VIII and IX from dioxane.

\*\*Literature value [8]: mp 212-213 °C.

Dibromocarbazole IX, in turn, was methylenated with HBr/DMSO at 120 °C to form compound VIII. These results confirm that bromination of the carbazole ring system occurs at a higher rate than the formation of bis(carbazolyl)methane VIII.

Thus, it is shown that the system HBr/DMSO can be used for the bromination of carbazoles and the preparation of bis(carbazolyl)methanes of type VIII in higher yield and greater purity than was previously feasible.

## EXPERIMENTAL

IR spectra were recorded on a UR-20 instrument (petrolatum oil) and PMR spectra were recorded on a BS-497 instrument (100 MHz) in DMSO-d<sub>6</sub> with HMDS as internal standard. The course of the reactions and the purity of the compounds obtained were monitored by TLC on Silufol UV-254 plates [elution system for compounds IIIa, b was benzene, while that for compounds VII, VIII, and IX was hexane-ether (2:1)]. The melting points were determined on a Boetius microheating stage.

The elemental analysis data corresponded to the calculated values.

Initial compounds Ia, b were synthesized by a method similar to that reported in [6] for the synthesis of (E,E)-3,6-bis(phenylethenyl)carbazole. The properties of compounds I-IX are given in Table 1.

**(E)-3-(2-Phenylethenyl)carbazole (Ia).** A mixture of 5.86 g (20 mmoles) of 3-iodocarbazole, 3.89 g (20 mmoles) of tributylamine, 3.24 g (30 mmoles) of styrene, 5 mg of Pd/C, and 30 ml of dimethylformamide was heated (see Table 1). On completion of the reaction, the mixture was poured into water, the precipitate that formed was filtered off, washed initially with water, then washed with hexane, and recrystallized.

**1-(6-Bromo-carbazol-3-yl)-2-phenylethane-1,2-dione (IIIa) and 1-(6-Bromo-9-methylcarbazol-3-yl)-2-phenylethane-1,2-dione (IIIb).** A mixture of 1 mmole of styrylcarbazole I, 5 ml of DMSO, and 1 ml of HBr was heated (see Table 1). After

cooling, the reaction mixture was poured into water and extracted with ether. The extracts were purified by filtration through a layer of silica gel. The ether was distilled off and the residue was crystallized.

**9-Methyl-3,6-dibromocarbazole (VII) and 3,6-Dibromocarbazole (IX).** A mixture of the respective carbazole, 18 ml of DMSO, and 1.4 ml of HBr was heated (see Table 1). The reaction mixture was cooled and poured into water. The precipitate that formed was filtered off, washed until neutral reaction, and crystallized.

**9,9'-Bis(3,6-dibromocarbazolyl)methane (VIII).** A. Compound VIII was obtained by the method indicated above at 120°C for 7 h. The IR spectra and TLC data of compound VIII were identical to those of a sample of the same compounds obtained from 3,6-dibromocarbazole and formaldehyde in acetic acid according to the method of [5]. B. A mixture of 0.325 g (1 mmole) of 3,6-dibromocarbazole IX, 10 ml of DMSO, and 1 ml of HBr was heated at 120°C for 10 h. After cooling, the reaction mixture was poured into water, the precipitate that formed was filtered off, washed until neutral reaction, and recrystallized.

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