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The thermally and photochemically induced 1,6- π -electrocyclization reaction of 3-vinyl-functionalized *N,N'*-dimethyl-2,2'-bisindolyls **4** has been analysed and some reactivity aspects are presented. On the basis of time dependent ^1H nmr and uv spectroscopic measurements the educt transformations can be observed in detail. Some results of the isomerization process of the educts are also given.

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Introduction.

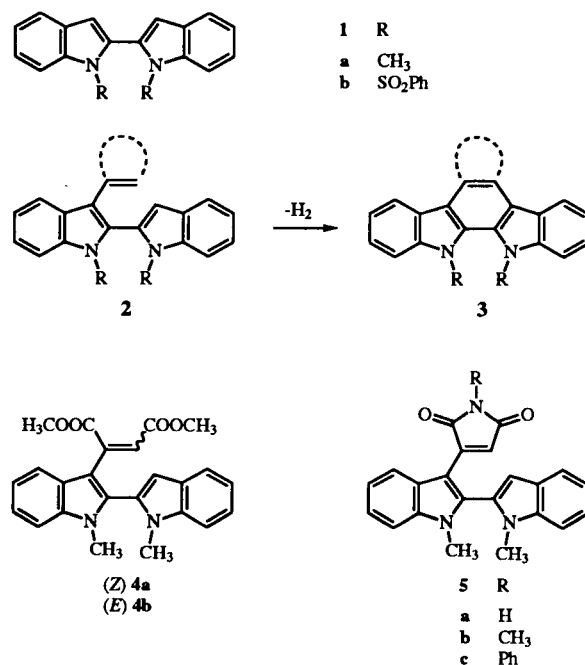
The pericyclic [*b*]annellation reactions of 3-vinylindoles belong to a highly attractive synthetic strategy giving rise to a variety of polycyclic indoles, carbazoles and carbazole alkaloids [1-4]. Among these products some antitumor active natural products like the ellipticines or variants of the staurosporine or rebeccamycin aglycons are of special interest in medicinal chemistry [1,2,5]. In recent years we have studied systematically the functionalization chemistry of 2,2'-bisindolyls **1a**, **1b** and have described new routes to 3-vinyl-2,2'-bisindolyl derivatives and to indolo[*a*]carbazoles [6-9]. In this context the electrocyclization reaction of 3-vinyl-substituted *N,N'*-dimethyl-2,2'-bisindolyl of type **2** to indolo[*a*]carbazoles of type **3** (Scheme 1) has become of preparative interest [10]. In order to expand the synthetic potential of this strategy and to rationalize this methodology it is worthwhile to study some of the structural and/or mechanistic aspects of this annellation procedure (Scheme 1). Thus in the present paper we describe the reactivity pattern/reaction path of electrocyclization of the (formally) 3-vinyl-substituted 2,2'-bisindolyls **4** and **5** which are readily available by Michael type addition of the *N,N'*-dimethyl-2,2'-bisindolyl **1a** with dimethyl acetylene dicarboxylate [7] and maleimides [8].

Results and Discussion.

Electrocyclization of Compounds **4a** and **4b**.

The analytically pure π -diastereomeric 3-vinylindoles **4a** and **4b** were submitted to the thermally induced electrocyclization process (*o*-dichlorobenzene, 230°, >4 hours) and yielded the indolo[*a*]carbazole **6** via a disrotatory ring closure [11] and a dehydrogenation step (Scheme 2). The

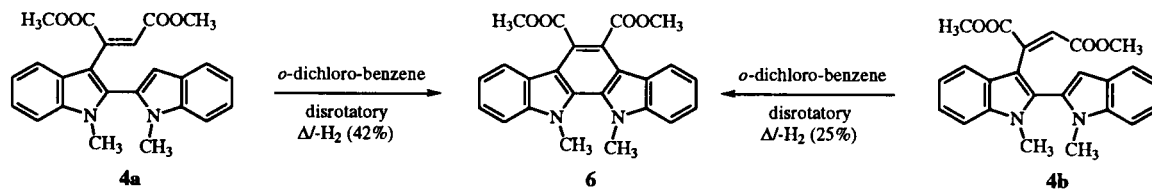
Scheme 1



(*E*)-isomer **4b** is less reactive. On the basis of Dreiding models, we suggest that the transition state formed from the (*Z*)-isomer **4a** is sterically less hindered. Moreover, the reaction control did not give any indication of an isomerization starting from the (*E*) or from the (*Z*) isomer under the specified thermal condition.

The photochemically induced electrocyclization of **4a** and **4b** gave rise in a conrotatory process [10] to the carbazole **6** from **4a** in 45% pure yield and from **4b** in 65% pure yield,

Scheme 2



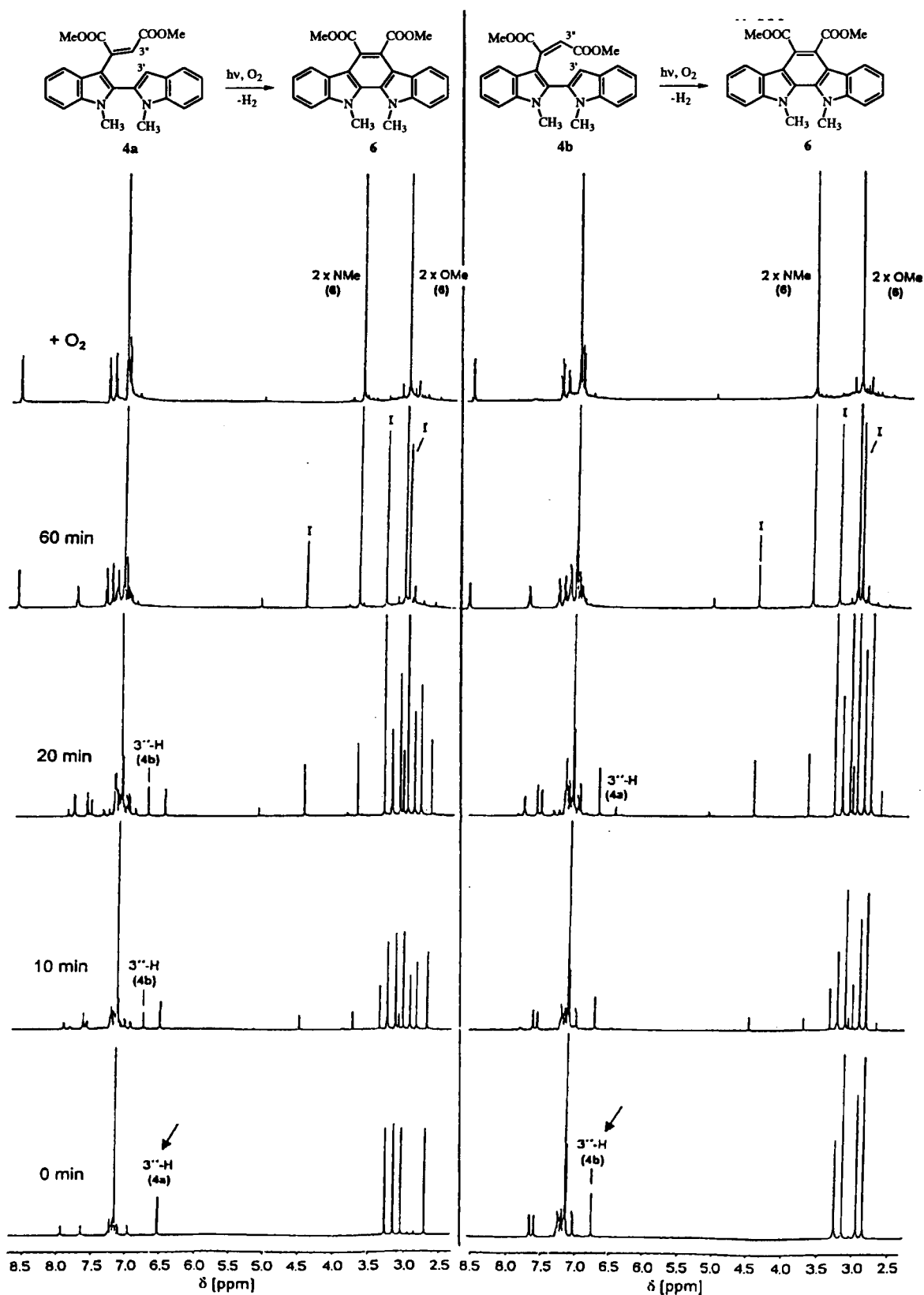


Figure 1. ^1H NMR spectroscopic analysis of electrocyclization reaction (400 MHz, d_6 -benzene); from the bottom: spectra recorded at 0 minutes, 10 minutes, 20 minutes, 60 minutes and after passage of oxygen; left: photochemical transformation of (Z)-4a; right: photochemical transformation of (E)-4b.

respectively. Otherwise the tlc reaction control revealed that the photochemical isomerization from (*Z*)-**4a** to (*E*)-**4b** was almost quantitative after a reaction time of 10 minutes. The analytically pure isomer (*E*)-**4b** did not equilibrate significantly by photochemical induction. The influence of the configuration of **4** on the reaction course was additionally analysed by ^1H nmr and uv spectroscopic measurements. For the nmr studies compound **4a** and separately compound **4b** were dissolved in d_6 -benzene and photochemically analysed under an argon atmosphere. The nmr spectra were recorded after 10, 20 and 60 minutes. According to Figure 1 the following results are of interest: Starting from **4a**, an isomerization reaction to **4b** is visible initially by analysis of the ^3H proton of the vinyl group. After the reaction time of about 1 hour some typical new signals (signals marked with \uparrow) are apparent. We suggest a dihydrocarbazole intermediate as the primary product of the electrocyclization process. After addition of oxygen, these signals disappear completely within the limits of nmr detection (see Figure 1) and are probably due to enhanced dehydrogenation.

For uv-analysis, qualitative uv/vis spectra were performed starting from (*Z*)-**4a** and (*E*)-**4b** in an oxygen atmosphere in order to shift the equilibrium to the full aromatic carbazole **6**. In Figure 2a the qualitative uv/vis spectra of (*Z*)-**4a**, (*E*)-**4b** and product **6** are recorded. In comparison to (*E*)-**4b** the uv/vis spectrum of (*Z*)-**4a** is significantly different and has a quite distinct absorption maxima at $\lambda = 261$ and 330 nm. Thus, this compound will be an appropriate probe for uv spectroscopic reaction control. In the uv radiation of (*E*)-**4b** (Figure 2b) a time dependent change of the spectrum is visualized by a hyperchromic shift of the shoulder at $\lambda = 261$ nm and of the maximum at $\lambda = 300$ nm. The disappearance of the shoulder at $\lambda = 248$ nm and the increase of intensity at $\lambda = 261$ nm can be rationalized by the formation of carbazole **6** at the expense of compound (*E*)-**4b**.

In Figure 2c the time dependent uv/vis spectral change of 3-vinylindole (*Z*)-**4a** is recorded. Already after the first

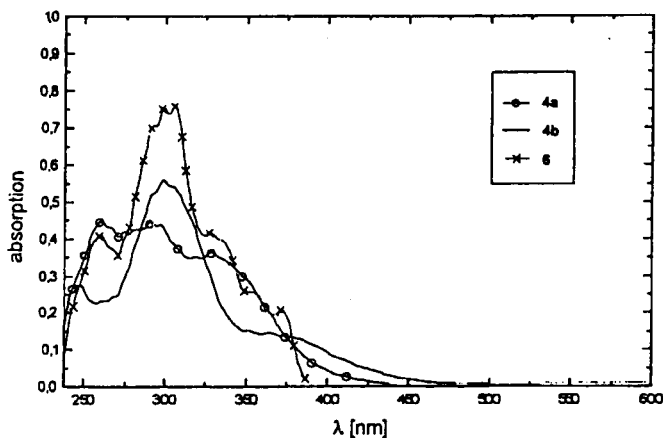


Figure 2a. The uv/vis spectra of (*Z*)-**4a**, (*E*)-**4b** and **6**.

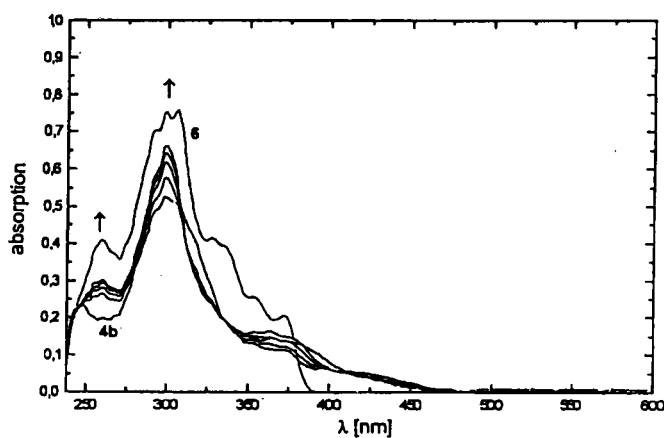


Figure 2b. Time dependent qualitative absorption change of uv/vis spectra of (*E*)-**4b**; traces from the baseline upwards recorded at 0 minutes (*E*-**4b**), 10, 20, 30, 40 and 50 minutes. Concentration of product **6** is increased.

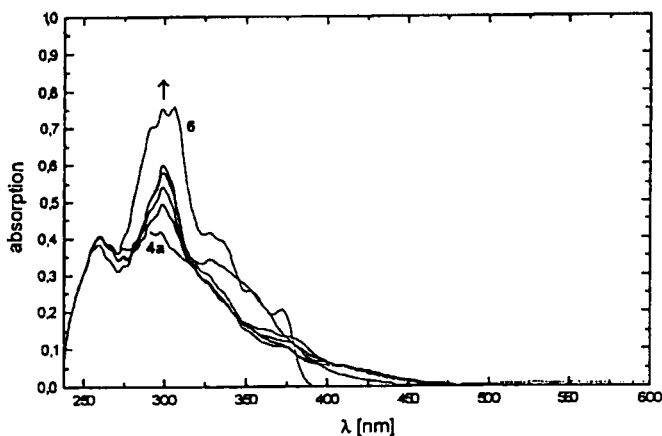
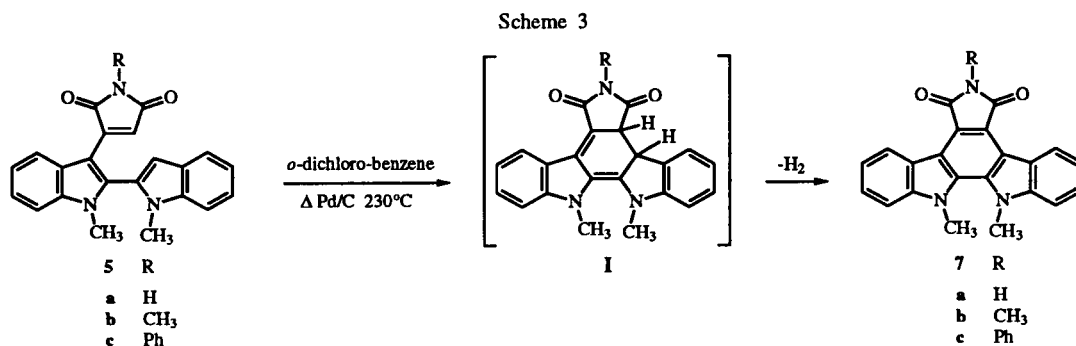


Figure 2c. Time dependent qualitative absorption change of uv/vis spectra of (*Z*)-**4a**; traces from the baseline upwards recorded at 0 minutes (*Z*-**4a**), 10, 20, 30, 40 and 50 minutes. Concentration of product **6** is increased.

10 minutes the flat shoulder at $\lambda = 330$ nm has disappeared. We suggest in this case a fast isomerization of (*Z*)-**4a** to (*E*)-**4b**, fully compatible with the tlc and ^1H nmr reaction control. Moreover saturation of the test solution with argon did not succeed in any retarding of the (*Z*)-(*E*) isomerization.

Electrocyclization of Compounds 5.

The thermally induced electrocyclization of **5a-5c** was performed in *o*-dichlorobenzene at 230° (24-72 hours) to produce the indolo[2,3-*a*]pyrrolo[3,4-*c*]carbazoles **7a-7c** in yields of 15, 25 and 28% respectively [8,9]. The presence of 10% Pd on carbon was necessary to achieve the dehydrogenation step (Scheme 3) and thus shift the equilibrium to the aromatized carbazole product **7**.



The photochemically induced reaction with *N*-phenyl-maleimido-substituted 2,2'-bisindolyl **5c** has been systematically studied as the series exemplar. The preparative yield could be photochemically enhanced about 10% in comparison to the thermally pure procedure. This electrocyclization reaction was also analysed by time dependent uv/vis spectroscopy in dichloromethane in the presence of oxygen in order to shift the electrocyclization equilibrium to the ring-closed product. During the uv radiation the spectra were recorded every 5 minutes. In Figure 3 the absorption curves are recorded up to a reaction time of 35 minutes. From the time dependent course of the spectra two principal products can be derived. The educt **5c** absorption maximum is at $\lambda = 292$ nm ($t = 0$ minutes). In the reaction time from 0-10 minutes a new absorption band appears at $\lambda = 366$ nm. After 15 minutes the product absorption band of the carbazole **7c** at $\lambda = 325$ nm has increased considerably. On the basis of these spectra we suggest, that in the electrocyclization reaction of maleimido-substituted bisindolyl **5c** via an intermediate **I** (Scheme 3) the dehydrogenation step **I** \rightarrow **7c** is probably slower than the electrocyclization step of the educt **5c** to **I** (Scheme 3). Thus, the aromatization reaction is the rate limiting step.

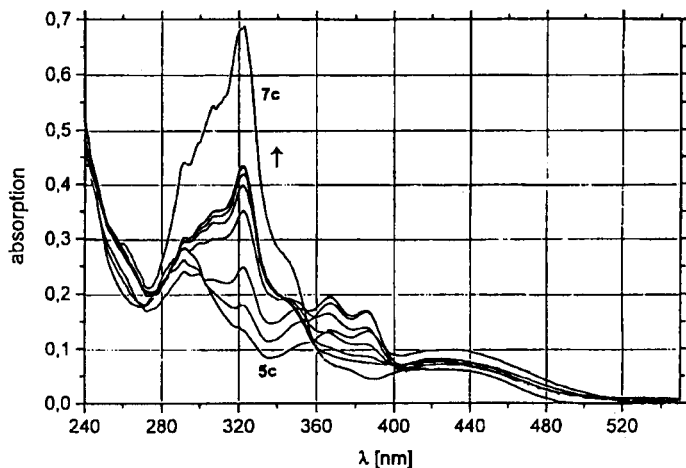


Figure 3. Time-dependent qualitative absorption change of uv/vis spectra of **5c**; traces from the baseline upwards recorded at 0 minutes (**5c**), 5, 10, 15, 20, 25, 30 and 35 minutes. Concentration of product **7c** is increased.

EXPERIMENTAL

Materials and Techniques.

The photochemical reactions were carried out in a water cooled pyrex immersion well apparatus with fluid circulation from Normag (Germany) using a UV-lamp TQ 150 from Heraeus or in a photoreactor A-5000 Q from AMKO using a XBO-1000 W OFR-Xenon-lamp from Osram. The uv/vis spectra were recorded on a MCS224/MCS234-diode array uv/vis-spectrometer. The ¹H-nmr spectroscopic analysis was carried out in a roundabout-radiation apparatus using a 450 W Hg lamp (Hanovia, middle pressure).

Reaction to 4,5-Bis(methoxycarbonyl)-10,11-dimethyl-10,11-dihydroindolo[2,3-*a*]carbazole (**6**) [12].

¹H-NMR spectroscopic Analysis.

Ten mg of compounds **4a** and **4b** were dissolved in 1 ml of *d*₆-benzene; the spectra were recorded after 10, 20, 60 minutes and additionally after 60 minutes and degassing of oxygen.

UV/Vis spectroscopic Analysis.

Compounds **4a** and **4b** 1.99 x 10⁻⁵ mmole/l were dissolved in dichloromethane; radiation wavelengths: $\lambda = 320$ -370 nm; the spectra were recorded after 10, 20, 30, 40 and 50 minutes.

The reaction to 5,6-dimethyl-12-phenyl-indolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-11,13-dione (**7c**) has been reported [12].

UV/Vis Spectroscopic Analysis.

Compound **5c** (1.99 x 10⁻⁵ mmole/l) was dissolved in dichloromethane; radiation wavelength: $\lambda = 405$ nm; the spectra were recorded after 5, 10, 15, 20, 25, 30 and 35 minutes.

Acknowledgements.

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