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[4 + 2]-Cycloadditions to 1′-Phenyl-Substituted 3-Vinylindoles with *N*-Phenylmaleimide: An Access to New [*a*]Anellated Carbazole Derivatives**

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Abstract: The $AlCl_3$-catalyzed [4 + 2]-cycloaddition of 1′-phenyl-substituted 3-vinylindoles with *N*-phenylmaleimide gives rise to new anellated carbazole derivatives with a high *endo*-preference. A dehydrogenative Diels-Alder reaction occurs on cycloaddition with the 3-vinylindole **1e**.

The general interest in the chemistry of carbazoles and structurally related indole derivatives has increased considerably in recent years[1–5] as some of these compounds, both natural products and synthetic compounds, have exhibited pronounced physiological and pharmacological activities. A synthetically attractive concept for the preparation of novel [*b*]anellated indoles and carbazole alkaloids consists of the [4 + 2]-cycloaddition to 3-vinylindoles as 4π-systems[1–7]. The pronounced enophile reactivity of this class of compounds results from the characteristically high HOMO energy[8]. As the synthetic potential of this reaction type, especially with regard to variation of the starting materials, has by no means been fully exploited and as comprehensive knowledge of the regio- and stereochemistry is still lacking, we now report on some new cycloadditions of selected, 1′-phenyl-substituted 3-vinylindoles with *N*-phenylmaleimide (carbo-Diels-Alder reactions).

The 3-vinylindoles **1a–d**[7], in contrast to cycloaddition reactions with 1,1-bis(3-indolyl)-ethenes[1], only react sufficiently rapidly with *N*-phenylmaleimide[9] in the presence of a Lewis acid ($AlCl_3$). Under these mild conditions, which were especially chosen above all to avoid polymerizations of the educts, the new anellated carbazole derivatives **2a-d** were obtained with a high *endo*-preference. The reaction with **1c** resulted in the formation of *endo*- and *exo*-epimers whereas the reactions with **1a**, **1b**, and **1d** led exclusively to the *endo*-cycloadducts (Scheme 1; in the reactions of **1b** and **1c**, the effective product distribution was determined also by quantitative TLC remission measurements(*)).

A time-dependent, quantitative investigation of the course of the reactions of **1b** and **1c** with the dienophile by thin-layer chromatography (TLC) showed a significantly delayed cycloaddition in the case of

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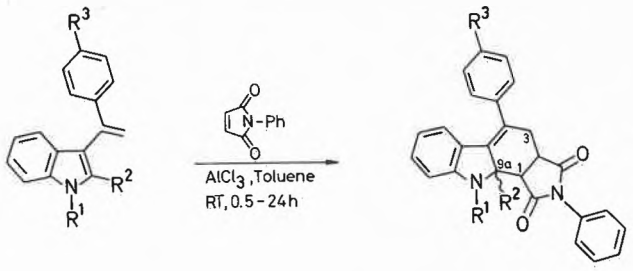
** Cycloadditions to [*b*]Anellated Indole Derivatives, Part 3. – Part 2: U. Pindur, L. Pfeuffer, *Tetrahedron Lett.*, in press.

Scheme 1

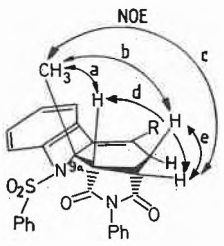


	R^1	R^2	R^3
1a	SO_2Ph	Me	OMe
1b	SO_2Ph	H	H
1c	Me	Me	H
1d	SO_2Ph	Me	H

	R^1	R^2	R^3	yield [%] endo	exo
2a	SO_2Ph	Me	OMe	11.5	-
2b	SO_2Ph	H	H	11.2(24)*	-
2c	Me	Me	H	43(43)*	11(13)*
2d	SO_2Ph	Me	H	4.3	-

1b as compared to that of **1c**. According to the FMO concept, the HOMO energy of the diene moiety in **1b** should be lowered by the *N*-acceptor group as compared to that of **1c** (this should also be valid for **1a** and **1d**)[8]. The pronounced *endo*-selectivity of these cycloadditons can, on the assumption of a $HOMO_{3\text{-vinylindole}}/LUMO_{dienophile}$ cycloaddition, be attributed to energetically favorable frontier orbital interactions[10–12] in the transition state.

Analysis of the relative configurations of the new cycloadducts **2** was based mainly on 400 MHz ^{1}H-NMR decoupling experiments and recordings of the $^1H\{^1H\}$-NOE difference spectra. As exemplarily shown below in the structural formula of **2a**[13], the significantly positive effects NOE (a–e) confirm the *endo*-configuration assigned (for clarity, only one enantiomer is shown).



endo - 2a
R = p-MeO-Ph

In the case of the *exo*-epimer of **2a**, the effect NOE (a) should not be observable as a result of the inversion of the configuration at C-9a. The *endo*-compounds **2b**, **2c**, and **2d** furnish analogous effects.

Scheme 2

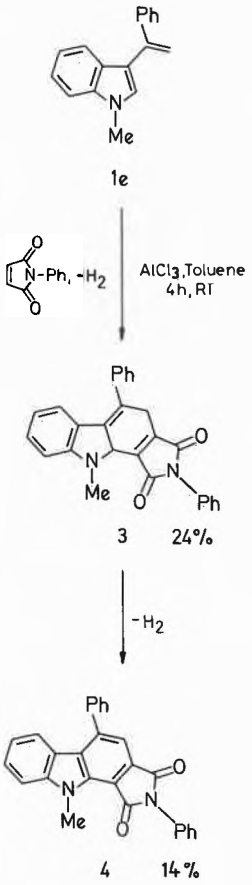


Table 1. Cycloadducts **2a–d**, **3**, and 4. ^{1}H-NMR spectra: Bruker WM 400 (δ scale); mass spectra (70 eV): Varian CH 7A; quantitative TLC analysis: Zeiss MQ 3, PMQ 3 TLC scanner, solvent: methanol or CCl_4, measurements at λ = 325 nm (**2b**), 370 and 385 nm (**2c**), 295 nm (**3**, **4**), silica gel plates 60 F_{254} Merck; *m.p.*: Mettler Fp 1; «flash»-chromatography: silica gel 60, Merck, particle size 0.040–0.063 mm, eluent: petrol ether (40–60 °C)/ethyl acetate.

Product[a]	*m.p.* [°C]	Reaction time [h]	^{1}H-NMR ($CDCl_3$)[b]	MS (70 eV) *m/z* (rel. int. %)
2a (*endo*)	164–165 (petrol ether/ ethyl acetate)	7	1.77 (s, 3H, 9a-CH_3), 3.03 (d, ^2J = 17.8 Hz, 1H, 3-Hβ), 3.20 (dd, ^2J = 17.8 Hz, ^3J = 8.3 Hz, 1H, 3-Hα), 3.39 (t (dd), 1H, 2-H), 3.83 (s, 3H, OCH_3), 4.54 (d, ^3J = 9.0 Hz, 1H, 1-H), 6.6–6.71 (mc, 2H, aromatic), 6.90 (d, ^3J = 8.5 Hz, 2H, methoxyphenyl-H), 7.05–7.13 (mc, 4H, aromatic), 7.27–7.58 (mc, 8H, aromatic), 8.20 (d, 2H, phenylsulfonyl-H)	576 (34), 435 (100)
2b (*endo*)	293 (MeOH)	24	2.64 (ddd, ^2J = 16.1 Hz, ^3J = 9.8 Hz, ^5J = 1.8 Hz, 1H, 3-Hβ), 3.14 (dd, ^2J = 16.1 Hz, ^3J = 7.5 Hz, 1H, 3-Hα), 3.28 (mc, 1H, 2-H), 3.34 (dd, $^3J_{9a,1}$ = 8.3 Hz, $^3J_{1,2}$ = 8.5 Hz, 1H, 1-H), 4.80 (dd, $^3J_{9a,1}$ = 8.3 Hz, ^5J = 1.8 Hz, 1H, 9a-H), 6.76 (t (ddd), 1H, aromatic), 6.81 (d (dd), 1H, aromatic), 7.16 (t (ddd), 1H, aromatic), 7.23 (d (dd), 1H, aromatic), 7.34–7.62 (mc, 13H, aromatic), 7.93 (d (dd), 2H, phenylsulfonyl-H)	304 (6), 134.9 (100)
2c (*endo*)	177–179 (MeOH)	0.5	1.47 (s, 3H, 9a-CH_3), 2.98 (dd, ^2J = 16.6 Hz, ^3J = 6.2 Hz, 1H, 3-H), 2.99 (s, 3H, NCH_3), 3.22 (dd, ^2J = 16.6 Hz, ^3J = 1.8 Hz, 1H, 3-H), 3.37 (ddd, 1H, 2-H), 3.60 (d, ^3J = 8.7 Hz, 1H, 1-H), 6.29 (t (dd), 1H, aromatic), 6.41 (d, ^3J = 7.9 Hz, 1H, 5,8-H), 6.63 (d, ^3J = 7.1 Hz, 1H, 5,8-H), 7.00–7.05 (mc, 3H, aromatic), 7.26–7.40 (mc, 8H, aromatic)	420 (71), 405 (100)
2c (*exo*)	214 (petrol ether/ ethyl acetate)		1.34 (s, 3H, 9a-CH_3), 2.86 (dd, ^2J = 16.4 Hz, ^3J = 10.8 Hz, 1H, 3-H), 3.05 (dd, ^2J = 16.4 Hz, ^3J = 8.0 Hz, 1H, 3-H), 3.15 (s, 3H, NCH_3), 3.33 (ddd, 1H, H-2), 3.57 (d, ^3J = 10.4 Hz, 1H, 1-H), 6.37 (t (dd), 1H, aromatic), 6.49 (d, ^3J = 7.9 Hz, 1H, 5,8-H), 6.62 (d, ^3J = 6.9 Hz, 1H, 5,8-H), 7.08 (t (dd), 1H, aromatic), 7.31–7.52 (mc, 10H, aromatic)	420 (71), 405 (100)
2d (*endo*)	267 (petrol ether)	7	1.77 (s, 3H, 9a-CH_3), 3.03 (d, ^2J = 17.5 Hz, 1H, 3-Hβ), 3.23 (dd, ^2J = 17.5 Hz, ^3J = 9.0 Hz, 1H, 3-Hα), 3.42 (t (dd), 1H, 2-H), 4.56 (d, ^3J = 8.9 Hz, 1H, 1-H), 6.55–6.62 (m, 2H, aromatic), 7.07–7.14 (mc, 4H, aromatic), 7.28–7.58 (mc, 11H, aromatic), 8.10–8.12 (d, 2H, phenylsulfonyl-H)	546 (62), 405 (100)
3[c]	183–184 (petrol ether/ ethyl acetate)	4	2.09 (s, 1H, 9a-H), 3.14 (d, ^2J = 19.4 Hz, 1H, 3-H), 3.39 (d, ^2J = 19.4 Hz, 1H, 3-H), 4.23 (s, 3H, NCH_3), 6.50 (d, ^3J = 8.1 Hz, 1H, 5-H), 6.86 (ddd, 2 × $^3J \approx$ 7.9 Hz, ^4J = 0.7 Hz, 1H, 6-H), 7.22 (t (ddd), 1H, 7-H), 7.35 (d, ^3J = 8.2 Hz, 1H, 8-H), 7.36–7.56 (mc, 8H, aromatic), 7.63–7.65 (mc, 2H, phenylsulfonyl-H)	decomposition
4	273 (petrol ether/ ethyl acetate)	4	4.49 (s, 3H, NCH_3), 7.04 (t (ddd), 1H, aromatic), 7.30–7.66 (mc, 14H, aromatic)[d]	402 (100), 357 (19)

[a] Compounds **2a–d** and **4** gave satisfactory elemental analyses. [b] The designations Hβ and Hα refer to the stereoformula of **2a**. [c] The constitution of **3** was confirmed by 400 MHz ^{1}H-NMR spectroscopic measurements. [d] Measured at 200 MHz.

The 3-vinylindole **1e** reacts with *N*-phenylmaleimide exclusively in the sense of a dehydrogenative Diels-Adler reaction (Scheme 2). The new cycloadducts **3** and **4** can be isolated by means of flash-chromatography. However, the anellated dihydrocarbazole **3** is rather unstable and undergoes ready transformation, albeit with decomposition, to the more stable, delocalized 14π-system **4** (quantitative TLC analysis of the reaction mixture: 62% of **4**). The constitution of **3** is unusual for a cycloadduct of this series[6], but was elucidated by differential $^1H\{^1H\}$-NOE measurements.

Typical Procedure for Cycloaddition of 3-Vinylindoles **1** *with N-Phenylmaleimide:* 111 mg (0.835 mmol) of $AlCl_3$ are suspended in 10 mL of absolute toluene and treated at room temperature with 115 mg (0.668 mmol) of *N*-phenylmaleimide. Then, 0.556 mmol of **1** are added and the resultant mixture is stirred for 0.5–24 h (see Table 1) at 20°C. Subsequently, the reaction mixture is poured into 20 mL of water and extracted with dichloromethane (3 × 25 mL). The organic phase is washed with water (2 × 30 mL), dried with calcium chloride, and concentrated. The residue is separated by flash-chromatography. For quantitative TLC measurements, the residue from the organic phase is dissolved in trichloromethane and chromatographically separated on silica gel 60 plates (Merck) with petrol ether/ethyl acetate (8/2).

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