First Synthesis of Chiral 3-Vinylindoles as 4π-Components for Diels-Alder Reactions

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Received April 25, 1994

The first syntheses of chiral 3- and 2-vinylindoles bearing sulfoxide or (−)-menthyloxy functional groups at the β-vinyl positions by way of procedures based on the Horner-Wadsworth-Emmons and Wittig reactions, respectively, are described. Some Diels-Alder reactions demonstrating the 4π-reactivity of these compounds are reported.

J. Heterocyclic Chem., **32**, 201 (1995).

Introduction.

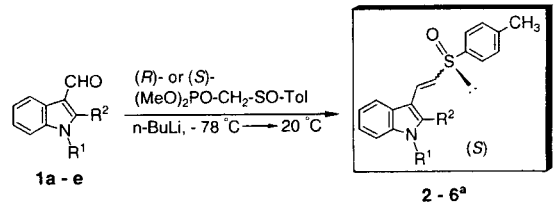
Selectively functionalized 2- and 3-vinylindoles have become versatile building blocks for highly regio- and stereoselective syntheses of a range of [*b*]anellated indoles and other physiologically active heterocyclic compounds by procedures in which a Diels-Alder reaction constitutes the key step [1-8]. Furthermore, the first asymmetric Diels-Alder reactions of vinylindoles to furnish enantiomerically pure tetrahydrocarbazoles were reported recently [4]. In this work, the chiral auxiliary was incorporated into the dienophile and a high π-facial diastereoselectivity was observed [4]. However, before investigations on the scope and limitations of asymmetric Diels-Alder reactions in the vinylheteroarene series can be initiated, there is a necessity to develop new synthetic strategies to the appropriate 3- and 2-vinylindoles for use as 4π-components bearing the chiral auxiliary. But, in general, only a limited number of homochiral 4π-systems is presently available [9]. In the present paper, we describe the first syntheses of chiral 3- and 2-vinylindoles by Horner-Wadsworth-Emmons and Wittig procedures.

Inspection of Dreiding models in combination with the concept of π-diastereofacial selectivity revealed that the incorporation of a chiral auxiliary onto the β-carbon atom of the vinyl function in 2- or 3-vinylindoles should in principle provide sufficient chiral discrimination in the Diels-Alder step for the *s-cis* conformation of the diene moiety.

Results and Discussion.

The application of enantiomerically pure sulfoxides as chiral auxiliaries in several types of asymmetric synthesis [10,13,14,19,21] and also in some Diels-Alder reactions [13,15-18,20] has been widely documented in recent years. Accordingly, the indole-3-carbaldehydes **1a-e** were subjected to a Horner-Wadsworth-Emmons reaction with dimethyl (*R*)- or (*S*)-4-toluenesulfinylmethanephosphonate/*n*-butyllithium [11,12] under mild conditions (Scheme 1). There was no discrimination towards the given *E*/*Z* configuration of the products formed in dependence on the absolute configuration (*R* or *S*) of the employed chiral reagent. But in all examples studied the *E*-π-diastereomer represented the main product and, in most cases, the *E*/*Z* ratio could be analyzed in the crude reaction mixtures (Scheme 1).

Scheme 1



1a - e **2 - 6**[a]

	R^1	R^2
1a	SO_2Ph	H
1b	Me	H
1c	Me	Me
1d	H	Me
1e	SO_2Ph	Me

[a] In the scheme, exemplarily the (*S*)-reagent is introduced.

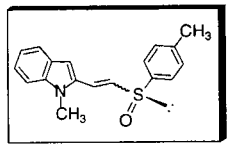
educt	product	config.[a]	*E*/*Z*[b]	yield [%]
1a[c]	**2a**	*S*, *E*	63:37	44
1a[c]	**2b**	*S*, *Z*	63:37	18
1b[c,d]	**3b**	*S*, *Z*	4:1	9
1c[e]	**4**	*R*, *E*	-	47
1d[e]	**5**	*R*, *E*	-	15
1e[e]	**6a**	*R*, *E*	68:32	25
1e[e]	**6b**	*R*, *Z*	68:32	27

[a] Clarified by application of chiral reagent and NMR spectroscopy
[b] *E*/*Z* ratio of crude mixture (^{1}H-NMR)
[c] (*S*)-reagent used
[d] *E*-isomer: yield ~ 35 %; unstable oil
[e] (*R*)-reagent used

The total yields of the respective 3-vinylindoles **2-6** (Scheme 1) reflect the reactivity of the aldehyde function in **1**. This approach appears to be limited to indolecarbaldehydes since neither 3-acetyl-1-methylindole nor 3-benzoyl-1-methylindole reacted with the α-phosphoryl sulfoxide in the expected manner. Nevertheless, both compounds afforded the respective 3-vinylindoles in satisfactory yields (*e.g.* 46 and 92%) when subjected to a Wittig procedure with *e.g.*, $[(Ph)_3PCH_3]^+ Br^-$/*n*-butyllithium. Thus, the generally assumed increased reactivity of phosphoryl-stablized carbanions cannot be invoked in this case. Here it is

postulated that the 3-acetylindole derivative is more likely to dissociate into an enolate whereas the 3-benzoyl derivative has been shown to dimerize within a few minutes; both alternative pathways are catalyzed by the slight excess of *n*-butyllithium employed. However, these two examples obviously extend beyond the scope of the reagent and the indole derivatives because of their reciprocal demands on reactivity, reaction rate, and steric requirements.

1-Methylindole-2-carbaldehyde reacted similarly with the chiral reagent to furnish the (*E*/*Z*)-2-vinylindoles **7** (ratio: 6:4 by ^{1}H nmr spectroscopy). According to tlc monitoring, this reaction proceeds almost quantitatively; the lower yields of products isolated are due to decomposition of the unstable oily products during workup. In general, vinylindoles with low melting points or of oily consistency - such as **4**, **6b**, **7a**, and (*E*)-**3b** - undergo decomposition even on storage at low temperature under inert gas atmospheres. Thus, we were not able to obtain samples of analytical purity.

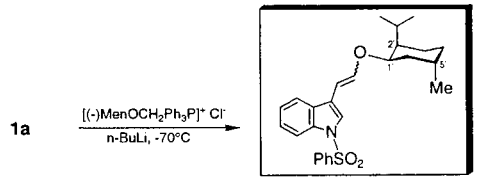


(*R*)-*E*-**7a** (40 %)[a]
(*S*)-*Z*-**7b** (23 %)[a]

[a] (*R*)- resp. (*S*)-reagent used; only the (*R*)-enantiomer is shown

Encouraged by the highly successful Diels-Alder reactions with alkoxy-3-vinylindoles [7], we next focussed our attention on the synthesis of chiral alkoxyvinylindoles and realized an example utilizing (−)-menthol as the chiral reagent for elaboration. Thus, the indole-3-carbaldehyde **1a** reacted with (−)-menthyloxymethyl(triphenyl)phosphonium chloride at −70° to furnish an (*E*/*Z*)-mixture (ratio 4:3 by ^{1}H nmr spectroscopy) of the novel chiral 3-vinylindoles **8a,b** (Scheme 2). The menthyloxymethyl(triphenyl)phosphonium chloride was readily prepared from the α-chloromethyl ether of (−)-menthol and triphenylphosphine as previously reported [22].

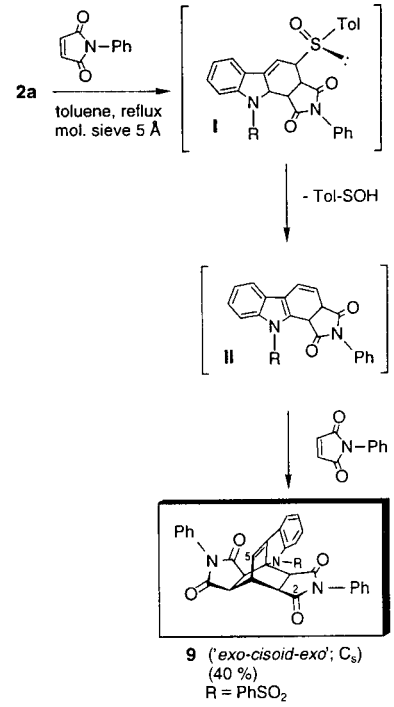
Scheme 2



8a 1'(*R*) 2'(*S*) 5'(*R*)-E (41%)
8b 1'(*R*) 2'(*S*) 5'(*R*)-Z (32%)

Having prepared the new chiral 3- and 2-vinylindoles, we then studied the Diels-Alder reaction of these 4π-systems towards a variety of carbodienophiles. However, in spite of several variations of the reaction conditions [23], the synthetic potential to produce enantiomerically pure carboazole derivatives *via* π-diastereoselection could not be verified. Even so, the Diels-Alder reactions with the optically pure 3-vinylindoles **2a** and **8a** were successful in two cases. Thus, **2a** reacted in a tandem sequence with *N*-phenylmaleimide to furnish the bridged carbazole **9** with a tetrahydrobarrelene skeleton (Scheme 3). This double Diels-Alder product, which had previously been obtained in a related, albeit achiral, procedure [24], probably originates from the primarily formed [4 + 2] cycloadduct **I** which immediately undergoes elimination of *p*-toluenesulfenic acid to furnish **II**. Subsequent trapping of **II** as a 4π-system by another molecule of *N*-phenylmaleimide then yields the more stable product **9** (Scheme 3).

Scheme 3



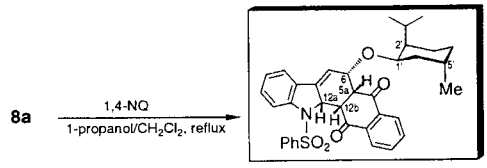
9 ('*exo-cisoid-exo*'; C_s)
(40 %)
R = $PhSO_2$

As a result of several 1-D, high resolution ^{1}H nmr nOe measurements, however, we have been forced to revise the reported [24] configuration of **9**: a diagnostically relevant nOe was observed from the *o*-phenyl proton of the imide ring to the H-5 vinyl proton on the bridge and *vice versa*. The thus established new configuration of **9**, namely *exo-exo* configuration of the imide rings, is in addition fully compatible with the structure of the related 1:2 cycloadduct from 1-methyl-3-propenylindole and maleimide described in ref [25].

From a series of tests of (*E*)-**8a** with several dienophiles, only the [4 + 2] cycloaddition with 1,4-naphthoquinone (1,4-NQ) was successful to furnish a 1:1 mixture (by hplc

and ^{1}H nmr) of the diastereomeric *endo* adducts **10a,b** as an inseparable mixture in a total yield of 62% (Scheme 4). Thus, no π-diastereoselection was observed. The configurations at the four newly formed stereocenters were established by ^{1}H nOe experiments and by the characteristic coupling constants (*e.g.*, $^3J_{6a\beta\text{-}H,5a\beta\text{-}H}$ = 4.97 Hz); of particular relevance are the nOe's from H-12a to H-12b, to H-5a, and to H-6 and *vice versa*.

Scheme 4



10[a]

10a 5a(*R*)6(*R*)12a(*S*)12b(*S*)

10b 5a(*S*)6(*S*)12a(*R*)12b(*R*)

[a] In the scheme exemplarily the configuration of compound **10a** is shown.

EXPERIMENTAL

Materials and Techniques.

For details of the instruments used, see ref [7]. Optical rotations were determined with a Perkin Elmer 241 MC polarimeter using a 10.001 cm cell, concentrations are given in % (w/v). Column chromatography was performed on silica gel 60 (Merck, 0.063-0.200 mm particle size) and "flash" chromatography on silica gel 60 (Merck, 0.04-0.063 mm particle size). The petroleum ether used throughout had the boiling range 40-60°.

All reactions were performed in oven-dried glassware under a nitrogen atmosphere and in solvents of high purity. The yields reported refer to isolated and, in most cases, analytically pure products; the yields in the crude reaction mixtures, as determined by tlc monitoring, were usually higher. Some of the low yields obtained may be attributed to the tendency of vinylindoles to undergo polymerization.

Chiral Vinylindoles **2-7**.

General Procedure.

To a solution of dimethyl (*S*)- or (*R*)-4-toluenesulfinylmethanephosphonate (prepared according to refs [11,12]) in dry tetrahydrofuran (10 ml) was added dropwise under a nitrogen atmosphere at −78° the stated amount of *n*-butyllithium (1.6 *M* solution in hexane). After 1 hour at −78°, a solution of the indolecarbaldehyde **1a-e** in dry tetrahydrofuran (10 ml) was added dropwise. The resultant mixture was stirred for 30 minutes and then allowed to warm to room temperature. The solvents were evaporated after the stated reaction time, the residue was then treated with water (50 ml) and extracted with chloroform (3 x 25 ml). The combined organic phases were washed with brine (30 ml), dried with sodium sulfate, and concentrated. The crude vinylindoles were purified by column or "flash" chromatography.

(*S*)-*E*-[2-(1-Phenylsulfonylindol-3-yl)ethen-1-yl] *p*-Tolyl Sulfoxide (**2a**).

Prepared from dimethyl (*S*)-4-toluenesulfinylmethanephosphonate (0.74 g, 2.8 mmoles), *n*-butyllithium solution (1.9 ml, 3.0 mmoles), and **1a** (0.81 g, 2.8 mmoles); reaction time 4 hours; purification by column chromatography (petroleum ether/ethyl acetate, 1:1) in 44% yield, ratio of **2a:2b** = 63.37 (by ^{1}H nmr), mp 141-142°, $[\alpha]_D^{20}$ = −119° (0.96, chloroform); ir (potassium bromide): ν 1365, 1175, 1045 cm^{-1}; ^{1}H nmr (400 MHz, deuteriochloroform): δ 8.19 (s, 1H, C2'-H), 8.05-8.03 (m, 3H, *o*-PhSO$_2$-H, C4'-H or C7'-H), 7.88 (d, 1H, ^{3}J = 7.9 Hz, C7'-H or C4'-H), 7.69-7.65 (m, 1H, *p*-PhSO$_2$-H), 7.62-7.56 (m, 4H, *o*- or *m*-tolyl-H, *m*-PhSO$_2$-H), 7.50 (d, 1H, ^{3}J = 15.5 Hz, C2-H), 7.42-7.36 (m, 3H, *o*- or *m*-tolyl-H, C5'-H or C6'-H), 7.31 (d, 1H, ^{3}J = 15.5 Hz, C1-H), 7.32-7.28 (m, 1H, C6'-H or C5'-H), 2.4 (s, 3H, *p*-tolyl-CH$_3$); ^{13}C nmr (100.6 MHz, deuteriochloroform): δ 141.8, 140.8, 137.8, 135.5, 134.2, 133.4, 130.2, 129.4, 128.1, 127.1, 126.9, 125.5, 124.9, 124.0, 120.3, 117.5, 113.8, 21.4; ei-ms: m/z (%) 421 (M$^{+\cdot}$, 2), 373 (68), 232 (98), 141 (42), 140 (41), 77 (100).

Anal. Calcd. for $C_{23}H_{19}NO_3S_2$ (421.54): C, 65.53; H, 4.54; N, 3.32. Found: C, 65.48; H, 4.50; N, 3.44.

(*S*)-*Z*-[2-(1-Phenylsulfonylindol-3-yl)ethen-1-yl] *p*-Tolyl Sulfoxide (**2b**).

The *Z*-isomer was obtained from the above preparation of **2a** in 18% yield, mp 155-157°, $[\alpha]_D^{20}$ = +572° (1.06, chloroform); ir (potassium bromide): ν 1375, 1180, 1045, 1035 cm^{-1}; ^{1}H nmr (400 MHz, hexadeuterioacetone): δ 8.24 (d, 1H, J = 0.7 Hz, C2-H), 8.11-8.06 (m, 3H, *o*- or *m*-PhSO$_2$-H, 1 indole-H), 7.75 (d, 1H, J = 7.9 Hz, C4'-H or C7'-H), 7.73-7.68 (m, 1H, *p*-PhSO$_2$-H), 7.64-7.60 (m, 4H, *o*- or *m*-tolyl-H, *o*- or *m*-PhSO$_2$-H), 7.47-7.41 (m, 3H, *o*- or *m*-tolyl-H, 1 indole-H), 7.38 (dd, 1H, J = 1.0 Hz, ^{3}J = 10.51 Hz, C2-H), 7.37-7.33 (pseudo-t, 1H, J = 7.87 Hz, J = 7.31 Hz, ^{4}J = 1 Hz, C5'-H or C6'-H), 6.64 (d, 1H, ^{3}J = 10.5 Hz, C1-H), 2.41 (s, 3H, tolyl-CH$_3$); ^{13}C nmr (100.6 MHz, deuteriochloroform): δ 141.7, 141.0, 137.9, 137.6, 134.6, 134.2, 130.2, 129.6, 129.5, 127.5, 127.0, 126.9, 125.6, 124.4, 123.9, 119.2, 116.0, 113.7, 21.4; ei-ms: m/z (%) 421 (M$^{+\cdot}$, 5), 373 (35), 232 (76), 217 (50), 141 (35), 77 (100).

Anal. Calcd. for $C_{29}H_{19}NO_3S_2$ (421.54): C, 65.53; H, 4.54; N, 3.32. Found: C, 65.60; H, 4.71; N, 3.39.

(*S*)-*Z*-[2-(1-Methylindol-3-yl)ethen-1-yl] *p*-Tolyl Sulfoxide (**3b**).

Compound **3b** was prepared from dimethyl (*S*)-4-toluenesulfinylmethanephosphonate (0.78 g, 3.0 mmoles), *n*-butyllithium solution (2.0 ml, 3.2 mmoles), and **1b** (0.47 g, 3.0 mmoles); reaction time 2 hours; purification by "flash" chromatography (petroleum ether/ethyl acetate, 1/1) in 9% yield, ratio of **3a:3b** after "flash" chromatography = approximately 4:1, mp 96-97° dec, $[\alpha]_D^{20}$ = +410° (0.88, chloroform); ir (potassium bromide): ν 2930, 1475, 1390, 1035 cm^{-1}; ^{1}H nmr (200 MHz, hexadeuterioacetone): δ 8.01 (s, 1H, C2'-H), 7.80 (d, 1H, ^{3}J = 7.7 Hz, C4'-H or C7'-H), 7.63 (d, 2H, ^{3}J = 8.2 Hz, *o*- or *m*-tolyl-H), 7.51 (d, 1H, ^{3}J = 7.9 Hz, C7'-H or C4'-H), 7.45 (d, 1H, ^{3}J = 10.7 Hz, C2-H), 7.39 (d, 2H, ^{3}J = 8.1 Hz, *o*- or *m*-tolyl-H), 7.34-7.26 (pseudo-t, 1H, J = 7.5 Hz, ^{4}J = 1 Hz, C5'-H or C6'-H), 7.24-7.16 (pseudo-t, 1H, J = 7.3 Hz, ^{4}J = 1 Hz, C6'-H or C5'-H), 6.24 (d, 1H, ^{3}J = 10.3 Hz, C1-H), 3.98 (s, 3H, N-CH$_3$), 2.40 (s, 3H, *p*-tolyl-CH$_3$); ^{13}C nmr (100.6 MHz, hexadeuterioacetone): δ 144.1, 141.5, 137.8, 132.5, 131.9, 130.7, 130.2, 128.8, 124.9, 123.3, 121.3, 119.1, 110.9, 110.0, 33.4, 21.2; ei-ms: m/z (%) 295 (M$^{+\cdot}$, 9), 280 (6), 279 (48), 247 (100), 246 (11), 156 (16), 155 (48), 91 (22).

Anal. Calcd. for $C_{18}H_{17}NOS$ (295.41): C, 73.19; H, 5.80; N, 4.74. Found: C, 73.13; H, 5.92; N, 4.82.

(*R*)-*E*-[2-(1,2-Dimethylindol-3-yl)ethen-1-yl] *p*-Tolyl Sulfoxide (**4**).

Compound **4** was prepared from dimethyl (*R*)-4-toluenesulfinylmethanephosphonate (0.78 g, 3.0 mmoles), *n*-butyllithium solution (2.0 ml, 3.2 mmoles), and **1c** (0.52 g, 3.0 mmoles); reaction time time 4 hours; purification by column chromatography (ethyl acetate) in 47% yield, mp 103-104°, $[\alpha]_D^{20}$ = +22° (1.18, chloroform); ir (potassium bromide): ν 2940, 1470, 1370, 1055 cm^{-1}; ^1H nmr (400 MHz, deuteriochloroform): δ 7.68 (d, 1H, ^3J = 7.9 Hz, C4'-H or C7'-H), 7.61-7.57 (m, 3H, *o*- or *m*-tolyl-H, C2-H), 7.30-7.26 (m, 3H, *o*- or *m*-tolyl-H, C7'-H or C4'-H), 7.20 [d (pseudo-t), 1H, ^4J = 1.0 Hz, C5'-H or C6'-H], 7.12 [d (pseudo-t), 1H, J = 7.5 Hz, ^4J = 1 Hz, C6'-H or C5'-H], 6.77 (d, 1H, ^3J = 15.5 Hz, C1-H), 3.67 (s, 3H, N-CH_3), 2.51 (s, 3H, CH_3), 2.38 (s, 3H, CH_3); ^{13}C nmr (100.6 MHz, deuteriochloroform): δ 142.2, 140.9, 140.5, 137.3, 131.8, 129.8, 125.5, 124.5, 122.1, 121.1, 119.6, 109.3, 107.8, 29.8, 21.3, 10.6; fd-ms: m/z (%) 309 ($M^{+\cdot}$, 100).

(*R*)-*E*-[2-(2-Methylindol-3-yl)ethen-1-yl] *p*-Tolyl Sulfoxide (**5**).

The lithium salt of 3-formyl-2-methylindole-1-carboxylic acid was prepared as previously described [26,27] from **1d** (0.64 g, 4.0 mmoles), dissolved in tetrahydrofuran (20 ml), and added to the simultaneously generated sulfoxide ylide; reaction time 20 hours; isolation by "flash" chromatography (petroleum ether/ethyl acetate, 2/1) to furnish **5** in 15% yield, mp 158-161°, $[\alpha]_D^{20}$ = +27° (1.02, chloroform); ir (potassium bromide): ν 3200, 1460, 1390, 1030 cm^{-1}; ^1H nmr (400 MHz, hexadeuteriodimethyl sulfoxide): δ 9.96 (s, 1H, N-H), 7.70 (d, 1H, ^3J = 7.8 Hz, C4'-H or C7'-H), 7.59 (d, 2H, ^3J = 8.1 Hz, *o*- or *m*-tolyl-H), 7.53 (d, 1H, ^3J = 15.5 Hz, C1-H), 7.37 (d, 2H, ^3J = 8.0 Hz, *o*- or *m*-tolyl-H), 7.33 (d, 1H, ^3J = 7.9 Hz, C7'-H or C4'-H), 7.09 (pseudo-t, 1H, C5'-H or C6'-H), 7.03 (pseudo-t, 1H, C6'-H or C5'-H), 6.85 (d, 1H, ^3J = 15.5 Hz, C2-H), 3.36 (s, 3H, C2'-CH_3), 2.34 (s, 3H, *p*-tolyl-CH_3); ^{13}C nmr (100.6 MHz, deuteriochloroform): δ 141.9, 141.0, 139.6, 136.4, 135.7, 132.3, 129.9, 126.1, 124.8, 122.2, 121.0, 119.2, 111.1, 108.1, 21.3, 12.1; fd-ms: m/z (%) 295 ($M^{+\cdot}$, 100).

Anal. Calcd. for $C_{18}H_{17}NOS$ (295.41): C, 73.19; H, 5.80; N, 4.74; S, 10.85. Found: C, 73.15; H, 5.92; N, 4.72; S, 10.90.

(*R*)-*E*-[2-(2-Methyl-1-phenylsulfonylindol-3-yl)ethen-1-yl] *p*-Tolyl Sulfoxide (**6a**).

Compound **6a** was prepared from dimethyl (*R*)-4-toluenesulfinylmethanephosphonate (0.61 g, 2.3 mmoles), *n*-butyllithium solution (2.0 ml, 3.2 mmoles), **1e** (0.70 g, 2.3 mmoles); reaction time 3 hours; purification by column chromatography (petroleum ether/ethyl acetate, 1:1) in 25% yield, ratio of **6a:6b** = 68:32 (by ^1H nmr), mp 169-170.5°, $[\alpha]_D^{20}$ = +129° (1.1, chloroform); ir (potassium bromide): ν 1370, 1190, 1050 cm^{-1}; ^1H nmr (200 MHz, hexadeuterioacetone): δ 8.24 (d, 1H, ^3J = 8.1 Hz, C4'-H or C7'-H), 7.96-7.92 (m, 2H, aromatic H), 7.77 (d, 1H, ^3J = 7.8 Hz, C7'-H or C4'-H), 7.69-7.47 (m, 6H, aromatic H, C2-H), 7.39-7.19 (m, 5H, aromatic H, C1-H), 2.80 (s, 3H, C2'-CH_3), 2.37 (s, 3H, *p*-tolyl-CH_3); ^{13}C nmr (100.6 MHz, deuteriochloroform): δ 141.8, 141.0, 138.9, 138.4, 136.6, 134.0, 133.6, 130.2, 129.4, 127.4, 126.9, 126.4, 124.9, 124.8, 124.1, 119.4, 115.3, 114.7, 21.4, 13.2; fd-ms: m/z (%) 435 ($M^{+\cdot}$, 100).

Anal. Calcd. for $C_{24}H_{21}NO_3S_2$ (435.57): C, 66.18; H, 4.86; N, 3.22; S, 14.72. Found: C, 66.15; H, 4.92; N, 3.34; S, 14.76.

(*R*)-*Z*-[2-(2-Methyl-1-phenylsulfonylindol-3-yl)ethen-1-yl] *p*-Tolyl Sulfoxide (**6b**).

Compound **6b** was isolated as a yellow oil together with **6a** in 27% yield, $[\alpha]_D^{20}$ = −309° (0.98, chloroform); ir (potassium bromide): ν 1380, 1180, 1040 cm^{-1}; ^1H nmr (400 MHz, deuteriochloroform): δ 8.22 (d, 1H, ^3J = 8.3 Hz, C4'-H or C7'-H), 7.80-7.77 (m, 2H, aromatic H), 7.51 (pseudo-t, 1H, aromatic H), 7.43-7.36 (m, 3H, *m*-$PhSO_2$-H, C7'-H or C4'-H), 7.34 (pseudo-t, 1H, C5'-H or C6'-H or *p*-$PhSO_2$-H), 7.27 (pseudo-t, 1H, C6'-H or C5'-H or *p*-$PhSO_2$H), 7.21 (d, 2H, ^3J = 8.4 Hz, *o*- or *m*-tolyl-H), 7.17 (d, 2H, ^3J = 8.3 Hz, *o*- or *m*-tolyl-H), 6.86 (dd, 1H, ^3J = 10.0 Hz, J = 0.8 Hz, C2-H), 6.60 (d, 1H, ^3J = 10.0 Hz, C1-H), 2.62 (s, 3H, C2'-CH_3), 2.34 (s, 3H, *p*-tolyl-CH_3); ^{13}C nmr (100.6 MHz, deuteriochloroform): δ 142.5, 141.6, 141.0, 139.0, 136.4, 134.8, 133.9, 130.0, 129.4, 128.7, 128.4, 126.3, 124.9, 124.2, 124.1, 119.0, 116.2, 114.8, 21.3, 14.4; fd-ms: m/z (%) 435 ($M^{+\cdot}$, 100).

(*R*)-*E*-[2-(1-Methylindol-2-yl)ethen-1-yl] *p*-Tolyl Sulfoxide (**7a**).

Compound **7a** was prepared as an oil from dimethyl (*S*)-4-toluenesulfinylmethanephosphonate (0.78 g, 3.0 mmoles), *n*-butyllithium solution (2.0 ml, 3.2 mmoles), and *N*-methylindole-2-carbaldehyde (0.47 g, 3.0 mmoles); reaction time 1 hour at room temperature; purification by "flash" chromatography (ethyl acetate) in 40% yield, ratio of **7a:7b** = 64:36 (by ^1H nmr), $[\alpha]_D^{20}$ = +12° (1.38, chloroform); ir (potassium bromide): ν 2950, 1465, 1385, 1050 cm^{-1}; ^1H nmr (400 MHz, deuteriochloroform): δ 7.57 (d, 2H, ^3J = 7.2 Hz, *o*- or *m*-tolyl-H), 7.54 (d, 1H, ^3J = 7.7 Hz, C4'-H or C7'-H), 7.47 (d, 1H, ^3J = 15.2 Hz, C2-H), 7.33-7.27 (m, 3H, *o*- or *m*-tolyl-H, C7'-H, or C4'-H), 7.23 (pseudo-t, 1H, J = 7.78 Hz, J = 6.93 Hz, ^4J = 1 Hz, C5'-H or C6'-H), 7.08 (pseudo-t, 1H, C6'-H or C5'-H), 6.85 (d, 1H, ^3J = 15.2 Hz, C1-H), 6.76 (s, 1H, C3'-H), 3.82 (s, 3H, N-CH_3), 2.40 (s, 3H, *p*-tolyl-CH_3); ^{13}C nmr (100.6 MHz, deuteriochloroform): δ 141.9, 140.6, 138.6, 134.2, 133.2, 130.2, 127.4, 125.0, 124.2, 123.2, 121.1, 120.3, 109.5, 102.8, 30.1, 21.4; ei-ms m/z (%) 295 ($M^{+\cdot}$, 14), 247 (46), 232 (5), 172 (17), 156 (31), 155 (100), 154 (27).

(*S*)-*Z*-[2-(1-Methylindol-2-yl)ethen-1-yl] *p*-Tolyl Sulfoxide (**7b**).

Compound **7b** was obtained together with **7a** as described above for the preparation of (*R*)-**7a** but using the (*S*)-reagent in 23% yield, mp 171-172° dec, $[\alpha]_D^{20}$ = +1378° (0.84, chloroform); ir (potassium bromide): ν 2930, 1460, 1390, 1030 cm^{-1}; ^1H nmr (400 MHz, deuteriochloroform): δ 7.66-7.61 (m, 3H, *o*- or *m*-tolyl-H, C4'-H or C7'-H), 7.33-7.30 (m, 3H, *o*- or *m*-tolyl-H, C7'-H or C4'-H), 7.28 [d (pseudo-t), 1H, ^4J = 1.0 Hz, C5'-H or C6'-H), 7.15-7.08 (m, 2H, C6'-H or C5'-H, C2-H), 7.07 (s, 1H, C3'-H), 6.49 (d, 1H, ^3J = 10.6 Hz, C1-H), 3.75 (s, 3H, N-CH_3), 2.40 (s, 3H, *p*-tolyl-CH_3); ^{13}C nmr (100.6 MHz, deuteriochloroform): δ 141.4, 138.2, 137.3, 132.3, 130.1, 127.3, 126.1, 124.3, 123.6, 121.5, 120.4, 109.5, 107.2, 30.0, 21.3; ei-ms: m/z (%) 295 ($M^{+\cdot}$, 71), 247 (41), 246 (30), 232 (10), 231 (23), 172 (76), 156 (27), 155 (100), 154 (57), 144 (59), 105 (11), 91 (18), 77 (19).

Anal. Calcd. for $C_{18}H_{17}NOS$ (295.41): C, 73.19; H, 5.80; N, 4.74; S, 10.85. Found: C, 73.19; H, 5.96; N, 4.73; S, 10.86.

Chiral Vinylindoles **8**.

General Procedure.

To a suspension of (−)-menthyloxymethyl(triphenyl)phosphonium chloride [22] (5.00 g, 10.7 mmoles) in dry tetrahydrofuran (30 ml) was added dropwise under a nitrogen atmosphere *n*-butyllithium (1.6 *M* solution in hexanes, 7 ml) at −70°. After 15 minutes, a solution of the indolecarbaldehyde **1a** (1.00 g, 5.7 mmoles) in dry tetrahydrofuran (10 ml) was also added dropwise at −70°. The resultant mixture was stirred at −40° for 12 hours, allowed

to warm to room temperature, and was then poured onto ice. The aqueous layer was extracted with diethyl ether (2 x 25 ml), the organic layers were combined, dried with magnesium sulfate, and concentrated. The residue was purified by "flash" chromatography with chloroform/*n*-hexane, 3/5 v/v).

1′(*R*),2′(*S*),5′(*R*)-*E*-1-(1-Benzenesulfonylindol-3-yl)-2-menthyloxyethene (**8a**).

Compound **8a** was isolated as a colorless oil in 41% yield, bp not determined, $[\alpha]_D^{20} = -161°$ (1.16, chloroform); ir (sodium chloride): ν 1590, 1350, 1160, 1070 cm^{-1}; ^1H nmr (400 MHz, deuteriochloroform): δ 7.98 (d, 1H, ^3J = 8.3 Hz, aromatic H), 7.85 (d, 2H, ^3J = 7.95 Hz, aromatic H), 7.55-7.47 (m, 3H, aromatic H), 7.41-7.37 (m, 3H, aromatic H), 7.32-7.25 (m, 1H, aromatic H), 6.93 (d, 1H, ^3J = 12.68 Hz, C2-H), 5.92 (d, 1H, ^3J = 12.67 Hz, C1-H), 3.60 (dt, 1H, ^3J = 4.29 Hz, ^3J = 10.72 Hz, menthyl H), 2.17-2.08 (m, 2H, menthyl H), 1.71-1.65 (m, 2H, menthyl H), 1.44-1.36 (m, 2H, menthyl H), 1.09-0.95 (m, 2H, menthyl H), 0.93 (d, 3H, ^3J = 6.47 Hz, CH_3), 0.92 (d, 3H, ^3J = 7.06 Hz, CH_3), 0.80 (d, 3H, ^3J = 6.96 Hz, CH_3); fd-ms: m/z (%) 437.2 ($M^{+\cdot}$, 100).

Anal. Calcd. for $C_{26}H_{31}NO_3S$ (437.60): C, 71.36; H, 7.14; N, 3.20; S, 7.40. Found: C, 71.08; H, 7.21; N, 3.18; S, 7.40.

1′(*R*),2′(*S*),5′(*R*)-*Z*-1-(1-Benzenesulfonylindol-3-yl)-2-menthyloxyethene (**8b**).

Compound **8b** was isolated as a colorless oil in 32% yield, bp not determined, $[\alpha]_D^{20} = -189°$ (1.11, chloroform); ir (sodium chloride): ν 1590, 1355, 1170, 1080 cm^{-1}; ^1H nmr (400 MHz, deuteriochloroform): δ 7.97 (m, 2H, aromatic H), 7.84 (d, 2H, ^3J = 7.60 Hz, C2-PhSO$_2$, C6-H), 7.52-7.46 (m, 2H, aromatic H), 7.40-7.36 (m, 2H, aromatic H), 7.30-7.26 (m, 1H, aromatic H), 7.23-7.19 (m, 1H, aromatic H), 6.42 (d, 1H, ^3J = 6.44 Hz, C2-H), 5.36 (d, 1H, ^3J = 6.44 Hz, C1-H), 3.63 (dt, 1H, ^3J = 6.37 Hz, ^3J = 10.75 Hz, menthyl H), 2.21-2.08 (m, 3H, menthyl H), 1.75-1.70 (m, 2H, menthyl H), 1.60-1.53 (m, 1H, menthyl H), 1.24-1.14 (m, 2H, menthyl H), 0.98 (d, 3H, ^3J = 7.07 Hz, CH_3), 0.94 (d, 3H, ^3J = 6.57 Hz, CH_3), 0.82 (d, 3H, ^3J = 6.94 Hz, CH_3); fd-ms: m/z (%) 437.2 ($M^{+\cdot}$, 100).

Anal. Calcd. for $C_{26}H_{31}NO_3S$ (437.60): C, 71.36; H, 7.14; N, 3.20; S, 7.40. Found: C, 71.11; H, 7.10; N, 3.07; S, 7.32.

2,14-Diphenyl-10-phenylsulfonyl-1,3,3aα,4α,10,10bα,12α,13,14,-15-decahydro-11α*H*,4β,10aβ-[3′,4′]-*exo*-pyrrolo-2*H*,10aα*H*-pyrrolo[3,4-*a*]carbazole-1,3,13,15-tetraone (**9**).

In a suspension of 5 Å molecular sieves (approximately 5 g) in dry toluene (15 ml) **2a** (100 mg, 0.24 mmoles) was dissolved at room temperature under a nitrogen atmosphere. After 30 minutes, *N*-phenylmaleimide (300 mg, 1.73 mmoles) was added in portions of 100 mg (two further 100 mg portions were added after 3.5 and 6 days). The resultant mixture was heated under reflux for 7 days. The molecular sieves were then filtered off, washed with toluene (5 x 10 ml), and the filtrate and washings were evaporated. The residue was purified by "flash" chromatography (petroleum ether/ethyl acetate, 1/1) to furnish the product in 40% (60 mg) yield, mp 239-243°; ir (potassium bromide): ν 1720, 1380 cm^{-1}; ^1H nmr (400 MHz, hexadeuterioacetone): δ 8.22 (m_c, 2H, *o*-PhSO$_2$-H), 7.82 (d, 1H, ^3J = 8.38 Hz, C9-H), 7.57-7.49 (m, 4H, C6-H, *m*- and *p*-PhSO$_2$-H), 7.35-7.25 (m, 7H, C8-H, *m*- and *p*-N-Ph-H), 7.00 (m_c, 1H, C7-H), 6.89 (m_c, 4H, *o*-N-Ph-H), 6.56 (d, 1H, ^3J = 6.20 Hz, C5-H), 4.52 (d, 2H, ^3J = 8.46 Hz, C10b-H, C11-H), 3.98 (m_c, 1H, ^3J = 6 Hz, ^3J = 3 Hz, C4-H), 3.70 (dd, 2H, ^3J = 2.9 Hz, ^3J = 8.5 Hz, C3a-H, C12-H); ^{13}C nmr (100.6 MHz, hexadeuterioacetone): δ 176.0, 172.9, 141.8, 133.9, 133.3, 131.7, 129.5, 129.0, 127.4, 124.1, 123.5, 122.2, 114.6, 112.8, 72.2, 45.0, 42.9, 36.8; ei-ms: m/z (%) 627.15 ($M^{+\cdot}$, 9), 454 (10), 194 (25), 167 (25), 166 (100), 77 (26).

Anal. Calcd. for $C_{36}H_{25}N_3O_6S$ (627.68): C, 68.89; H, 4.01; N, 6.69; S, 5.11. Found: C, 68.76; H, 4.30; N, 6.53; S, 5.21.

Cycloaddition Reaction of Vinylindole **8a** with 1,4-Naphthoquinone.

Preparation of **10**.

A solution of 1,4-naphthoquinone (250 mg, 1.58 mmoles) in 1-propanol (15 ml) was rapidly added to a solution of **8a** (310 mg, 0.71 mmoles) in a mixture of 1-propanol (30 ml) and dichloromethane (5 ml) under a nitrogen atmosphere. The resultant mixture was heated under reflux for 24 hours and then stirred at room temperature for further 72 hours. The solution was concentrated under reduced pressure whereupon colorless crystalline plates began to separate. The crystals were filtered off and dried to furnish a mixture of **10a** and **10b**.

1′(*R*),2′(*S*),5′(*R*),5a(*R*),6(*R*),12a(*S*),12b(*S*)-12-Benzenesulfonyl-6-menthyloxy-5,5a,6,12a,12b,13-hexahydro-12*H*-naphtho[2,3-*a*]carbazole-5,13-dione (**10a**) and 1′(*R*),2′(*S*),5′(*R*),5a(*S*),6(*S*),12a(*R*),-12b(*R*)-12-Benzenesulfonyl-6-menthyloxy-5,5a,6,12a,12b,13-hexahydro-12*H*-naphtho[2,3-*a*]carbazole-5,13-dione (**10b**).

The yield was 62%, ratio of compound **A**:compound **B** = 1:1 (by hplc and ^1H nmr), mp 194-195°; ir (potassium bromide): ν 2880, 2860, 2840, 1690, 1590, 1460, 1445, 1360, 1170 cm^{-1}; ^1H nmr (400 MHz, dideuteriodichloromethane): δ 8.07-8.05 (m, 1H, aromatic H), 8.02-7.99 (m, 1H, aromatic H), 7.86-7.78 (m, 8H, aromatic H), 7.72-7.58 (m, 6H, aromatic H), 7.49-7.35 (m, 8H, aromatic H), 7.13-7.09 (m, 2H, aromatic H), 5.95 (pseudo-t, 1H, ^3J = 3.17 Hz, C7-H of **A**), 5.85 (pseudo-t, 1H, ^3J = 3.23 Hz, C7-H of **B**), 4.64-4.61 (m, 1H, C12a-H of **A**), 4.59-4.56 (m, 1H, C12a-H of **B**), 4.44-4.41 (m, 2H, C12b-H of **A**, C12b-H of **B**), 4.29 (pseudo-t, 1H, ^3J = 4.97 Hz, C6-H of **A**), 4.23 (dd, 1H, ^3J = 4.97 Hz, ^3J = 5.39 Hz, C6-H of **B**), 3.57-3.54 (m, 4H, C5a-H of **A**, C5a-H of **B**, menthyl H), 3.06-3.00 (m, 2H, C1′-H of **A**, C1′-H of **B**), 1.97-1.94 (m, 2H, menthyl H), 1.59-1.44 (m, 4H, menthyl H), 1.38-1.15 (m, 6H, menthyl H), 0.92 (d, 3H, ^3J = 7.41 Hz, CH_3 of **A**), 0.89 (d, 3H, ^3J = 7.42 Hz, CH_3 of **B**), 0.84 (d, 3H, ^3J = 7.55 Hz, CH_3 of **A**), 0.83 (d, 3H, ^3J = 7.55 Hz, CH_3 of **B**), 0.81-0.55 (m, 4H, menthyl H), 0.40 (d, 3H, ^3J = 6.82 Hz, CH_3 of **A**), 0.39 (d, 3H, ^3J = 6.89 Hz, CH_3 of **B**); fd-ms: m/z (%) 563.2 ($M^{+\cdot}$, 100).

Anal. Calcd. for $C_{36}H_{37}NO_3S$ (563.75): C, 76.60; H, 6.62; N, 2.48; S, 5.69. Found: C, 76.57; H, 6.49; N, 2.50; S, 5.39.

Acknowledgments.

The authors are grateful to the Deutsche Forschungsgemeinschaft (Bonn, FRG) for financial support of this work (Project Pi 135/8-1).

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