118. First Synthesis of 2-Vinylindole and its *Diels-Alder* Reactions with CC-Dienophiles[1])

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Dedicated to Prof. Dr. *h.c.mult. H. Böhme* (Marburg, FRG) with the best wishes for his 80th birthday

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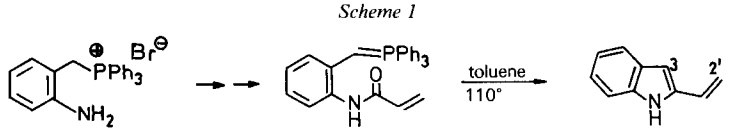
By means of an intramolecular *Wittig* process, 2-vinylindole (**2**) was prepared. The indole **2** functions as a heterocyclic, donor-activated 1,3-diene and undergoes [4 + 2] cycloaddition reactions with dimethyl acetylenedicarboxylate, *N*-phenylmaleimide, and *p*-benzoquinone leading to the novel carbazole derivatives **3**, **4**, **5c**, **6**, and **7**, respectively. The reaction of **2** with acceptor(A)-substituted dienophiles (*e.g.* ACH=CH_2, AC≡CH) does not yield products that can be isolated.

Vinylindoles are able to take part in various cycloaddition processes, *e.g. Diels-Alder* reactions. In these transformations, the vinylindoles may react both as dienes and as dienophiles. In this way, they have been used by us and by others in several syntheses of heterocyclic compounds and alkaloids [1–6]. Up till now, mostly selectively functionalized vinylindoles have been the reaction partners since as a consequence of stability factors [3] [7], these compounds are more easily accessible in higher yields than the parents.

Of the series of parent vinylindole compounds, only 3-vinylindole has been prepared previously by means of a *Cope* elimination from *N*,*N*-dimethyltryptamine *N*-oxide, and its *Diels-Alder* reactions were only superficially investigated [8]. In the present publication, we report on the first synthesis of the parent 2-vinylindole (**2**) and its cycloadditions with dienophiles.

The 2-vinylindole (**2**) is prepared without difficulty in 38% yield from (2-aminobenzyl)triphenylphosphonium bromide (**1a**) as starting material *via* **1b** by way of an intramolecular *Wittig* process according to *Le Corre*'s method [9] *(Scheme 1)*.

Scheme 1

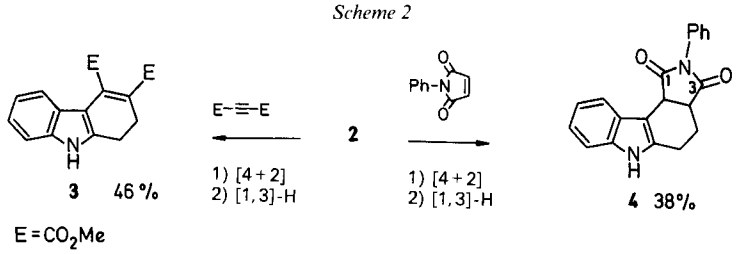


1a **1b** **2** 38%

The thermally stable, crystalline vinylindole **2** functions as a 4π-component in [4 + 2] cycloadditions with symmetrical carbodienophiles. Under reflux conditions in absolute toluene, reactions of **2** with the dienophiles tested by us, namely dimethyl acetylenedicarboxylate and *N*-phenylmaleimide, give rise to the carbazole derivatives **3** and **4**,

[1]) Part VI in the series 'Cycloadditions of Vinylindoles to Annellated Indole Derivatives'; Part V: [1].

Scheme 2

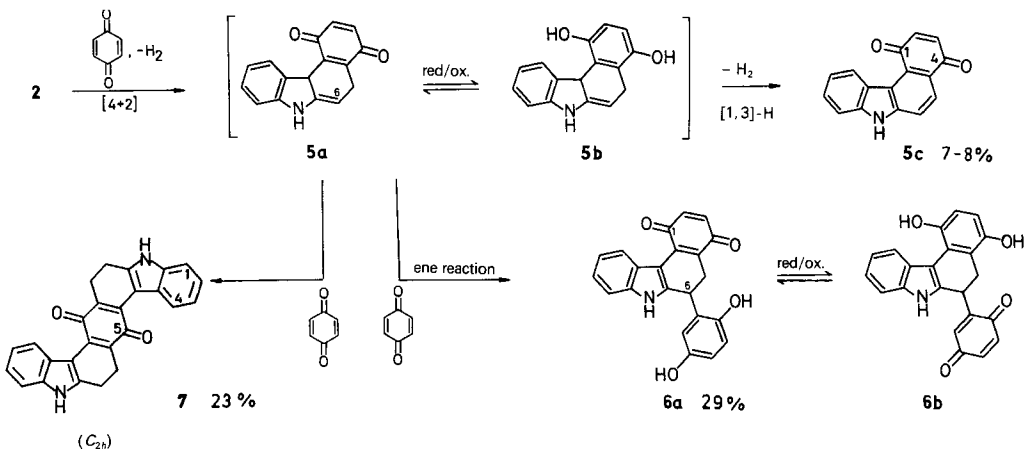


respectively *(Scheme 2)*. The primarily formed cycloadducts are apparently stabilized by a formal [1,3]-H shift[2]) to furnish the products. Dehydrogenation to form a 14π-carbazole skeleton, as observed in other cases [5], does not take place.

The [*c*]annellated carbazole **5c** and the double *Diels-Alder* adduct **7** are obtained, after chromatographic purification, from the reaction of **2** with *p*-benzoquinone in boiling toluene *(Scheme 3)*. Product **5c** tenaciously retains the hydroquinone that is always present in the reaction mixture; similarly, product **7** is obtained as an inseparable mixture with quinhydrone (^{1}H-NMR analysis)[3]). In the double *Diels-Alder* reaction of **2** with *p*-benzoquinone proceeding *via* **5a**, two constitutionally isomeric products with C_{2v} and C_{2h} symmetry, respectively, are expected as a consequence of the two possible orientations in the transition state of the final step. The constitution of the exclusively formed product **7** with C_{2h} symmetry is finally elucidated by a *J*-modulated, spin-echo ^{13}C-NMR spectrum (among others, a single resonance for the 2 carbonyl C-atoms is found, see *Exper. Part*).

From the reaction of **2** with *p*-benzoquinone in EtOH at room temperature, the dihydroxyphenyl-substituted carbazole **6a** was isolated in addition to **5c** (by-product). In

Scheme 3



[2]) The mechanism of the [1,3]-H shifts [4] frequently observed in reactions of this type has not yet been clarified; for more information, see [10].

[3]) Hydroquinone and quinhydrone, respectively, cannot be separated from **5c** and **7** without concomitant decomposition of the carbazole derivatives. This tenacious retention is presumably favoured by the formation of charge-transfer complexes.

solution, **6a** is in equilibrium (^{1}H-NMR experiment in $CDCl_3$) with the constitutionally isomeric carbazole **6b** (redox reaction) [11]. Product **6a** is the direct result of an ene reaction of **5a** with a further molecule of *p*-benzoquinone[4]). Under the mild reaction conditions employed (20°), the life time of **5a** is sufficiently long for the ene reaction to take place.

Inspite of numerous variations of the reaction conditions (*e.g. Lewis*-acid catalysis, molecular-sieve catalysis, use of higher temperatures in an autoclave) and in contrast to 3-vinylindole [8], its isomer **2** does not undergo [4 + 2] cycloadditions with acceptor-substituted dienophiles such as methyl propynoate, phenyl vinyl sulfone, methyl acrylate, and methyl phenylpropynoate, to give definable products (monitoring by TLC). Thus, no statement can be made yet on the regiochemistry of the *Diels-Alder* reactions [8] with **2**[5]).

The constitutions of the new carbazole derivatives **3**, **4**, **5c**, **6a**, and **7** have been confirmed unambiguously by ^{1}H-NMR spectroscopic measurements (400 MHz, ^{1}H-decoupling, NOE, and INDOR experiments).

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Experimental Part

General. All reactions must be performed in highly pure, anh. solvents under inert-gas atmospheres. Column chromatography: silica gel *60* (*Merck*, 0.063–0.200 mm particle size). M.p.: *Büchi SMP-20*; not corrected. ^{1}H-NMR and ^{13}C-NMR spectra: *Bruker WM 400* and *Bruker WH 90* spectrometers, δ [ppm] scale, coupling constants J in Hz, TMS as internal standard. EI-MS (70 eV): *Varian MAT 7*, data given as *m/z* (%). FI- and FD-MS: *Varian MAT 711*. C,H,N Analyses: *Carlo Erba Strumentazione*.

2-Vinylindole (**2**). (2-Aminobenzyl)triphenylphosphonium bromide (**1a**; 4.48 g, 10 mmol) was suspended in anh. CH_2Cl_2 (200 ml) and propenoyl chloride (1.0 g, 11 mmol) added slowly. Pyridine (1.2 g, 15 mmol) was then added dropwise and the mixture heated under reflux for 30 min and then allowed to cool to r.t. The mixture was washed with 15% aq. Na_2CO_3 soln. (15 ml) and 1N aq. HCl (15 ml). The aq. phase was extracted with CH_2Cl_2 (100 ml), the combined org. phases were washed with 2 portions of H_2O (100 ml each), dried (Na_2SO_4), and evaporated to give 4.5 g (89%) of [2-(propenoylamino)benzyl]triphenylphosphonium bromide. M.p. 276° (sintered above 239° with appearance of a brown discoloration).

The phosphonium bromide (2.52 g, 5 mmol) was supended in abs. toluene (200 ml) and the mixture heated under reflux for 30 min. Then, 50 ml of toluene were distilled off. The resultant mixture was heated to 60°, K(*t*-BuO) (0.67 g, 6 mmol) added in 6 portions, the mixture heated under reflux for further 40 min, allowed to cool to r.t., and filtered. The filtrate was concentrated to *ca.* 50 ml and Et_2O added dropwise to precipitate as much of the formed Ph_3PO as possible. The org. phase was concentrated and the residue purified by column chromatography using petroleum ether (40–60°)/AcOEt 3:1: 272 mg (38%) of **2**. Colorless, light- and air-sensitive crystals. M.p. 92° (petroleum ether (40–60°)). ^{1}H-NMR (90 MHz, (D_6)acetone): 5.23 (*dd*, J = 0.9, 17.9,1 H–C(2′)); 5.75 (*dd*, J = 0.9, 17.9,1 H–C(2′)); 6.48 (*s*, H–C(3)); 6.8 (*q*, J = 11.2, 11.6, 18, H–C(1′)); 6.84–7.55 (*m*, H–C(4), H–C(5), H–C(6), H–C(7)); 9.80 (*s*, NH). ^{13}C-NMR (100.6 MHz, (D_6)acetone): 103.25 (C(3)); 111.72 (C(7)); 112.62 (C(2′)); 120.25 (C(4)); 121.60 (C(6)); 123.04 (C(5)); 128.89 (C(1′)); 129.70 (C(3a)); 137.65 (C(2)); 138.22 (C(7a)). MS: 143 ($M^{+\cdot}$). Anal. calc. for $C_{10}H_9N$ (143.07): C 83.87, H 6.34, N 9.79; found: C 83.64, H 6.75, N 9.54.

*Dimethyl 1,2-Dihydro-9*H*-carbazole-3,4-dicarboxylate* (**3**). A soln. of **2** (143 mg, 1 mmol) and dimethyl acetylenedicarboxylate (284 mg, 2 mmol) in toluene (10 ml) was heated under reflux for *ca.* 6 h and then allowed to cool to r.t. The major portion of **3** separated as a colorless precipitate on cooling; precipitation was completed by

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[4]) For further information on dehydrogenative *Diels-Alder* reactions with *p*-benzoquinone, see [3] [4] [6].

[5]) MNDO calculations demonstrate [12] that the reactions of **2** (E_{HOMO} = −8.25 eV) with acceptor-substituted dienophiles are $HOMO_{diene}$-$LUMO_{dienophile}$-controlled reactions according to the FMO concept [13].

addition of petroleum ether (40–60°): 130 mg (46%) of **3**. Colorless crystals. M.p. 217° (toluene). ^{1}H-NMR (400 MHz, (D_6)acetone): 2.79–2.84 (*'quint.'*, H–C(1) or H–C(2)); 2.97–3.01 (*'quint.'*, H–C(2) or H–C(1)); 3.71 (*s*, $COOCH_3$); 3.93 (*s*, $COOCH_3$); 7.03–7.13 (*m*, H–C(6), H–C(7)); 7.34 (*d*, J = 7.6, H–C(5)); 7.39 (*d*, J = 7.8, H–C(8)); 10.7 (*s*, NH). MS: 285 ($M^{+\cdot}$). Anal. calc. for $C_{16}H_{15}NO_4$ (285.10): C 67.34, H 5.30, N 4.91; found: C 67.21, H 5.43, N 4.78.

2-Phenyl-4,5,6,10c-tetrahydropyrrolo[3,4-c]carbazole-1,3(2H,3aH)dione (**4**). To a soln. of **2** (357 mg, 2.5 mmol) in toluene (20 ml), *N*-phenylmaleimide (433 mg, 2.5 mmol) was added in one portion. The resultant mixture was heated under reflux for 24 h, allowed to cool to r.t., concentrated, and the residue purified by column chromatography using pertroleum ether (40–60°)/AcOEt 1:1: 300 mg (38%) of **4**. Colorless crystals. M.p. 206° (petroleum ether (40–60°)/AcOEt). ^{1}H-NMR (400 MHz, (D_3)nitromethane): 2.05–2.15 (*m*, H–C(4)); 2.49–2.56 (*m*, H–C(4)); 2.74–2.89 (*m*, H–C(5)); 3.64–3.68 (*sext.*, J(3a,10c) = 8.1, J(3a,4) = 5, H–C(3a)); 4.49 (*dd*, J(10c,3a) = 8.1, J(10c,4) = 0.9, H–C(10c)); 7.07–7.57 (*m*, 5 arom. H, H–C(7), H–C(8), H–C(9)); 7.86 (*d*, J = 7.6, H–C(10)); 8.81 (*s*, NH). ^{13}C-NMR (100.6 MHz, (D_6)DMSO): 20.9 (C(4)); 23.2 (C(5)); 41.8 (C(3a)); 49.6 (C(10c)); 104.6 (C(10b)); 112.3 (C(7)); 120.8 (C(8)); 120.9 (C(10)); 122.9 (C(9)); 127.99, 128.59, 129.79, 130.37, 130.56, 137.27 (arom. C); 137.51, 134,34 (C(5a), C(7a)); 128.37 (C(10a)); 178.27 (CO); 180.10 (CO). MS: 316 (49, $M^{+\cdot}$), 168 (100). Anal. calc. for $C_{20}H_{16}N_2O_2$ (316.12): C 75.92, H 5.10, N 8.86; found: C 75.45, H 4.99, N 8.22.

7H-Benzo[c]carbazole-1,4-dione (**5c**) *and 6-(2,5-Dihydroxyphenyl)-5,6-dihydro-7H-benzo[c]carbazole-1,4-dione* (**6a**). A soln. of **2** (286 mg, 2 mmol) in EtOH (5 ml) was added by syringe to a soln. of *p*-benzoquinone (540 mg, 5 mmol) in EtOH (20 ml), the resultant mixture was stirred at r.t. for 16 h, and then evaporated carefully. The residue was purified by column chromatography using petroleum ether (40–60°)/AcOEt 3:1 to give **5c** and **6a**.

5c: Yield 32 mg (7%). Red crystals. M.p. 157–164° (a 1:1 mixture with hydroquinone according to ^{1}H-NMR). ^{1}H-NMR (400 MHz, (D_6)DMSO): 7.03 (*d*, J = 10.2, H–C(2) or H–C(3)); 7.11 (*d*, J = 10.2, H–C(3) or H–C(2)); 7.56 (*t*, J = 7.5, 7.4, H–C(10)); 7.60 (*d*, J = 7.7, H–C(8)); 7.92 (*t*, J = 7.0, 7.0, H–C(9)); 7.93 (*d*, J = 8.5, H–C(5) or H–C(6)); 8.13 (*d*, J = 8.5, H–C(6) or H–C(5)); 9.29 (*d*, J = 8.2, H–C(11)); 12.2 (*s*, NH); signals for hydroquinone: 6.54, 8.62 (2 br. *s*). MS: 247 (67, $M^{+\cdot}$), 219 (18), 110 (100).

6a: Yield 105 mg (29%). Deep blue crystals. M.p. 221–226° (dec.). UV/VIS (MeOH): 581 (CT bands). ^{1}H-NMR (400 MHz, (D_6)DMSO): 2.89 (*dd*, J = 17.5, 8.8, H_α–C(5) or H_β–C(5)); 3.18 (*dd*, J = 17.5, 4.7, H_β–C(5) or H_α–C(5)); 4.62 (*dd*, J = 8.7, 4.7, H–C(6)); 5.91 (*d*, J = 2.8, H–C(3')); 6.40 (*dd*, J = 8.5, 8.8, H–C(5')); 6.66 (*d*, J = 8.5, H–C(6')); 6.77 (*d*, J = 10.0, H–C(2) or H–C(3)); 6.83 (*d*, J = 10.0, H–C(3) or H–C(2)); 7.12 (*t*, J = 4.0, 4.0, H–C(8), H–C(11)); 7.35 (*t*, J = 5.0, 4.1, H–C(9) or H–C(10)); 8.20 (*t*, J = 5.0, 4.0, H–C(10) or H–C(9)); 8.51 (*s*, OH); 9.08 (*s*, OH); 11.82 (*s*, NH). MS: 357 (100, $M^{+\cdot}$), 273 (19), 250 (10). Anal. calc. for $C_{22}H_{15}NO_4$ (357.37): C 73.94, H 4.23, N 3.92; found: C 73.79, H 4.15, N 3.69.

6,7,8,14,15,16-Hexahydrobenzo[1,2-c:4,5-c']dicarbazole-5,13-dione (**7**) *and* **5c**. To a soln. of *p*-benzoquinone (270 mg, 2.5 mmol) in toluene (10 ml) over molecular sieve (0.4 nm; 3 g) was added dropwise by syringe a soln. of **2** (143 mg, 1 mmol) in toluene (5 ml). The mixture was stirred and heated under reflux for 6 h and then carefully concentrated in a rotary evaporator. The residue was separated by column chromatography on silica gel using petroleum ether (40–60°)/AcOEt 3:1 to give **5c** (20 mg, 8%) and **7** (45 mg, 23%). **7**: M.p. 156–158° (a 3:2 mixture with quinhydrone according to ^{1}H-NMR). UV/VIS (MeOH): 590 (CT bands). ^{1}H-NMR (400 MHz, (D_6)DMSO): 2.76 (*m*, 1 H–C(6), 1 H–C(14), 1 H–C(7), 1 H–C(15)); 2.92 (*m*, 1 H–C(6), 1 H–C(14), 1 H–C(7), 1 H–C(15)); 7.05–7.12 (*m*, H–C(2,10), H–C(3,11)); 7.35 (*dd*, J = 6.6, 1.5, H–C(1,9)); 8.07 (*t*, J = 8.2, 1.4, H–C(4,12)); 11.94 (*s*, NH); signals for quinhydrone: 6.54 (*s*, 4 H); 6.82 (*s*, 4 H); 8.64 (*s*, 2 H, OH). ^{13}C-NMR (100.2 MHz, (D_6)DMSO): 20.2 (C(6), C(14) or C(7), C(15)); 20.4 (C(7), C(15) or C(6), C(14)); 105.6 (C(4b), C(12b)); 111.6 (C(1), C(9)); 120.6 (C(2), C(10)); 121.6 (C(3), C(11)); 122.2 (C(4), C(12)); 124.1 (C(7a), C(15a)); 130.1 (C(4a), C(12a)); 135.5 (C(8a), C(16a)); 136.8 (C(4c), C(12c) or C(5a), C(13a)); 138.0 (C(5a), C(13a) or C(4c), C(12c)); 185.4 (2 CO), signals for quinhydrone: 115.6, 136.3, 149.6 (2 COH), 187.2 (2 CO). FD-MS (MeOH): 390 (5, $M^{+\cdot}$), 388 (4), 386 (10), 294 (100). FI-MS (MeOH): 392 (23, $M^{+\cdot}$ + 2), 390 (16, $M^{+\cdot}$), 388 (23), 386 (32), 294 (100). EI-MS: 252 (18), 251 (100), 250 (44), 247 (84).

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