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# A New Access to 3-(2′-Aminovinyl)indoles and Their First Diels-Alder Reactions

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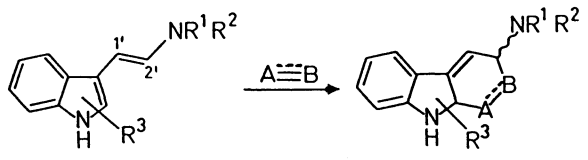
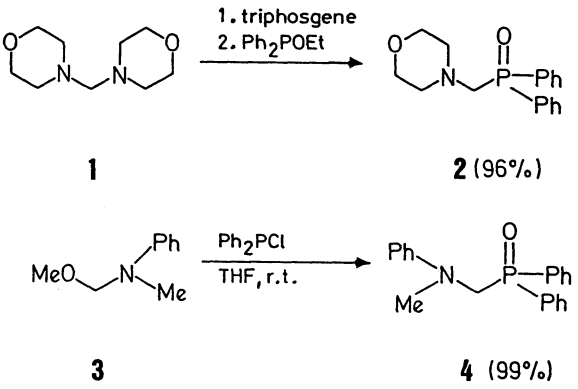
3-Acylindoles react with α-amino-α′-diphenylphosphinoyl-substituted carbanions to 3-(2′-aminovinyl)indoles (**7** and **12**) via carbinols. The electron-rich 3-vinylindoles **7** and **12** undergo Diels-Alder reactions with *N*-phenylmaleimide.

Diels-Alder reactions of 2- and 3-vinylindoles as 4π-electron components are versatile procedures for regio- and stereocontrolled syntheses of [*b*]annelated indoles and/or carbazoles, including alkaloids.[1-5] This concept also facilitates attractive new syntheses of heteroatom-functionalized carbazoles and annelated indoles, i.e. compounds selectively functionalized with alkoxy, alkylthio, or amino groups.[4-6] In this context, 3-(2′-aminovinyl)indoles **A** are of interest[6] since they possess the structural feature (indole-C-C-$NR_2$) of dehydrotryptamine and some alkaloids of *Aristotelia*.[7] On the other hand, indolylenamines **A** are also useful as building blocks for compounds exhibiting antidepressive and/or antitumor activity as well as indole alkaloids biogenetically derived from L-tryptophan/tryptamine.[7] On reactivity considerations, the two enamine functions in **A** can operate independently, in concert, or in opposition. Exemplarily performed π-SCF-MO and σ/π-charge calculations on (*E*)-3-[2′-(morpholin-4-yl)-vinyl]indole revealed[6] that **A** can, in principle, be involved both in HOMO(diene)-LUMO(dienophile)-controlled [4 + 2] cycloadditions to produce [*b*]annelated indoles **B** (Scheme 1) and in charge-controlled, simple, one-bond formations at C1′ (a Michael-type addition). However, syntheses of **A** from, e.g. indole-3-acetaldehyde and morpholine or pyrrolidine, are laborious. The relatively unstable species thus obtained are difficult to characterize and undergo polymerization rather than Diels-Alder reactions.[6,9]




**Scheme 1.**

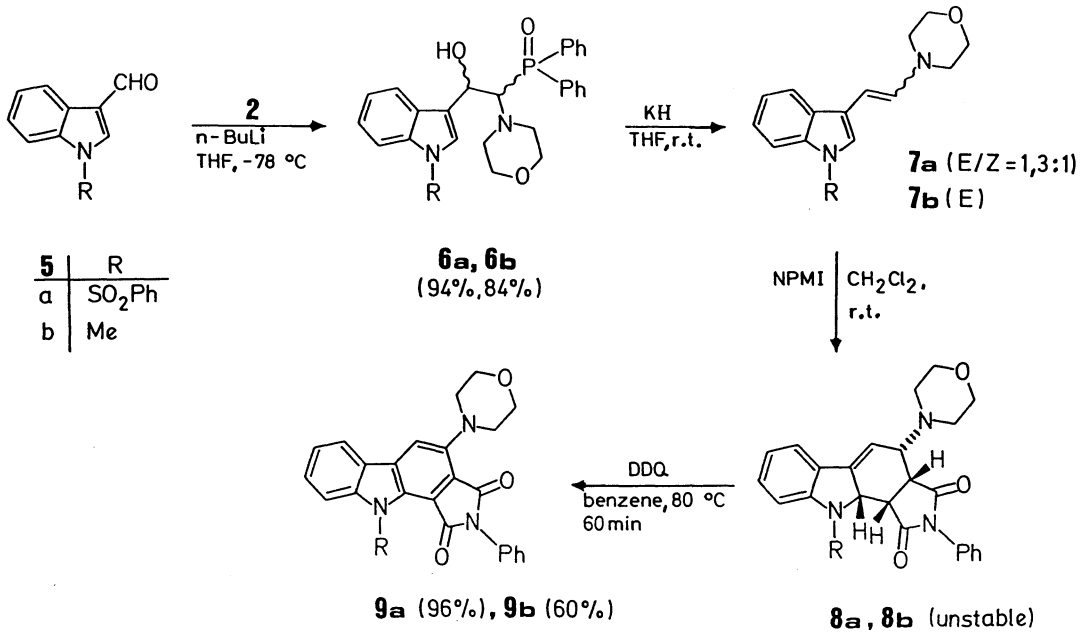
We now report on a new synthesis of three previously unknown 3-(2'-aminovinyl)indoles of type **A** starting from aminal or aminal ether substrates and their enophilic reactivity towards *N*-phenylmaleimide (NPMI). Diphenyl(*N*-morpholinomethyl)phosphine oxide (**2**)[10] was obtained by aminal cleavage[11] of **1** with phosgene (reagent used: triphosgene). Subsequent reaction with ethyl diphenylphosphinite[12] gave **2** (mp 160 °C; Scheme 2) in high yield. Analogously, the aminal ether **3**[13] was converted to **4** (mp 122 °C, 99%) by an Arbuzov reaction with chloro(diphenyl)phosphine.[14]




**Scheme 2.**

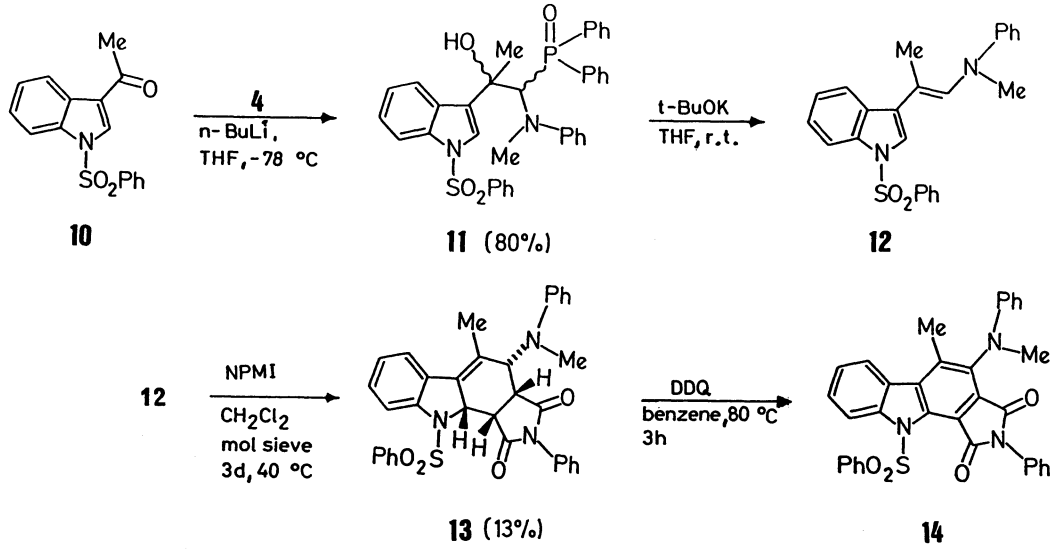
In the key step, a modified Horner-Wadsworth-Emmons reaction (Scheme 3), the indole-3-carbaldehydes **5a,b** each reacted with the *in situ* generated, reactive α-amino-α'-diphenylphosphinoyl carbanion derived from **2** to produce inseparable diastereoisomeric mixtures of the indole-3-carbinols **6a,b** (mp 189 °C). Potassium hydride-catalyzed 1,2-elimination of **6a,b** furnished the *N*-substituted 3-[2-(morpholin-4-yl)vinyl]indoles **7a,b** with a preference for (*E*)-stereoselectivity, but **7a,b** are unstable (like the *N*-unsubstituted indole analog)[6] and undergo rapid oligomerization and polymerization. The $^1$H-NMR vinylic proton pattern is indicative for the constitution and stereochemistry of **7** [*E*-**7a**: $\delta$ = 5.86 and 6.64 ppm (d, $J$ = 14.2 Hz), *Z*-**7a**: $\delta$ = 5.29 and 5.94 ppm (d, $J$ = 9.2 Hz); *E*-**7b**: $\delta$ = 5.65 and 6.57 ppm (d, $J$ = 14.2 Hz)]. Under nitrogen, however, freshly prepared **7a,b** undergo HOMO(diene)-LUMO(dienophile) controlled, stereoselective Diels-Alder reactions with NPMI to give the "endo"-cycloadduct **8a** (mp 198 °C) and the less stable and difficult to purify **8b**. $^1$H-NMR configurational analyses of **8** showed retention of the "*E*"-stereochemistry of **7**. 2,3-Dichloro-5,6-dicyano-*p*-benzoquinone (DDQ)-catalyzed dehydrogenations of **8** gave the 14π-carbazoles **9a,b** (mp 112 °C and 131 °C) in good yields.

Similarly (Scheme 4), the 3-acetylindole **10** reacted with the *in situ* generated carbanion of **4** to furnish diastereomers of **11** (mp 192 °C and 175 °C, 80%). Potassium *t*-butoxide-induced 1,2-elimination stereoselectively furnished the oily *E*-3-vinylindole **12**. The electron-rich **12** exhibits the same instability as **7a,b**. However, freshly prepared **12** also




**Scheme 3.**

undergoes a Diels-Alder reaction with NPMI to give exclusively the "endo"-cycloadduct **13** (mp 219 °C). As outlined, DDQ-catalyzed dehydrogenation of **13** gave the unstable carbazole **14** (mp 252 °C; characterized by FD-MS).




**Scheme 4.**

The constitutions of **6**, **9**, **11** and the configurations of **7a,b**, **12**, **13** (**8b** was too unstable) were elucidated by 400 MHz $^{1}$H-NMR and, in some cases, by 100.6 MHz $^{13}$C-NMR as well as $^{1}$H,$^{1}$H-NOE experiments.[15]

In summary, a new preparation some 3-(2'-aminovinyl)indoles and, above all, the first Diels-Alder reactions of this compound class are presented. The carbazoles **8** and **14** with a coplanar framework (chromophoric group) are of interest as antitumor active intercalators to human B-DNA.[16]

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15) Selected 400 MHz $^{1}$H- and 100.6 MHz $^{13}$C-NMR data. **8a**: $^{1}$H-NMR ($CDCl_3$) $\delta$ = 2.4 (m, 2H, $CH_2$-morpholine), 2.91 (m, 3H, $CH_2$-morpholine and C4-H), 3.72 (dd, $^{3}J$ = 8.5 Hz, $^{3}J$ = 6.2 Hz, 1H, C3a-H), 3.83 (m, 4H, $CH_2$-morpholine), 4.15 (pseudo-t, $^{3}J$ = 8.4 Hz, $^{3}J$ = 7.4 Hz, 1H, C10b-H), 4.74 (dd, $^{3}J$ = 7.4 Hz, $^{4}J$ = 1.0 Hz, 1H, C10a-H), 6.19 (dd, $^{3}J$ = 8.5 Hz, $^{4}J$ = 1.0 Hz, 1H, C5-H), 6.9-7.9 (m, 14H, aromatic). $^{13}$C-NMR ($CDCl_3$) $\delta$ = 28.4, 43.8, 52.9 (2 x $CH_2$), 61.33, 66.70 (2 x $CH_2$), 115.3, 115.8, 120.9, 124.1, 125.7, 126.4, 127.2, 128.4, 128.8, 129.3, 130.8, 131.6, 133.6, 136.3, 137.6, 144.9, 172.0 (CO), 173.1 (CO). **9a**: $^{1}$H-NMR ($CD_2Cl_2$) $\delta$ = 3.37 (m, 4H, $CH_2$-morpholine), 4.01 (m, 4H, $CH_2$-morpholine), 7.30-7.60 (m, 10H, aromatic), 7.67 (s, 1H, C5-H), 7.84-7.95 (m, 2H, aromatic). **13**: $^{1}$H-NMR (DMSO-$d_6$) $\delta$ = 1.85 (s, 3H, C5-$CH_3$), 3.07 (s, 3H, $NCH_3$), 4.00 (m, 1H, C3a-H), 4.18 (pseudo-t, $^{3}J$ = 8.05 Hz, $^{3}J$ = 7.2 Hz, 1H, C10b-H), 4.65 (d, $^{3}J$ = 5.18 Hz, 1H, C4-H), 5.26 (dd, $^{3}J$ = 7.2 Hz, $^{5}J$ = 1.9 Hz, 1H, C10a-H), 6.72-7.68 (m, 17H, aromatic), 8.0 (d, $^{3}J$ = 7.5 Hz, C2/6-H of phenyl-$SO_2$).
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