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# Diels–Alder reactions of 2- and 3-nitroindoles. A simple hydroxycarbazole synthesis

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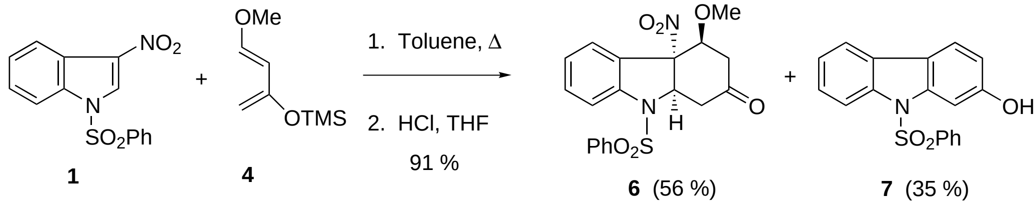
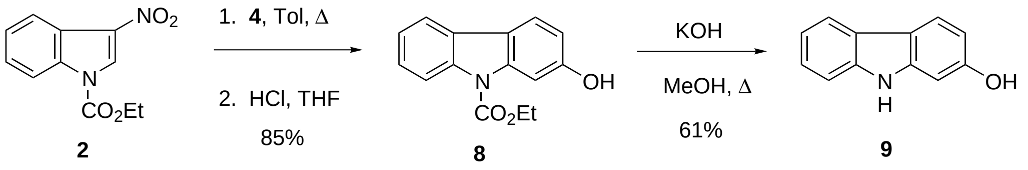
**Abstract**—A Diels–Alder reaction of 3- and 2-nitroindoles with Danishefsky's diene gives the expected 2- and 3-hydroxycarbazoles in very good to excellent yields (73–91%) and with apparent complete regioselectivity. © 2001 Elsevier Science Ltd. All rights reserved.

It is well established that the indole 2,3-double bond can serve as a dienophile in inverse electron demand Diels–Alder reactions.[1] The recent work of Snyder is particularly noteworthy in this regard.[2] Fewer examples exist of indole reacting with electron-rich dienes in normal demand Diels–Alder reactions. Raasch described the Diels–Alder reaction of indole with tetrachlorothiophene-1,1-dioxide.[3] Wenkert showed that indoles with electron-withdrawing groups on both the C-3 position and nitrogen react with simple dienes (isoprene, 2,3-dimethyl-1,3-butadiene) to give tetrahydrocarbazoles.[4] Kraus achieved the first intramolecular Diels–Alder reactions of the indole double bond.[5] Steckhan has effected a photoinduced electron-transfer-catalyzed step-wise reaction between indole and 1,3-cyclohexadienes.[6] Markgraf achieved the cycloaddition of *N*-methylindole and *o*-xylylene.[7] Padwa has employed an intramolecular indole-furan Diels–Alder reaction strategy to craft several hexahydroindolinones.[8] During the course of our work, Mancini reported Diels–Alder reactions between *N*-tosyl-3-nitroindole and *N*-acyl-*N*-alkylamino-1,3-butadienes.[9]

In continuation of our interest in the cycloaddition chemistry of 2- and 3-nitroindoles,[10] we now describe the Diels–Alder reactions of nitroindoles **1**–**3** with Danishefsky's diene (**4**) (1-methoxy-3-(trimethylsiloxy)-1,3-



**Scheme 1.**



**Scheme 2.**

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*Keywords*: 2-nitroindole; 3-nitroindole; Diels–Alder reaction; 2-hydroxycarbazole; 3-hydroxycarbazole.

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butadiene) and 1-dimethylamino-3-*tert*-butyldimethylsiloxy-1,3-butadiene (**5**).[11]

Treatment of 3-nitro-1-(phenylsulfonyl)indole (**1**)[12] with diene **4** in refluxing toluene afforded a mixture of *exo* adduct **6**[13] (56% yield) and 2-hydroxy-9-(phenylsulfonyl)carbazole (**7**)[13] (35% yield) following acid hydrolysis. Both compounds were fully characterized, including X-ray structure determinations.[14] In refluxing THF the cycloaddition of **1** and **4** gave a lower yield (47%) of a mixture of **6** and the *endo* isomer by NMR (Scheme 1).

Similarly, 1-ethoxycarbonyl-3-nitroindole (**2**)[12] reacted with **4** under the same conditions to afford 9-ethoxycarbonyl-2-hydroxycarbazole (**8**)[13] in 85% yield. The intermediate cycloadduct was not observed in this case. Hydrolysis of **8** with KOH/MeOH/reflux gave the known 2-hydroxycarbazole (**9**)[15] (Scheme 2).

A Diels–Alder reaction under the usual conditions between 1-ethoxycarbonyl-2-nitroindole (**3**)[16] and **4** gave 9-ethoxycarbonyl-3-hydroxycarbazole (**10**)[13] in 73% yield, after acidic treatment. Base cleavage of the carbamate afforded the known 3-hydroxycarbazole (**11**)[17] (Scheme 3).

In contrast to these relatively smooth Diels–Alder reactions with Danishefsky's diene (**4**), nitroindole **1** and 3-nitro-1-pivaloylindole[12] failed to produce isolable products with Rawal's diene (**5**). However, **5** did react with 2-nitroindole **3** in refluxing toluene to afford cycloadduct **12**[13] in 51% yield, along with 2-nitroindole (37% yield). Deprotonation of **12** with TBAF gave carbazole **10** (quantitative) (Scheme 4).

The comparable Diels–Alder reactions of dienes **4** and **5** with 2-nitro-1-(phenylsulfonyl)indole (**13**)[16] were quite sluggish and only **5** behaved appropriately to afford carbazole **14**[13] in low yield (Scheme 5).

We have also pursued a Diels–Alder approach to 1- and 4-hydroxycarbazoles with two dienes. A vinylketene equivalent, 3-hydroxy-2-pyrone,[18,19] failed to undergo a cycloaddition with either 2-nitroindole **3** or 3-nitroindole **2** even when refluxed in xylene. Kraus has recently used 1-trimethylsilyloxy-1,3-butadiene in a Diels–Alder sequence to synthesize tetrangulol.[20] We had hoped to employ a similar reaction sequence to access the 1- and 4-hydroxycarbazoles. However, the cycloaddition between 1-trimethylsilyloxy-1,3-butadiene and 3-nitroindole **2** in refluxing in xylene afforded only 9-ethoxycarbonylcarbazole in 47% yield (46% recovered starting material). With 2-nitroindole **3**, no reaction was observed under these conditions.

In summary, 2- and 3-nitroindoles **1**–**3** react efficiently with dienes **4** and **5** in normal electron demand Diels–Alder reactions to give the expected carbazole cycloadducts with high or complete regioselectivity. Applications of this chemistry to the synthesis of carbazole natural products are underway.

## Acknowledgements

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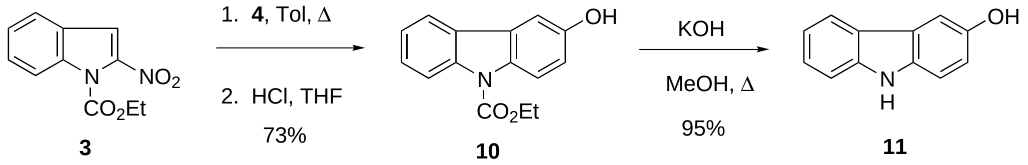
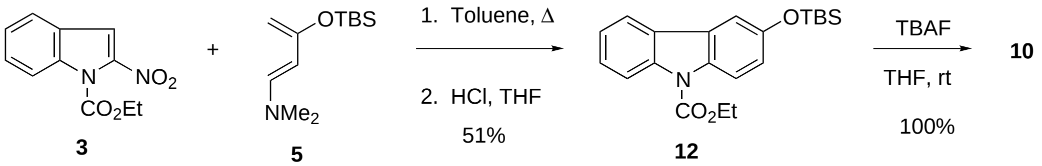
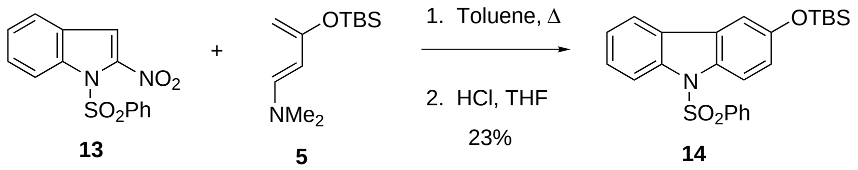


**Scheme 3.**



**Scheme 4.**



**Scheme 5.**

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13. Compound **6**: mp 178–179°C; IR (film) $\nu_{max}$ 1722 (C=O), 1361 ($SO_2$), 1166 ($SO_2$) cm$^{-1}$; (EtOH) $\lambda_{max}$ 256 nm. $^1$H ($CD_2Cl_2$): $\delta$ 7.73–7.80 (m, 3H), 7.55–7.62 (m, 2H), 7.42–7.52 (m, 3H), 7.15–7.20 (m, 1H), 5.70 (dd, 1H, 2, 6 Hz), 4.67 (m, 1H), 3.46 (s, 3H), 3.20 (dd, 1H, 6, 16 Hz), 3.15 (dd, 1H, 2, 16 Hz), 2.67 (dd, 1H, 3, 19 Hz), 1.92 (dd, 1H, 3, 19 Hz). $^{13}$C ($CD_2Cl_2$): $\delta$ 204.2, 142.7, 136.2, 134.4, 133.5, 129.6, 127.9, 125.9, 125.6, 125.4, 116.8, 96.1, 20.5, 62.0, 58.3, 44.5, 37.7; Anal. calcd for $C_{19}H_{18}N_2O_6S$: C, 56.71; H, 4.51; N, 6.96; S, 7.97. Found: C, 56.40; H, 4.45; N, 6.88; S, 7.91. Compound **7**: IR (film) $\nu_{max}$ 3347 (OH), 1367 ($SO_2$), 1176 ($SO_2$) cm$^{-1}$; UV (EtOH) $\lambda_{max}$ 224, 260 nm; $^1$H ($CD_3COCD_3$): $\delta$ 8.84 (s, 1H), 8.27 (d, 1H, 7.5 Hz), 7.84–7.91 (m, 5H), 7.34–7.59 (m, 5H), 6.95 (dd, 1H, 2, 8 Hz); $^{13}$C ($CD_3COCD_3$): $\delta$ 158.7, 140.7, 139.0, 138.6, 135.2, 130.3, 127.8, 127.3, 126.8, 125.2, 122.0, 120.2, 119.8, 115.7, 113.9, 102.5. Compound **8**: mp 172–172.5°C; IR (film) $\nu_{max}$ 3328 (OH), 1702 (C=O) cm$^{-1}$; (EtOH) $\lambda_{max}$ 230, 264, 294, 330 nm. $^1$H ($CD_3COCD_3$): $\delta$ 8.74 (s, 1H), 8.26 (d, 1H, 8 Hz), 7.88–7.96 (m, 3H), 7.29–7.40 (m, 2H), 6.94 (d, 1H, 8 Hz), 4.58 (q, 2H, 7 Hz), 1.53 (t, 3H, 7 Hz); $^{13}$C ($CD_3COCD_3$): $\delta$ 158.6, 153.1, 140.7, 139.0, 127.1, 126.4, 124.2, 121.4, 119.6, 119.2, 116.9, 112.9, 103.9, 63.9, 14.8; Anal. calcd for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.20; H, 5.13; N; 5.41. Compound **10**: mp 197–198°C; IR (film) $\nu_{max}$ 3401 (OH), 1723 (C=O) cm$^{-1}$; (EtOH) $\lambda_{max}$ 232, 274, 296, 304 nm. $^1$H ($CD_3COCD_3$): $\delta$ 8.42 (s, 1H), 8.30 (d, 1H, 8 Hz), 8.15 (d, 1H, 9 Hz), 8.01 (m, 1H), 7.44–7.52 (m, 2H), 7.32–7.37 (m, 1H), 7.03 (dd, 1H, 2.5, 9 Hz), 4.58 (q, 2H, 7 Hz), 1.53 (t, 3H, 7 Hz). $^{13}$C ($CD_3COCD_3$): $\delta$ 154.9, 152.9, 139.7, 132.9, 128.1, 127.8, 126.7, 123.9, 120.7, 117.9, 117.1, 116.5, 106.1, 63.8, 14.8. Anal. calcd for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.19; H, 5.20; N, 5.38. Compound **12**: $^1$H ($CDCl_3$): $\delta$ 8.32 (d, 1H, 8 Hz), 8.20 (d, 1H, 9 Hz), 7.93 (d, 1H, 7 Hz), 7.45–7.52 (m, 2H), 7.34–7.39 (m, 1H), 7.03 (dd, 1H, 2, 9 Hz), 4.60 (q, 2H, 7 Hz), 1.57 (t, 3H, 7.32 Hz), 1.10 (t, 9H, 3 Hz), 0.31 (t, 6H, 3 Hz); $^{13}$C ($CDCl_3$): $\delta$ 152.6, 152.2, 139.1, 133.4, 127.5, 127.3, 126.1, 123.3, 120.2, 119.9, 117.2, 116.6, 110.5, 63.2, 30.0, 26.1, 26.0, 18.6, 14.8, −2.6, −4.1; MS $m/z$ 404 ([M+Cl]), 370 (MH$^+$), HRMS $m/z$ calcd for $C_{21}H_{27}NO_3Si$ (M$^+$) 369.1760, found 369.1763. Compound **14**: $^1$H ($CDCl_3$): $\delta$ 8.34 (d, 1H, 8 Hz), 8.21 (d, 1H, 9 Hz), 7.86 (d, 1H, 7 Hz), 7.78–7.82 (m, 2H), 7.30–7.54 (m, 6H), 7.03 (dd, 1H, 2, 9 Hz), 1.06 (s, 9H), 0.27 (s, 6H). $^{13}$C ($CDCl_3$): $\delta$ 152.9, 139.2, 137.9, 133.9, 133.3, 129.1, 127.9, 127.7, 126.8, 126.7, 124.1, 120.4, 120.3, 116.3, 115.7, 110.6, 25.9, 18.4, −2.7, −4.2.
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