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THE 3-VINYLINDOLE PARENT COMPOUND AND ITS ANION: NEW REACTIVITY ASPECTS

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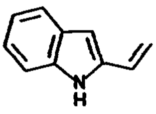
SUMMARY: Synthesis and reactivity of the parent 3-vinylindole and its anion are described. These compounds react as dienes in $\mathrm{HOMO}_{\mathrm{diene}}$-controlled Diels-Alder reactions. In the presence of dichloromethane, the 3-vinylindole anion undergoes an S_N reaction to furnish a dimeric product.

Both structural analysis and evaluation of the reactivity of the parent compounds in the vinylheteroarene series are of general interest for predicting the outcome of Diels-Alder reactions and other pericyclic processes, especially with regard to synthesis planning[1-3]. In the vinylindole series, we have reported the first synthesis of the parent 2-vinylindole (1) by way of an intramolecular Wittig process[4]. Compound 1 possesses sufficient thermal stability [mp 92 °C, ΔH_f s-cis (MNDO) = 71.1 kcal·mol^{-1}] and its Diels-Alder reactivity as a 4π-reaction component [E_{HOMO} (MNDO) = -8.25 eV] has been investigated thoroughly by us[4]. Although the parent 3-vinylindole (2) was described for the first time in Ref.[5], our reinvestigation of the experimental and physical data reported have shown that these are not sufficient from structural and reactivity points of view. According to MNDO calculations, compound 2 (ΔH_f s-cis = 72.9 kcal·mol^{-1}) is expected to possess a similar thermodynamic stability and reactivity to those of 1.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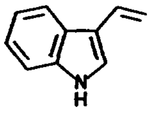
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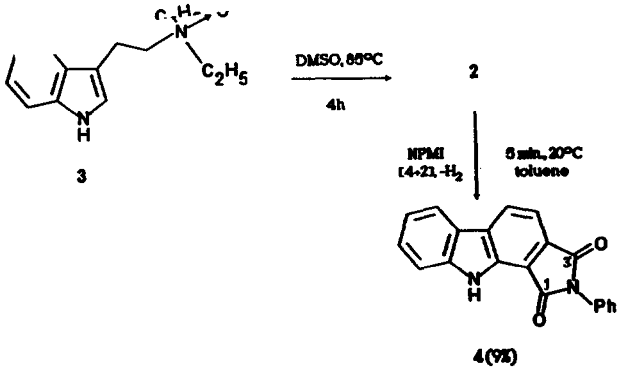
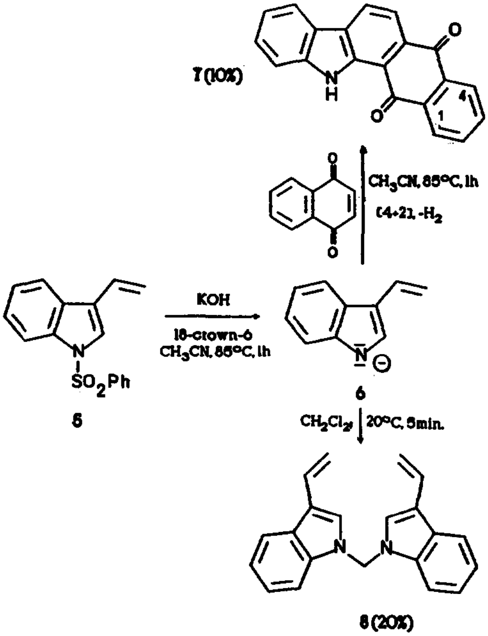
We have now repeated the multi-step reaction sequence leading to N,N-diethyltryptamine N-oxide (3) which, according to Ref.[5], can be converted to 2 via a Cope elimination. We obtained 3 as a syrupy product and its structure was confirmed as the picrate (mp 192 °C). The subsequent Cope elimination of 3 took place at about 85 °C in absolute DMSO. TLC analysis showed the presence of a single product but, in spite of various work-up conditions and in contrast to Ref.[5], we could not obtain compound 2 in crystalline form. The viscous oily product 2 is thermally labile and susceptible to polymerization. Hence, the constitution of 2 was confirmed indirectly via its Diels-Alder reaction with N-phenylmaleimide to yield 4 (mp 332 °C). According to MNDO calculations, compound 4 resulting from a dehydrogenative Diels-Alder reaction should represent the product of a $\mathrm{HOMO}_{\mathrm{diene}}$-$\mathrm{LUMO}_{\mathrm{dienophile}}$-controlled cycloaddition[3] (E_{HOMO} of 2 = -8.16



eV). In addition, according to MMX force field calculations[6] the coplanar s-cis and s-trans conformations of 2 represent the energetically minimum conformers and they exhibit only slight differences in their thermodynamic stabilities ($\Delta\Delta H_f$ = 1.0 kcal·mol^{-1})[6]. Thus, a sufficient population of the essential s-cis conformer of 2 can be assumed to be present in the reaction mixture for the construction of the [4 + 2] transition state.

Since the direct physical characterization of 2 in this way was unsuccessful, we attempted to realize an alternative concept for the synthesis of 2. The 3-vinylindole 5 (80%, mp 67 °C) can be prepared readily by a Wittig reaction from N-phenylsulfonylindole-3-carbaldehyde[7]. The protecting group of 5 can be cleaved under extremely mild conditions with KOH/ 18-crown-6 to furnish the 3-vinylindole anion 6. However, neutralization attempts led to polymerization so that again an indirect structural characterization via [4 + 2] cycloaddition with, in this case, 1,4-naphthoquinone added directly to the reaction mixture in which 6 had been generated was necessary. The cycloadduct 7 (mp 230 °C) was thus isolated and also represents the result of a dehydrogenating Diels-Alder reaction[5]. When the alkaline solution of the anion 6 was treated with an excess of dichloromethane, an S_N reaction occurred with the solvent to produce the bis(3-vinylindol-1-yl)methane 8, a physically extremely stable compound (mp 108 °C). The reaction products 7 and 8 without doubt represent further unequivocal structural evidence for the constitutions of 2 and 6. The constitutions of products 4, 7, and 8 were confirmed by ^{1}H- and ^{13}C-NMR spectroscopy, EI mass spectroscopy, and elemental analyses[8].



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5. W. E. Noland, R. J. Sundberg, J. Org. Chem. **28**, 884 (1963) and references cited therein.
6. MMX force field program (MM2/MMP1 Pi) from Serena Software, Bloomington, Indiana, U.S.A.
7. U. Pindur, L. Pfeuffer, Monatsh. Chem. **120**, 157 (1989).
8. 400 MHz ^{1}H-NMR data [δ (ppm), J (Hz)]: **4** (DMSO-d_6): 7.30 (dd, 2 x J = 7.5, 1H, C8-H or C7-H), 7.45 (m, 1H, C8-H or C7-H), 7.50-7.57 (m, 5H, phenyl), 7.66 (d, J = 8.1, 1H, C9-H), 7.71 (d, J = 7.8, 1H, C4-H), 8.31 (d, J = 7.9, 1H, C6-H), 8.63 (d, J = 7.9, 1H, C5-H), 12.25 (s, 1H, NH). **7** (DMSO-d_6): 7.26 (dd, 2 x ^3J = 7.7, 1H, C9-H or C10-H), 7.52 (dd, ^3J = 7.9 and 8.2, 1H, C10-H or C9-H), 7.80 (d, ^3J = 8.2, 1H, C11-H), 7.89 (mc, ^3J = 6.9 and 7.4, 2H, C2-H and C3-H), 7.98 (d, ^3J = 8.0, 1H, C6-H or C7-H), 8.17 (dd, ^3J = 7.3, ^4J = 0.8, $1H_{arom}$), 8.23 (mc, $2H_{arom}$), 8.58 (d, ^3J = 8.0, 1H, C7-H or C6-H), 12.21 (s, 1H, NH). **8** ($CDCl_3$): 5.25 (dd, ^2J = 1.3, $^3J_{cis}$ = 11.4, 2H, C2'-H_{trans}), 5.76 (dd, ^2J = 1.3, $^3J_{trans}$ = 17.8, 2H, C2'-H_{cis}), 6.28 (s, 2H, -CH_2-), 6.87 (dd, $^3J_{cis}$ = 11.4, $^3J_{trans}$ = 17.8, 2H, C1'-H), 7.31 (mc, 6H, C2-H, C5-H, C6-H), 7.48 (dd, ^3J = 8.1, ^4J = 0.7, 2H, C7-H), 7.94 (dd, ^3J = 7.9, ^4J = 0.9, 2H, C4-H).

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