Pergamon

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Isolation of 3H-Indole-3,3 Bis-Sulfides as Intermediates in the Second Sulfenylation of Indole

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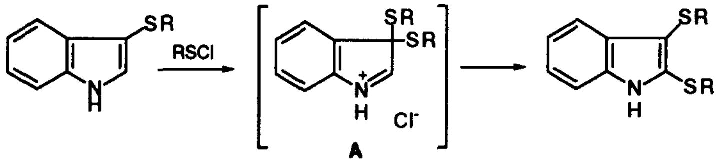
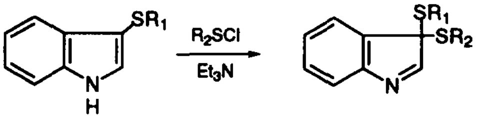
Abstract: 3H-Indole-3,3 bis sulfides have been isolated as probable intermediates in the second sulfenylation of indole with sulfenyl halides. © 1997 Published by Elsevier Science Ltd.

Recently,[1] we reported a study of the mechanism of the second sulfenylation of indole with sulfenyl halides, which provided strong support to the hypothesis[2] that initial attack occurs at the 3-position of the ring, leading to an intermediate 3,3-substituted indolenium species A. Subsequent migration of one of the sulfide groups, possibly via an episulfonium species, would lead to the 2,3-bis sulfide end-product. In our previous experiments,[1] we performed the second sulfenylation using a sulfenyl chloride that introduces a second sulfide which is different from the one already present. The fact that we obtained mixtures of the two possible mixed 2,3-bis sulfides indicated that initial formation of an intermediate of type A had occured, followed by migration of either of the two sulfide groups.



A

Further strong support for the hypothesis would be provided by the isolation of an intermediate of type A. We reasoned that it might be possible to isolate such a species by performing the second sulfenylation in the presence of a base which would neutralize the "hydrochloride" of A, allowing the isolation of 3H-indole-3,3 bis sulfides of type 1.



1a, $R_1 = R_2 =$ Ph
b, R_1=Ph R_2=p-tolyl

Indeed, when 3-phenylthioindole was subjected to sulfenylation with 1 eq. of benzenesulfenyl chloride, under the usual conditions[1,3] but in the presence of 1.2 eq of triethylamine , a new species was observed by tlc. This material was much less polar than the starting material, and was isolated by column chromatography on silica gel as an off-white, stable solid, mp 114-116°C. A recovery of 55% of the starting 3-phenylthioindole was also obtained, and no trace of 2,3-bis(phenylthio)indole could be detected. In a separate experiment, a second eq of benzenesulfenyl chloride was added to the mixture, leading to the almost complete transformation of the unknown material to 2,3-bis(phenylthio)indole. The proton NMR spectrum[4] of the intermediate species revealed that two phenylthio groups were present, with no sign of a NH signal. The presence of a singlet at δ 7.84 ppm was consistent with the presence of a proton at the 2-position of the ring. An infrared spectrum (KBr) did not show any absorption in the 3200-3500 cm^{-1} region, also indicating the absence of a NH proton. Elemental analysis[5] agreed with structure **1a** for the intermediate, and a mass spectrum indicated the correct molecular mass. The yield based on this structure was 33%. In a similar experiment, a sulfenylation was performed using p-toluenesulfenyl chloride, and mixed 3,3-bis sulfide **1b** was isolated in 27% yield, as a white solid, mp 112-114°C. To our knowledge, no examples of such 3H-indole-3,3 bis sulfides have been reported previously. A surprising property of the type **1** compounds is the fact that, when subjected to acidic conditions, such as trifluoroacetic acid or anhydrous HCl in DMF/1,2-dichloroethane (reaction solvents), or even in neat trifluoroacetic acid, they do not rearrange to indole-2,3 bis sulfides as might be expected. In a proton NMR experiment, addition of TFA to the acetone-d_6 solution did not cause the shift of any of the protons, indicating that the compounds of type **1** do not protonate.

We are pursuing our studies of the mechanism of the second sulfenylation of indole. The isolation of intermediates of type **1** will allow us to determine the conditions which promote their rearrangement to indole-2,3 bis sulfides

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4. ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.09-7.29 (m, 9H); 7.33-7.39 (m, 3H); 7.51 (d, j = 7 Hz, 1H); 7.71 (d, j = 7.5 Hz, 1H); 7.84 (s, 1H).
5. Calc'd for $C_{20}H_{15}NS_2$: C,72.04; H, 4.53; N, 4.20; S, 19.23. Found: C,71.91; H, 4.57; N, 3.83; S, 19.11.

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