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SYNTHESIS OF INDOLES FROM N-ARYL-1-ALKENYLSULPHINAMIDES

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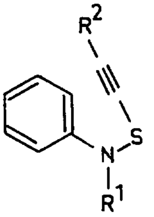
Summary: Reaction of 1-alkenylmagnesium bromides with N-sulphinyl-benzenamines affords the title sulphinamides 5. On heating in toluene, these sulphinamides 5 are transformed into the corresponding indoles.

A previous communication has described the thermal transformation of N-aryl-1-alkynesulphenamides 1, which undergo [3.3]-sigmatropic rearrangements followed by cyclisation of the intermediate thioketenes yielding indoline-2-thiones [1].



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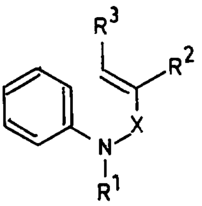
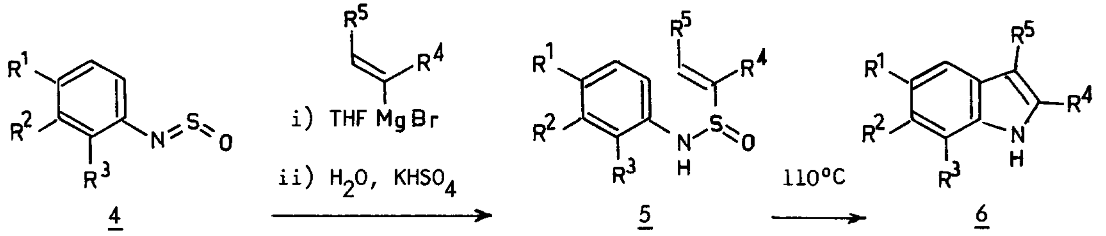


2 X = O
3 X = S

The known 1-aza-1'-oxa-[3.3]-sigmatropic rearrangement [2] of the compounds 2 has led us to investigate the properties of N-aryl-1-alkenylsulphenamides 3. These substrates 3 were obtained through a new procedure and generally on heating, they do not give the expected 1-aza-1'-thia-[3.3]-sigmatropic rearrangement [3].

The substrates that came next to our attention were the title sulphinamides 5, on account of their easy access and of the presence of the polar sulphinyl group which could allow the seeked [3.3]-sigmatropic rearrangement.

Many additions of various organometallic reagents [4] to N-sulphinyl-anilines [5] 4 are known. Most of the new N-aryl-1-alkenylsulphinamides 5 [6] were smoothly obtained from vinylic Grignard reagents [7] first at - 30°C then 2 hrs at + 18°C. Reaction of diisobutylaluminum hydride with 1-hexyne afforded the corresponding vinylalane which adds to N-sulphinylaniline yielding the compound 5b.



	R^1	R^2	R^3	R^4	R^5	yield %	yield % *
a	H	H	H	H	H	85	75 **
b	H	H	H	H	n.C_4H_9	82	19
c	CH_3O	H	H	H	H	97	52
d	H	CH_3O	H	H	H	95	25 ***
e	H	H	CH_3O	H	H	94	45
f	Cl	H	H	H	H	96	48
g	H	H	Cl	H	H	97	30
h	Br	H	H	H	H	95	49
i	CH_3	H	H	H	H	96	51
j	CH_3	H	H	CH_3	H	96	20

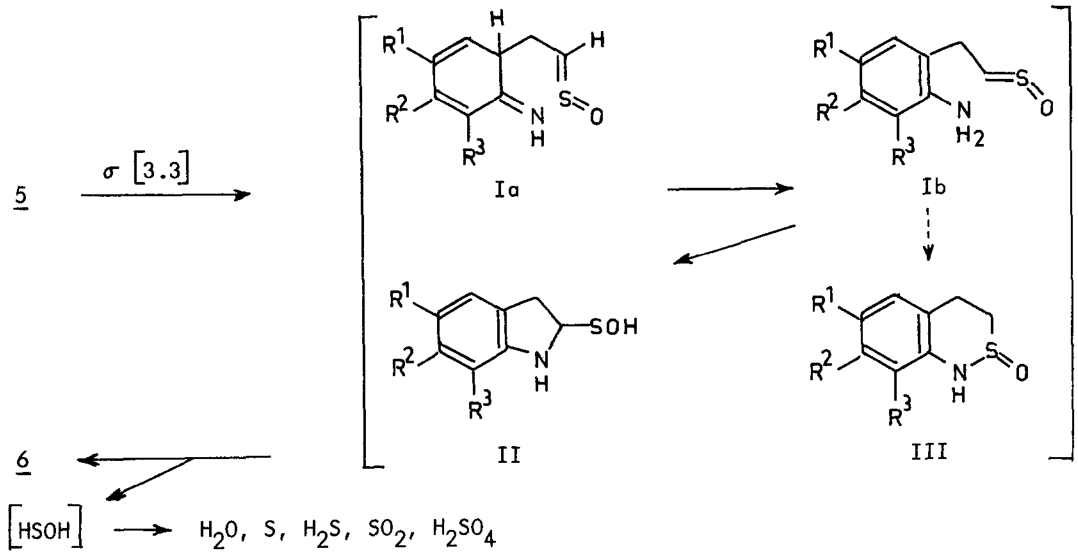
* All the isolated indoles showed m.p., NMR (^1H, ^{13}C) and Mass spectra consistent with literature data.

** The same yield was obtained after heating a solution of sulphinamide 5a in benzene for 90 min.

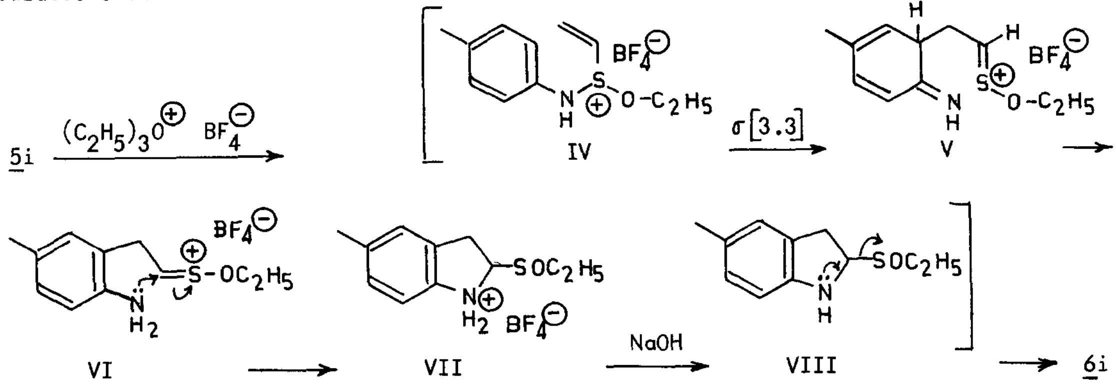
*** The thermal transformation of the sulphinamide 5d gave also 5 % of 4-methoxy-indole.

Slow distillation of an anhydrous 0.2 M solution of sulphinamide 5 in toluene with concomitant slow addition of fresh toluene over 1 hr afforded an azeotropic distillate containing sulphur and acidic water which probably arose from the decomposition of sulphenic acid HSOH. The remaining solution contains the indole 6 and the aniline $R^1R^2R^3(C_6H_2)\text{-}NH_2$ which were easily separated by flash chromatography. The yields are summarised in the table.

It is probable that during the thermal transformation of the sulphinamide, the aminosulphine I occurred as the intermediate formed through a [3.3] sigmatropic rearrangement [8]. Then the sulphine I could undergo either a carbophilic (→ II) or a thiophilic (→ III, not yet isolated) reaction with the nucleophilic neighbouring amino group. The unstable indoline-2-sulphenic acid II would readily explain the formation of the final products. However a recent review on the chemistry of sulphines [9] points out that the reactivity of simple sulphines with amines is unknown and that carbophilic reactions with nucleophiles are less frequently encountered.



When the sulphinamide 5i was treated with 1,2 equiv. of triethyloxonium tetrafluoroborate in methylene chloride at - 30°C for 16 hrs, the work up with dilute sodium hydroxide afforded indole 6i (30 %) and N,N-diethyl-4-toluidine (45 %). As some sulphinamides are known to be alkylated to the corresponding sulphonium salts by triethyloxonium tetrafluoroborate [10] or by methyl trifluoromethanesulphonate [11], the following intermediates seemed to be reasonable:



The cationic charge-accelerated process known for other unsaturated sulphonium salts [12] may explain the fact that the alkylated species IV rearranges at much lower temperature than the sulphinamides 5. However in the only case studied, the indole 6i was obtained in a lower yield. Efforts to verify this point with other examples and to obtain a better understanding of chemical reactivity of the N-aryl 1-alkenylsulphinamides in order to increase the yields of the indoles are underway and will be reported in due course.

In conclusion, we have developed a new method for the preparation of the indole ring system which is an important structural subunit of numerous natural products.

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