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Rapid Communication

Regiochemical control in the addition of aryl N-sulphinylamines to juglone and juglone derivatives

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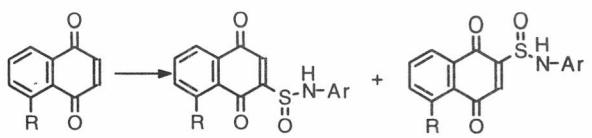
Regiochemistry of the addition of *N*-aryl-sulphinylamines to juglone and juglone derivatives is controlled by the nature of the oxygen function at 5-position.

Inhoffen and Muxfeldt in their studies directed towards the tetracycline synthesis reported an interesting observation[1], that the nature of the oxygen function in 5-hydroxy-1,4-naphthoquinone (juglone) and juglone acetate profoundly influences the regiochemical course of the cycloaddition with 1-acetoxybutadiene. Similar reactions have been observed when 1-methoxy-dienes are used as well[2]. Enhancement in the regiochemical directing ability of 5-hydroxy group in juglone has been found when the Lewis acid catalysts are used in the Diels-Alder reaction[3,4]. Kelly *et al.* In their studies on the synthesis of Adriamycinone have observed a reversal in the regiochemistry when juglone acetate is used instead of juglone as the dienophile[5]. Further, they have explained these regiochemical effects by using H-bonding in juglone and selective electron feeding from *peri*-acetoxy group in acetoxyjuglone. In a detailed study on factors influencing the regiochemical control in the Diels-Alder reaction between juglone derivatives and a wide range of dienes, Boeckman[6] has rationalised the results as regiochemistry is dominated by the diene polarity and the juglone and related systems are weakly polarised. Therefore, good regioselectivities are found only with highly polarised dienes in the uncatalysed reactions. Regioselective cycloaddition in juglone and related systems has been reported with a 1-azadiene as well[7].

Recently we have found that *N*-arylsulphinylamines add smoothly to 1,4-naphthoquinone when an equimolar mixture in benzene is allowed to stand at room temperature to give 2-arylsulphimoyl-1,4-naphthoquinones[8]. This reaction has been explained as an initial 2+2 cycloaddition of the N=S bond of the sulphinylamine to alkene to give a thiazitidinone oxide followed by the fragmentation of this intermediate with a 1,3-H shift. One can expect more pronounced regiochemical effects from 5-substitutes in the 2+2 cycloaddition where a highly polarised N=S bond is involved. In an attempt to develop methodology for regiocontrolled functionalisation of the alkene bond of 1,4-naaphthoquinone we have investigated the reactions of *N*-arylsulphinylamines with juglone, juglone acetate and juglone methyl ether (cf. **Scheme I**). The reaction between juglone and *N*-(*p*-methylphenyl)sulphinyl-amine gave only one product **1** and not even a trace of the other regioisomer **2** was seen in the 200MHz ^{1}H NMR. According to Kelly's hypothesis[5], H-bonding of the 5-hydroxy group makes the 4-C=O group a weaker polarising group, and the C-1 carbonyl directs the polarisation of the alkene. Using these arguments in the 2+2 cycloaddition with N=S bond, one can predict that the 3-arylsulphimoyl isomer is the only product formed in the reaction. To establish the structure, the product was hydrolysed (20% aq. HCl, reflux, 1 hr) giving 3,5-dihydroxy-1,4-naphthoquinone in 88% yield. The structure of this isomer was unambiguously confirmed by comparison of the ^{13}C NMR[9a] and mp[9b]. Acid[10a] or base [10b] hydrolysis of the sulphimoyl function in cyclic systems are known to give sulfinic acids with the cleavage of N-S bond. Hydroxylation of the alkene with the cleavage of C-S



1 **2**

R = OH, OAc, OMe
+ Ar - N=S=O
Ar = C_6H_5, *p*-CH_3-C_6H_4

R	Ar	Yield %	1 : 2
OH	C_6H_5	76	1 : 0
OH	*p*-CH_3-C_6H_4	70	1 : 0
OAc	*p*-CH_3-C_6H_4	90	1 : 8.2
OMe	*p*-CH_3-C_6H_4	78	1 : 4.7

Scheme I

bond is an unusual reaction, and as far as we are aware, this is the first example of such reaction in the sulphimoyl function. Addition of *N*-phenylsulphinylamine to juglone also gave only one isomer **1** and the hydrolysis of this adduct also resulted in 3,5-dihydroxy-1,4-naphthoquinone. Addition of *N*-(*p*-methylphenyl)-sulphinylamine to juglone acetate gave a mixture of adducts **2** and **1** in 8.2:1 ratio. The major isomer was 5-acetoxy-2-(*p*-methylphenylsulphimoyl)-1,4-naphthoquinone **2**. The structures of these products were also confirmed by hydrolysing to 2,5-dihydroxy-1,4-naphthoquinone[9] and 3,5-dihydroxy-1,4-naphthoquinone. This is in agreement with the Kelly's hypothesis[5], and the best regioselectivity reported[3] for 4+2 cyclôaddition is 3:1; this significant improvement in the regioselectivity is due to the highly polarised N=S bond which is involved in 2+2 cycloaddition. Methoxyjuglone gave a mixture of adducts **2** and **1** in 4.7:1 ratio (cf. **Scheme I**). Methoxy group is known to have regiochemical directing ability similar to OAc in the 4+2 reaction as well[5]. The present method can be used in the regioselective hydroxy-lation of juglone.

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