PREPARATION OF 1-TOSYL-2- AND 3-PYRROLIDINONES 'VIA' KETENES AND CARBENES

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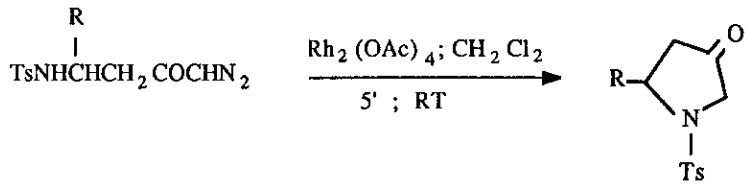
Abstract - Catalytic decomposition of 1-diazo-4-tosylamino-2-butanone **1a**, -2-pentanone **1b**, and -2-hexanone **1c**, results in the quantitative formation of the 1-tosyl-3-pyrrolidinones **2a**, **2b** and **2c**, while the photolysis afforded the rearranged esters, **3a**, **3b** and **3c**, or the unexpected 1-tosyl-2-pyrrolidinones **4a**, **4b** and **4c** depending on the solvent employed.

Following our interest in the reactivity of carbenes generated by catalytic decomposition of 1-diazocarbonyl compounds in order to obtain intramolecular cyclizations to 6- and 5-membered heterocycles[1,2], recently we have described how some carbenoids[3] derived from N-tosyl-α-aminoacids produce small ring heterocycles in good yields[4]. Here we report the decomposition of the homologous 1-diazo ketones which show unusual behaviour. The required substrates N-(4-diazo-3-oxobutyl)-4-methylbenzenesulfonamide, **1a**[5], N-(4-diazo-1-methyl-3-oxobutyl)-4-methylbenzenesulfonamide, **1b**, and N-(4-diazo-1-ethyl-3-oxobutyl)-4-methylbenzenesulfonamide, **1c** were easily prepared from the appropriate N-tosyl-β-amino acid by reacting the corresponding acid chloride with CH_2N_2.

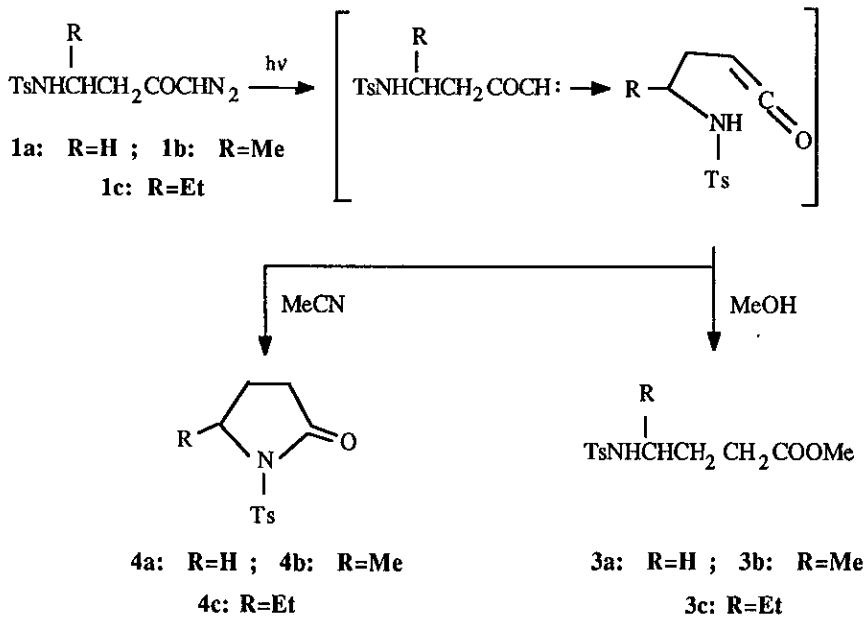


1a: R=H; 1b: R=Me
1c: R=Et

2a: R=H; 2b: R=Me
2c: R=Et

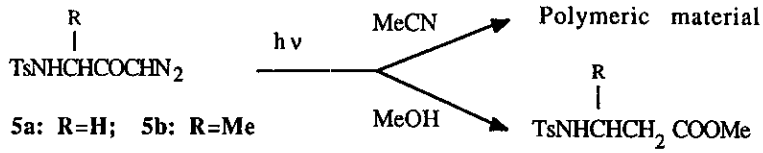
Treatment of **1a, 1b** and **1c** with catalytic amounts of rhodium acetate II (1% by wt) in dichloromethane at RT for 5' quantitatively afforded, after removal of the catalyst by filtration on neutral Al_2O_3, the 1-(4-methylphenyl)sulfonyl-3-pyrrolidinone, **2a**[5], the 1-(4-methylphenyl) sulfonyl-5-methyl-3-pyrrolidinone, **2b** and the 1-(4-methylphenyl) sulfonyl-5-ethyl-3-pyrrolidinone, **2c**, respectively. This reaction is due to the 'normal' intramolecular carbene insertion into the N-H bond. The diazo ketones **1a,b,c** were then submitted to photolysis[6] at 254 nm in MeOH solution giving, as the only products, the rearranged methyl 4-tosylaminobutanoate, **3a**,-pentanoate, **3b** and -hexanoate, **3c**, respectively. Surprisingly, when the irradiation of **1a, 1b**, and **1c** was performed in MeCN solution at the same reaction conditions, the unexpected 1-(4-methylphenyl)sulfonyl-2-pyrrolidinone, **4a**[7], 1-(4-methylphenyl)sulfonyl-5-methyl-2-pyrrolidinone, **4b** and 1-(4-methylphenyl)sulfonyl-5-ethyl-2-pyrrolidinone, **4c**, were recovered in >70% yield[8]. A probable mechanism to explain the different reaction course observed simply by changing the solvent is tentatively depicted in the Scheme: while the formation of the methyl esters **3a,b,c** could be explained in terms of the expected Wolff rearrangement, the intramolecular trap by the nitrogen atom of the intermediate ketene probably takes place in acetonitrile solution leading to γ-lactams, **4a,b.c**

SCHEME



A similar intramolecular trapping by an amidic nitrogen atom was previous observed as an undesired reaction, in a photo-decomposition of a more complex cyclic diazo ketoester[9], while the presence of a neighbouring heteroatom can generally interfere with the Wolff rearrangement or lead to secondary products[10]. In the present case, the reduced nucleophilicity of the nitrogen due to the electron withdrawing sulfonyl group could make it unable to interfere with the carbene-ketene rearrangement, while it is still able to internally trap the latter reactive intermediate. Thus the Wolff rearrangement is the only one of the processes occurring under photolytic conditions[11] and the selective cyclization by the keto carbenoid N-H insertion is observed in the catalytic decompositions: since the protective group can be easily removed[12], both catalytic and photolytic reactions are convenient preparations of the 2- and 3-pyrrolidinone ring systems.

In keeping with the aim of developing procedures or new entries for the preparation of N-unsubstituted β-lactams in the monobactam synthesis[13], these unexpected results suggested the photolysis of the α'-tosylamino-α-diazo ketones, **5a,b** whose acid and catalytic treatment afforded the 3-azetidinone ring system[4].



5a: R=H; 5b: R=Me

6a: R=H; 6b: R=Me

No traces of the rearranged 2-azetidinones were obtained by irradiating **5a** and **5b** in methanolic solution, but the ω-sulfonamido-methyl esters, **6a**[14] and **6b**[15] in quantitative yield. The photo-decomposition performed in MeCN solution, afforded a polymeric material which is under investigation. The lack of formation of the β-lactam ring is probably due to unfavourable strain factors.

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