

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

Antonio Saba^{*a} and Antonio Selva^b

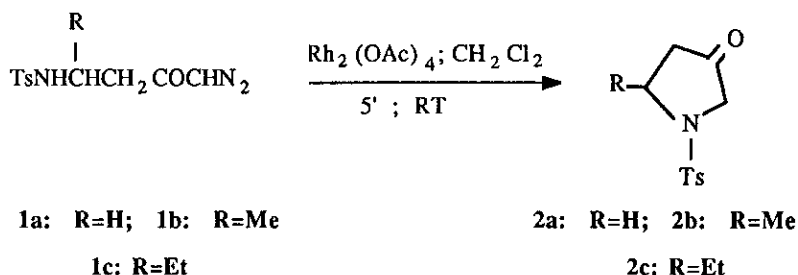
a) Dipartimento di Chimica dell'Università. Via Vienna, 2

I-07100 Sassari, Italy

b) C.N.R. Centro di studio di Chimica delle Sostanze Organiche Naturali, C/O Politecnico, Dipartimento di Chimica, P.zza Leonardo da Vinci, 32. I-20133 Milano, Italy

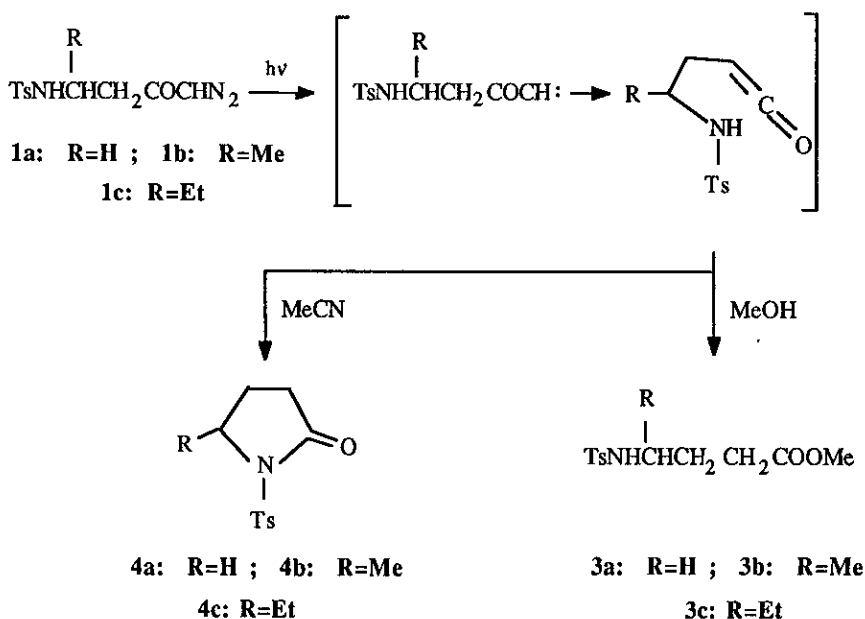
Abstract - Catalytic decomposition of 1-diazo-4-tosylamino-2-butanone **1a**, -2-pentanone **1b**, and -2-hexanone **1c**, results in the quantitative formation of the 1-tosyl-3-pyrrolidinones **2a**, **2b** and **2c**, while the photolysis afforded the rearranged esters, **3a**, **3b** and **3c**, or 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 carbenoids³ derived from N-tosyl- α -aminoacids produce small ring heterocycles in good yields⁴. 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 .



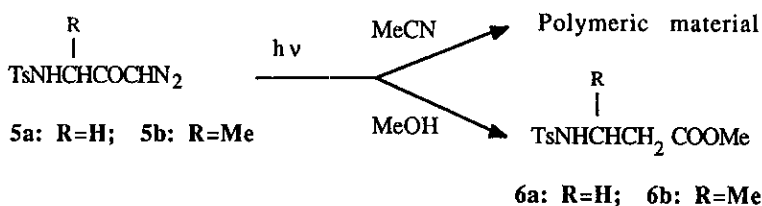
Treatment of **1a**, **1b** and **1c** with catalytic amounts of rhodium acetate II (1% by wt) in dichloromethane at RT for 5' quantitatively afforded, after removal of the catalyst by filtration on neutral Al_2O_3 , the 1-(4-methylphenyl)sulfonyl-3-pyrrolidinone, **2a**⁵, the 1-(4-methylphenyl)sulfonyl-5-methyl-3-pyrrolidinone, **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 photolysis⁶ at 254 nm in MeOH solution giving, as the only products, the rearranged methyl 4-tosylamino-butanoate, **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% yield⁸. 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 previously observed as an undesired reaction, in a photo-decomposition of a more complex cyclic diazo ketoester⁹, while the presence of a neighbouring heteroatom can generally interfere with the Wolff rearrangement or lead to secondary products¹⁰. 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 conditions¹¹ and the selective cyclization by the keto carbenoid N-H insertion is observed in the catalytic decompositions: since the protective group can be easily removed¹², 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 synthesis¹³, 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 system⁴.



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.

ACKNOWLEDGMENTS

We wish to thank prof. Tullio Caronna for helpful discussions and Mr. Mauro Mucedda for experimental assistance. Financial support from the 'Ministero della Pubblica Istruzione' is gratefully acknowledged.

REFERENCES AND NOTES

- 1) A. Saba, Synthesis, 1984, 268.
- 2) A. Pusino, A. Saba, and V. Rosnati, Tetrahedron, 1986, 42, 4319.
- 3) The term 'carbenoid' is referred here to a carbene complex generated by catalytic decomposition of diazo compounds (as opposed to a free carbene generated photochemically): S. D. Burke and P. Grieco, Org. Reactions, 1979, 26, 364.
- 4) A. Pusino, A. Saba, G. Desole, and V. Rosnati, Gazz. Chim. Ital., 1985, 115, 33.
- 5) Acid decomposition (MeCOOH) of 1-diazo-4-tosylamino-2-butanone, **1a**, was reported to afford 49% 3-pyrrolidinone, **2a**, and N-(4-acetoxy-3-oxobutyl)-4-methylbenzenesulfonamide: V. G. Kartsev and M. A. Sipyagin, Zh. Org. Chim., 1979, 15, 2603 (Russ.), C. A. 92, 1980, 215189d.
- 6) Photolyses were carried out through quartz vessels using a Rayonet apparatus equipped with 2537 Å lamps and operating at 35°. The reactions were run until the diazo stretching absorption was no longer visible in the infrared spectrum (usually 60-90').
- 7) W. Reppe, Ann., 1955, 596, 80.
- 8) All new compounds presented correct composition by elemental analysis in accordance with the proposed structure.
- 9) H. Meyer and K. P. Zeller, Angew. Chem. Int. Ed. Engl., 1975, 14, 32.
- 10) R. W. Ratcliffe, N. T. Salzmann, and B. G. Christensen, Tetrahedron Lett., 1980, 21, 31.
- 11) W. Kirmse, Carbene Chemistry, 2nd., Edn., Academic Press, New York 1971, pp 475-492.
- 12) I. W. Green, Protective groups in Organic Synthesis, J. Wiley and Sons, New York 1981, 285.
- 13) Chemistry and Biology of β -lactam antibiotics, R. B. Morin and M. Goldmann, Eds., Academic Press, New York 1982.
- 14) P. Buckus and R. Stonite, Zh. Obshch. Khim. 1963, 33, 624 (Russ.), C. A. 75, 1972, 151656t.
- 15) A. Cromarty, K. E. Haque, and G. R. Proctor, J. Chem. Soc. C, 1971, 3536.

Received, 20th November, 1987