Metalloporphyrin-catalysed Rearrangement of Oxaziridines: An Efficient and Regioselective Synthesis of Lactams Using Ring-enlargement of *N*-Phenyl-spirooxaziridines

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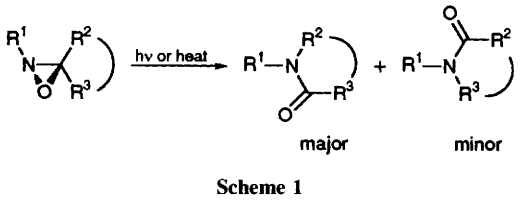
Manganese(III) tetraphenylporphyrin, Mn(tpp)Cl, is a new and specific catalyst for stereo- and regio-selective rearrangement of *N*-phenyl-spirooxaziridines into lactams.

Oxaziridines, strained three-membered ring compounds bearing a configurationally stable nitrogen atom,[1] have attracted considerable interest because of their photochemical and thermal rearrangements into amides or lactams.[2] These rearrangements into lactams are regioselective where the C-3 substituent *trans* to the lone pair of the ring nitrogen preferentially migrates to the nitrogen[3,4] (Scheme 1). The photochemical rearrangement is a valuable alternative to Schmidt and Beckmann rearrangements which usually require strongly acidic conditions, causing serious problems such as low regioselectivity of the reactions or decomposition of products.[5] The corresponding thermal rearrangement of spirooxaziridines is, however, substrate-dependent and inferior to the photochemical process with respect to the efficiency and selectivity.[3] Only one catalyst has been developed for the synthesis of a lactam from a spirooxaziridine.[6] We have recently reported that high valent metalloporphyrins work as a mild and characteristic Lewis-acid catalyst for the rearrangement of oxaziridines into amides.[7] Therefore, we expected these metalloporphyrins could be used in the ring-expanding rearrangement of spirooxaziridines into lactams. Reported herein is a new and highly efficient transformation of *N*-arylspirooxaziridines **1** into lactams **2** with high valent metalloporphyrins, especially manganese(III) tetraphenylporphyrin, Mn(tpp)Cl.

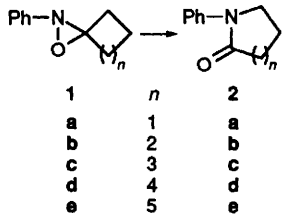
To find effective Lewis-acid catalysts for the rearrangement, the reaction of 2-phenyl-1-oxa-2-azaspiro[2,5]hexane **1c** with various Lewis acids was studied as it has been reported that the photochemical rearrangement of **1** into **2** is less promising than the corresponding thermal rearrangement.[3b,8] This rearrangement, however, could not be catalysed by common Lewis acids such as $AlCl_3$, $FeCl_3$, $TiCl_4$ and BF_3–Et_2O in aprotic solvents; these Lewis acids only decomposed **1c** into cyclohexanone along with tarry materials.

We then examined catalytic activity of the tetraphenylporphyrin complexes of the first series transition metals. Trivalent metallo-tpp complexes with chloride as an axial ligand such as Mn(tpp)Cl, Fe(tpp)Cl and Co(tpp)Cl were found to be mild and specific catalysts for the rearrangement. In the presence of these catalysts the rearrangement smoothly proceeded in aprotic solvents with high dielectric constant but low nucleophilicity. Mn(tpp)Cl was the most effective catalyst examined, the order of catalytic activity was Mn(tpp)Cl≫ Fe(tpp) > Co(tpp)Cl. Indeed, the reaction of **1c** (5 mmol) with a catalytic amount of Mn(tpp)Cl (0.1 mmol) at 30 °C in acetonitrile (20 ml) gave lactam **2c** (97%) after 20 min, whereas without the catalyst no rearrangement was observed under the same conditions. Divalent metallo-tpp complexes such as Cu(tpp), Fe(tpp) and Co(tpp) showed no catalytic activity for the rearrangement. These results suggest that the rearrangement proceeds *via* an ionic not an electron transfer process.



Scheme 1

The catalyst, Mn(tpp)Cl, was applied to the rearrangement of *N*-phenylspirooxaziridines, **1a–e**, with a different carbon ring size (Scheme 2). The rearrangements proceeded efficiently in acetonitrile under mild reaction conditions and were essentially independent of the size of the carbon-ring of the spirooxaziridines used (Table 1). The advantage of these

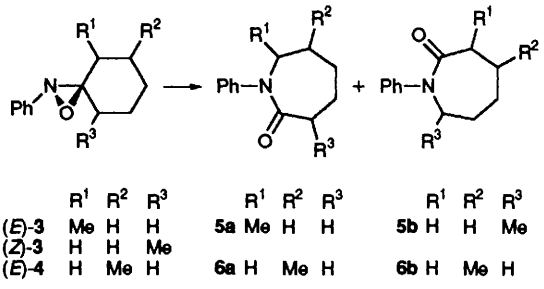


Scheme 2

Table 1 Rearrangement of *N*-phenylspirooxaziridines into lactams in the presence (A) and in the absence (B) of Mn(tpp)Cl in acetonitrile

Run	Oxaziridine 1		Conditions t	T/°C	Lactam 2	Yield/ %[a]
1	**a**	B	15 min	30	**a**	0[b]
2	**a**	A	15 min	30	**a**	60[b]
3	**b**	B	40 min	30	**b**	34[b]
4	**b**	A	15 min	30	**b**	77[b]
5	**c**	B	20 min	30	**c**	trace
6	**c**	A	20 min	30	**c**	97
7	**d**	B	24 h	reflux	**d**	62[b]
8	**d**	A	7.5 h	50	**d**	72[b]
9	**e**	B	24 h	reflux	**e**	58
10	**e**	A	5 h	50	**e**	90

[a] Isolated yields. [b] Isolated yields based on the ketone used.



Scheme 3

Table 2 Rearrangement of unsymmetric *N*-phenylspirooxaziridines in the presence of Mn(tpp)Cl in acetonitrile

Run	Oxaziridine	t/min	T/°C	Lactam	Yield/ %[a]	Isomer ratio[a] a : b
1	(*E*)-**3**	50	40	**5a,5b**	98	98 : 2
2	(*Z*)-**3**	50	40	**5a,5b**	94	2 : 98
3	(*E*)-**4**	80	40	**6a,6b**	96	94 : 6

[a] Determined by HPLC.

catalytic rearrangements over the corresponding thermal and photochemical reactions were shown in the rearrangements of spirooxaziridines with a small carbon-ring size, **1a** and **1b**. **1a** is unstable at room temp. and neither the photochemical nor the thermal rearrangement of it into **2a** has ever been reported. Although attempted non-catalysed thermal rearrangement of **1a** was unsuccessful, the catalytic rearrangement with Mn(tpp)Cl rapidly proceeded at 30 °C and gave **2a** in a good yield. Similar results were obtained with **1b**.

Spirooxaziridines with a larger carbon-ring size, **1d** and **1e**, were relatively stable but their non-catalysed thermal rearrangements required a long reaction time for the consumption of the substrates under reflux in acetonitrile and gave lactams **2d** and **2e**, respectively, in sufficient yields. On the other hand, the catalytic reactions proceeded smoothly at 50 °C and the yields of the lactams were essentially quantitative.

We further investigated the stereo- and regio-chemistry of the rearrangement of unsymmetrically substituted *N*-phenylspirooxaziridines, in which one should expect the formation of two regioisomeric lactams depending on the migration aptitude and bond energy of the two cleavable C–C bonds of the spirooxaziridines (Scheme 3 and Table 2). *N*-phenylspirooxaziridine **3** was prepared *via* peracid oxidation of the corresponding imines as a mixture of (*E*)- and (*Z*)-stereoisomers. They were separated into pure stereoisomers (*E*)-**3** and (*Z*)-**3**.[3b] When (*E*)-**3** was treated with Mn(tpp)Cl (2 mol% to the substrate used) in acetonitrile at 40 °C for 50 min, a mixture of lactams **5a** and **5b** was obtained in 98% total yield (run 1). The regioisomer ratio **5a**/**5b** = 98/2 was determined by HPLC. As shown in Table 2, the observed high regioselectivity is surprisingly reverse to those reported on the corresponding thermal and photochemical rearrangements (30/70 and 5/95).[3] These results mean that the new catalytic rearrangements take place with the migration of the C-3 substituent *cis* to the lone pair of the ring nitrogen. The rearrangement of the stereoisomer (*Z*)-**3** with this catalyst under the same conditions, on the other hand, led to **5b** almost exclusively and the regioisomer ratio was, in this time, **5a**/**5b** = 2/98 (run 2). Hence, stereoselective migration of the C-3 substituent *cis* to the lone pair of the ring nitrogen is also obvious in these reactions.

In order to confirm this new stereoselective event, we further investigated the rearrangement of spirooxaziridine (*E*)-**4**. For the photochemical rearrangement of (*E*)-**4** into lactams **6a** and **6b**, a high regioselectivity has been reported (**6a**/**6b** = 5/95).[3d] Treatment of (*E*)-**4** with Mn(tpp)Cl under similar conditions (in acetonitrile at 40 °C) gave a mixture of the lactams in a high yield with an excellent reverse regioselectivity (**6a**/**6b** = 94/6, run 3). Again, stereoselective migration of the C-3 substituent *cis* to the lone pair of the ring nitrogen was confirmed. In the catalytic rearrangement of unsymmetric *N*-phenylspirooxaziridines, substitution pattern in the carbon-ring size seems to have little effects on the migration aptitude of the C-3 substituents.

It is well known that the reactivity of oxaziridines toward pyrolysis or thermal decomposition varies very much depending on the structure of substituents on the ring.[9]

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