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ARENE-CHROMIUM-TRICARBONYL COMPLEXES : STEREOSELECTIVE REACTIONS WITH ISOCYANIDE*

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ABSTRACT : *More than 98 % of A.I. is obtained during addition of TosMic with chiral complexes* **2** *and* **3**. *The diastereoselectivity of the formation of the oxazolines is studied and the diastereomers clearly assigned. Orbital-interactions and electronic repulsions seem to be responsable for the presence of the cis isomers.*

During studies on the use of chiral arene-chromium-tricarbonyl complexes in enantioselective synthesis (1), we have investigated the reaction of tosyl methyl isocyanide **1** (TosMic) (2a) with complexes **2** and **3**. Many papers have been devoted to the reaction of this reagent with carbonyl compounds and other functional groups (2b) ; however all studies concerning aromatic aldehydes have been directed toward the synthesis of oxazoles. The oxazolines obtained as intermediates were neither isolated nor investigated (2c). We have thus focussed our attention on the formation of oxazolines **4** and **5**, as a route to optically pure amino alcohols, after $LiAlH_4$ reduction (2b).

We report here our preliminary results concerning the diastereoselectivity of the addition of TosMic **1** on complexed aldehydes **2**, **3** and, for comparison, on uncomplexed aldehydes **6**, **7** and **8**.

Oxazolines (**4**, **5**, **9** - **11**) are obtained by reacting equimolar quantities of TosMic **1** and aldehydes (**2**, **3**, **6** - **8**) with K_2CO_3 in methanol (2c), followed by addition of one molar equivalent of acetic acid. The results are given in Table 1.

Among the four diastereomers expected from complexes **2** and **3**, only one or two are obtained (entries 1,3 and 2,4 respectively). After decomplexation, diastereomer **4b** (entry 1) and mixture **4a/4b** = 1/2 (entry 2) give diastereomer **9b** and mixture **9a/9b** = 1/2 respectively ; therefore diastereomers **4a**, **4b** have been ascribed to cis/trans oxazoline-ring isomerism. Assignment of diastereomers **9a** and **9b** to cis and trans structures respectively has been done using 200 MHz proton-NMR (3) on the following observations :

1) the non-equivalence between H-4 and H-5 (4) is larger in isomer trans (1.2 ppm) than in isomer cis (0.3 ppm), as expected,
2) a usual non-equivalence of about 0.45 ppm between ortho and meta-protons of ring B in the trans isomer where the aromatic rings are away from each-other, and a small non-equivalence (0.05 ppm) between those protons in the cis isomer due to shielding of the ortho-protons by ring A (cf. Figure 1) are observed.

Assignments of diastereomers **5a**, **10a** and **5b**, **10b**, **11b** have been obtained in the same way.

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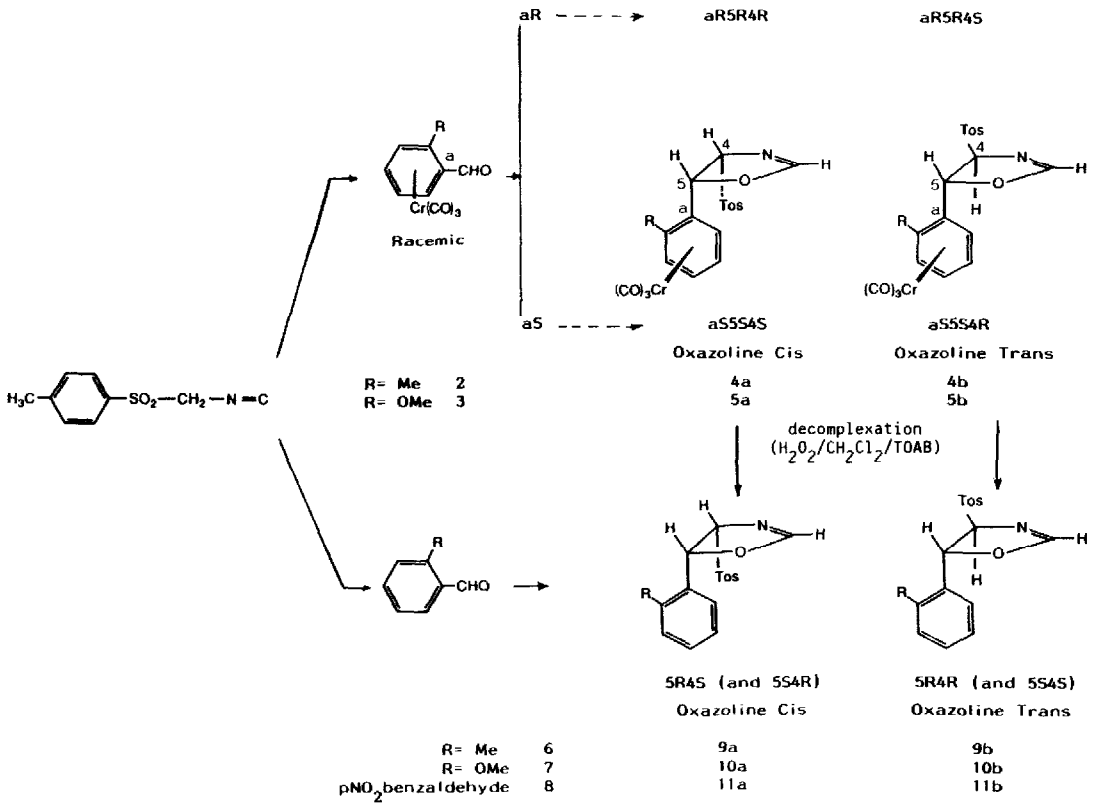
Scheme 1 :



The exclusive formation of trans isomer **4b** and/or **5b** (entries 1,4) shows that the asymmetric induction at C-5 induced by the complex's chirality is > 98 % which is consistent with previous results (1,5). Therefore according to our model of approach (6) one can postulate that S complex **2** (or **3**) will give the aS5S4R trans oxazoline (scheme 1 and Figure 2) which, after decomplexation and reduction (2b), will lead to the optically pure R amino-alcohol.

It must be noticed that the cis oxazolines formed (Figure 2) has also the S configuration at C-5, therefore decomplexation and reduction of the cis/trans mixtures (**4a/4b** or **5a/5b**) will also lead to optically pure R amino alcohols.

We have been surprised to note : i) an increase of the percentage of cis isomer with the temperature in the cases of complexes **2, 3** and free ligands **6, 7**. ii) that the cis isomer was prefered in the case of free ligand **6** ; which cannot be justified on the basis of steric interactions.

One could postulate that an attractive interaction involving the electron-rich phenyl ring A and the electron-poor phenyl ring B would compete with the steric interaction and increase the percentage of cis isomer. This hypothesis is consistent with the 100 % trans isomer obtained with p-nitrobenzaldehyde **8**, here, the phenyl ring A being also electron-poor, the attractive interaction between the two phenyl rings is nil or at least very small.

This orbital interaction is also consistent with the decrease of the percentage of the cis isomer on going from the free ligand (**6, 7**) to the complexed one (**2, 3**) due to lowering of the aromatic π orbitals on complexation

Table 1 : Reactions of TosMic with aldehydes (2, 3, 6, 7, 8)

Entry	Substrate	T (° C)	Time (hrs)	Complexed oxazoline cis : trans[a]	uncomplexed oxazoline cis : trans[a]	yield[b] (%)
1	2	0	0.5	0 : 100	0 : 100	100[c]
2	2	20	0.5	33 : 66	33 : 66	100[c]
3	3	0	3.5	1 : 99	-	100[c]
4	3	20	0.5	15 : 85	-	100[c]
5	6	0	6.5	-	66 : 33	55[d]
6	6	20	2.0	-	94 : 6	95[d]
7	7	0	6.0	-	30 : 70	95[d]
8	7	20	2.0	-	55 : 45	90[d]
9	8	0	0.5	-	0 : 100	100[d]

a) averaged over 2 to 3 reactions. b) determined on NMR spectra of crude products and refered to the starting aldehyde. c) percentage of recovered crude products = 90-95 %. d) percentage of recovered crude products = 70-85 %.

Figure 1 :

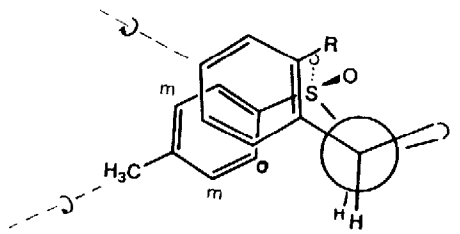
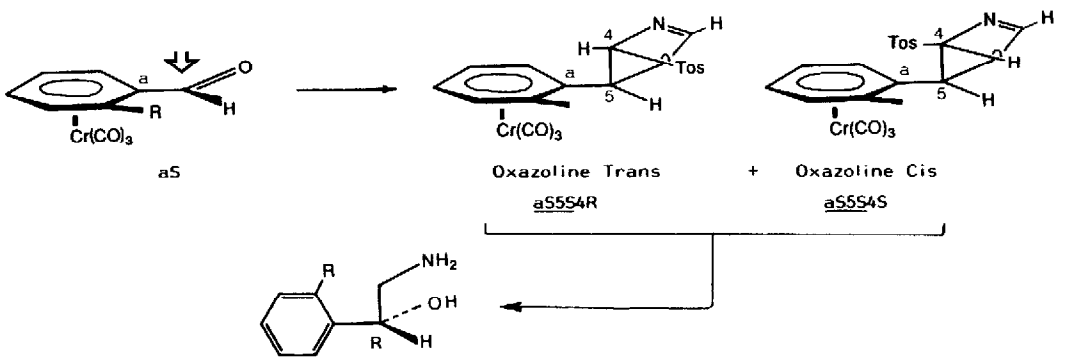


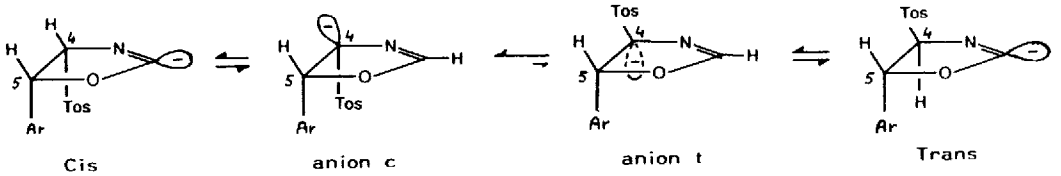
Figure 2 :



(7). The decrease of the percentage of the cis isomer in the case of compounds **3** and **7** could be a consequence of the larger steric demand of the methoxy group.

The increase in the percentage of cis isomer with the temperature is more intriguing ; one might envisage a temperature dependent equilibrium between the different anions involved (2d), the cis-anion **c** being stabilized by a $\sigma . \pi$ hyperconjugative interaction while the trans-anion **t**- could be destabilized by electronic repulsions (8), scheme 2.

Scheme 2:



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3) cis-oxazoline : 2.39 (3H, s, Me ring B), 3.54 (3H, s, Me ring A), 5.12 (1H, d.d, H-5, ^3J = 4.3 Hz, ^4J = 0.9 Hz), 5.42 (1H, d, H-4, ^3J = 4.3 Hz), 7.2 (9H, m, 4H, ring A + 4H ring B + H-2)
trans-oxazoline : 2.46 (3H, s) and 2.55 (3H, s) = Me on ring A and B, 5.08 (1H, d.d, H-4, ^3J = 5 Hz, ^4J = 1 Hz), 6.27 (1H, d, H-5, ^3J = 5 Hz), 7.2 (5H, m, 4H, ring A + H-2), 7.38 (2H, d, H_m, ring B, ^3J = 9Hz), 7.84 (2H, d, H_o ring B, ^3J = 9 Hz)

4) Assignment of H-4 and H-5 has been done using NOE-DIF technic :
4b : irradiation of Me on ring A gives 13 % effect on H-5 and 0.5 % on H-4 ;
9b : irradiation of Me on ring A gives 23 % effect on H-5 and 4 % effect on H-4.

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8) We are grateful to Dr. Wipff G. for the suggestion dealing with anion stability.

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