

[A0041]

REDUCTIVE RING OPENING OF  $\text{Cr}(\text{CO})_3$ -COMPLEXED  $\beta$ -LACTAM RING:

## STEREOSELECTIVE SYNTHESIS OF DIHYDROBENZOPYRAN

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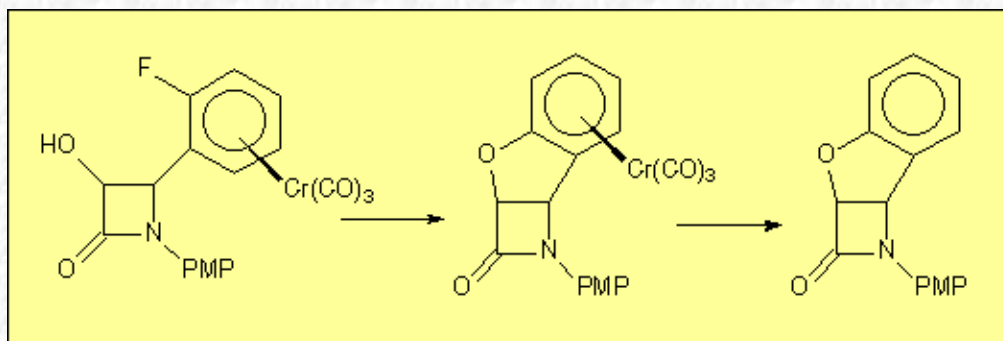
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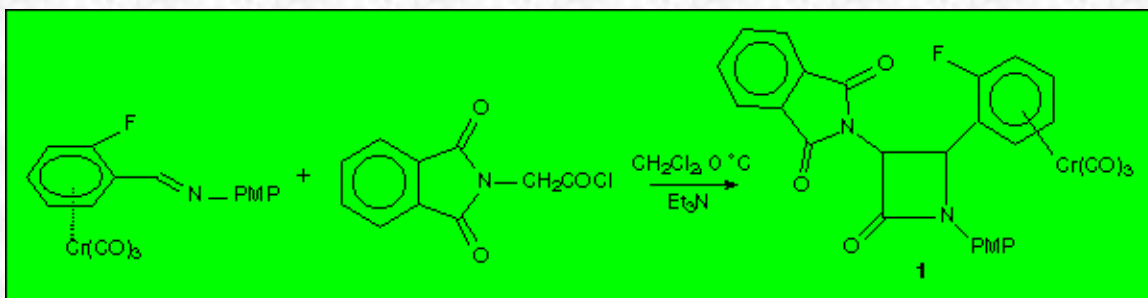
### Introduction:

In a preceding paper we have reported the stereoselective synthesis of a  $\beta$ -lactam tricyclic structure exploiting the chirality induced by *ortho* substituted chromiumarenes as well as its activation to the nucleophilic aromatic substitution, according the following Scheme:



### Aim of the work:

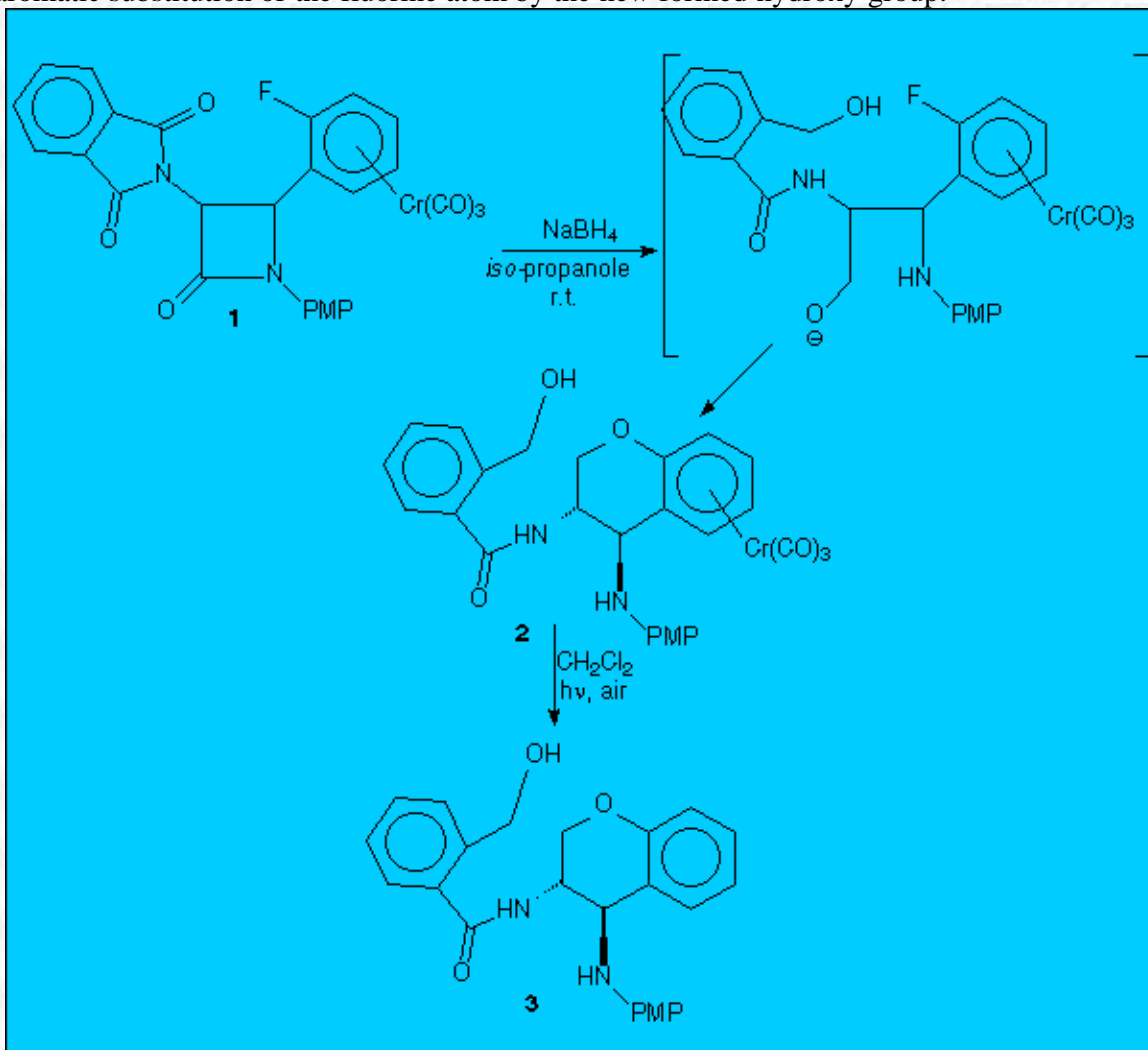
The scope was the extension of the above reaction to nitrogen containing products; therefore we have synthesised the  $\beta$ -lactam **1**, first in racemic and then in enantiomeric pure form, by [2+2] cycloaddition starting from tricarbonyl[N-(2-fluorobenzylidene)-4-methoxyaniline]chromium and phthalimidoacetyl chloride in the presence of  $\text{Et}_3\text{N}$  as a base:



### Results:

From the phthalimido protecting group, the 3-amino-b-lactam can be obtained normally with treatment by hydrazine or by reduction with  $\text{NaBH}_4$  followed by the acidic hydrolysis. In this case, the treatment with hydrazine was completely unsuccessful, while  $\text{NaBH}_4$  in *iso*-propanol gave rise only to product 2 in 65% yield to which we assigned a dihydrobenzopyran structure on the basis of spectroscopic and analytical data.

The dihydrobenzopyran ring should arise from an unusual reductive ring opening of azetidinone followed by the nucleophilic aromatic substitution of the fluorine atom by the new formed hydroxy group.



### Conclusions:

This reaction, made possible only by the presence of  $\text{Cr}(\text{CO})_3$  group, represents an interesting method to transform the  $\beta$ -lactam ring in dihydrobenzopyran compounds in stereoselective manner.

### Experimental data:

**Product 1:** Yield 94%; mp 198 °C (from petroleum ether); IR (nujol)  $\text{cm}^{-1}$  1972, 1903, 1869, 1762, 1723.  $^{19}\text{F}$  NMR d -141.6.  $^1\text{H}$  NMR d 3.8 (s, 3H); 4.7 (dt, 1H,  $J=6.2, 1.9$  Hz); 5.1 (t, 1H,  $J=5.7$  Hz); 5.3 (dt, 1H,  $J=6.5, 2.8$  Hz); 5.6 (m, 2H); 5.8 (d, 1H,  $J=5.5$  Hz);  $\delta$  7.0-7.7 (AB system, 4H); 7.8 (m, 4H).  $[\alpha]_D^{25} = -25.5$  (c 0.114  $\text{CHCl}_3$ ).

**Product 2:** Yield 65%; mp 105/6 °C (from petroleum ether); IR (nujol)  $\text{cm}^{-1}$  3336, 1959, 1871, 1640.  $^1\text{H}$  NMR d 3.8 (s, 3H); 3.85 (m, 2H, OH and NH); 4.2 (dd, 1H+NH,  $J=11.6$  and 4.2 Hz); 4.4 (dd+d, 2H,  $J=7.5, 11.6$  and 2.0 Hz); 5.0 (t, 1H,  $J=6.2$  Hz); 5.3 (d, 1H,  $J=6.8$  Hz); 5.5 (t, 1H,  $J=6.7$  Hz); 5.6 (d, 1H,  $J=6.2$  Hz); 6.8-7.0 (AB system, 4H,  $J=8.9, 6.5$  Hz); 7.4-7.6 (m, 4H).  $^{13}\text{C}$  NMR d 47.16, 53.1, 56.19, 65.16, 66.42, 81.29, 87.93, 92.65, 94.12, 94.46, 115.12, 115.72, 128.53, 128.65, 131.23, 132.18, 134.7, 138.18, 140.05, 140.66, 153.76, 170.57, 232.82.  $[\alpha]_D^{25} = +161.8$  (c 0.092  $\text{CHCl}_3$ ).

**Product 3:** Yield 94%; mp 75 °C (from petroleum ether); IR (nujol) cm<sup>-1</sup> 3367, 1635. <sup>1</sup>H NMR δ 1.6 (m, 1H, NH); 3.7 (m, 1H, NH); 3.8 (s, 3H); 3.9 (t, 1H, OH, J=6.3 Hz); 4.3 (dt, 1H, J=11.5, 2.5 and 4.6 Hz); 4.5-4.65 (m, 4H); 4.7 (dq, 1H, J=2.6, 4.2 and 7.8 Hz); 7.0 (m, 4H); 7.5 (m, 8H). <sup>13</sup>C NMR δ 46.14, 52.45, 56.25, 64.61, 65.1, 114.55, 114.75, 114.79, 115.45, 115.65, 115.53, 122.34, 128.50, 128.66, 130.12, 131.30, 131.81, 132.14, 112.57, 135.64, 139.88, 140.73, 153.08, 154.06, 170.25. [α]<sub>D</sub> = -156.1 (c 0.132 CHCl<sub>3</sub>).

**References:**

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- [4] Baldoli, C.; Del Buttero, P.; Molteni, G.; Pilati, T. *Tetrahedron:Asymmetry* **2000**, 11, 1927.

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