

This article was downloaded by: [University of Kiel]

On: 27 October 2014, At: 06:50

Publisher: Taylor & Francis

Informa Ltd Registered in England and Wales Registered Number: 1072954

Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



## Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/lcyc20>

### Studies on Pyrrolidinones. A New Rearrangement of Pyrrolo[1,2-b]isoquinolines Derivatives

Benoît Rigo <sup>a</sup>, Didier Barbry <sup>b</sup> & Daniel Couturier <sup>b</sup>

<sup>a</sup> Laboratoire de Synthèses Organiques, Ecole des Hautes Etudes Industrielles, 13 rue de Toul, 59046, Lille, France

<sup>b</sup> Laboratoire de Synthèse Organique, Université des Sciences et Techniques de Lille-Flandres-Artois, 59655, Villeneuve d'Ascq, France

Published online: 23 Sep 2006.

To cite this article: Benoît Rigo, Didier Barbry & Daniel Couturier (1991) Studies on Pyrrolidinones. A New Rearrangement of Pyrrolo[1,2-b]isoquinolines Derivatives, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 21:6, 741-747, DOI: [10.1080/00397919108019753](https://doi.org/10.1080/00397919108019753)

To link to this article: <http://dx.doi.org/10.1080/00397919108019753>

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness,

or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at <http://www.tandfonline.com/page/terms-and-conditions>

**STUDIES ON PYRROLIDINONES. A NEW REARRANGEMENT  
OF PYRROLO[1,2-b]ISOQUINOLINES DERIVATIVES**

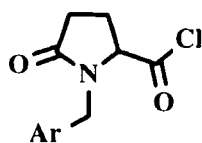
**Benoît Rigo<sup>a\*</sup> Didier Barbry<sup>b</sup> and Daniel Couturier<sup>b</sup>**

**a) Laboratoire de Synthèses Organiques, Ecole des Hautes Etudes Industrielles, 13 rue de Toul, 59046 Lille, France**

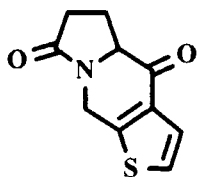
**b) Laboratoire de Synthèse Organique, Université des Sciences et Techniques de Lille-Flandres-Artois, 59655 Villeneuve d'Ascq, France**

**Abstract :** *New lactones are obtained as by-products during the Friedel-Crafts cyclization of N-arylmethyl pyroglutamoyl chlorides. A mechanism based on N-acyliminium salts is proposed to explain their formation.*

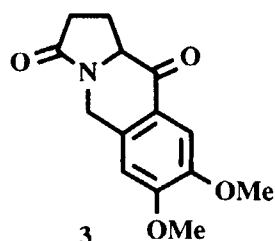
Pyroglutamic acid has been an efficient starting material for the synthesis of many condensed nitrogen heterocycles;<sup>1</sup> for example, Friedel-Crafts reaction of acid chlorides 1 led to ketones such as 2-5 (catalyst :  $\text{SnCl}_4$ ).<sup>2</sup>



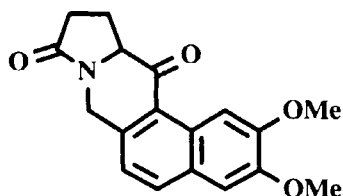
1



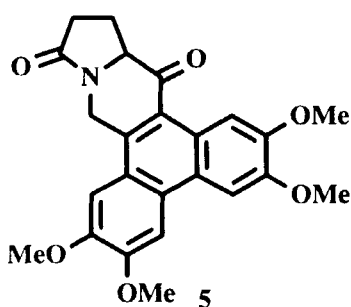
2



3

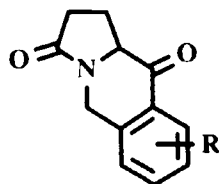


4

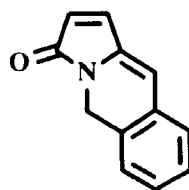


5

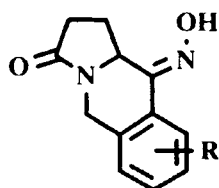
We have recently reported that a PPA treatment of ketone 6c, belonging to this series, gives the unsaturated lactam 7 in good yield,<sup>5</sup> and it has been shown that heating oximes 8 with PPA leads to lactams 9.<sup>4</sup>



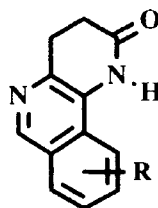
6 c R = H



7



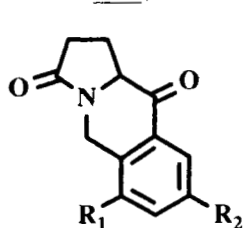
8



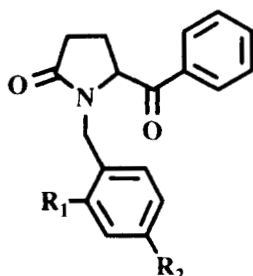
9

Herein we report that the structure of the by-products 11, 12 obtained during Friedel-Crafts synthesis of ketones 6, gives a supporting evidence for the intermediacy of N-acyliminium salts in these reactions. Indeed, we have reexamined this synthesis, catalyzed by aluminum chloride. According to previous results,<sup>2a</sup> ketones 10 as well as 6 can be obtained when benzene is chosen as solvent. However, in all cases examined (solvent : benzene<sup>2a</sup> or methylene dichloride<sup>4</sup>), small amounts of lactones 11 or their hydrolysis (12b,c) or methanolysis (12d) products (according to the final treatment of the reaction medium), are also formed.

Structural assignments are obtained by spectrometric methods (ir, <sup>1</sup>H nmr, <sup>13</sup>C nmr, MS) and by chemical methods (refluxing acid 12c with PTSA in toluene gives lactone 11c, and ring opening of lactone 11b yields acid 12b).



**6** a 5% b 10%  
c 81% d 64%



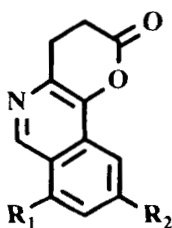
**10** a 31% b 14%

a  $R_1 = H$   $R_2 = Cl$

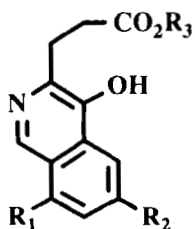
b  $R_1 = OMe$   $R_2 = H$

c  $R_1, R_2, R_3 = H$

d  $R_1, R_3 = Me$   $R_2 = H$

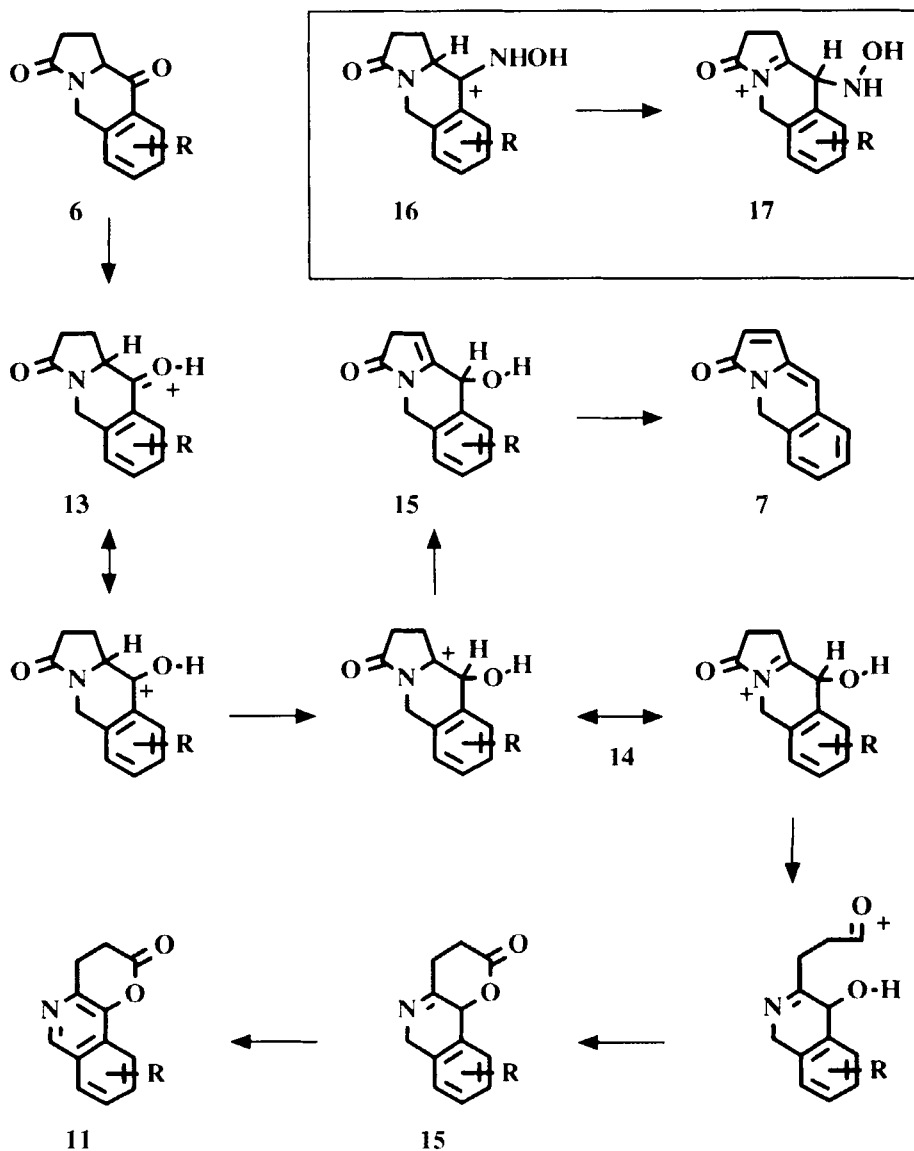


**11** a 2% b 16%



**12** c 4% d 0.9%

A similar mechanism can explain the formation of by-products 11 and 12 as well as the formation of lactam 7 :



A protonation of ketone 6 gives rise to cation 13. It is followed by a hydrogen shift yielding the more stabilized N-acyliminium salt 14. Opening of the lactam ring, recyclization to lactone 15 and air oxidation gives lactones 11. On the other hand, N-acyliminium salts 14 can lead to intermediate enamide 15.<sup>6</sup> The dehydration of this allyl alcohol then produces lactam 7. Similarly, the rearrangement of oxime 8 to lactam 9 can be explained by an initial nitrogen protonation (16) followed by a hydrogen shift giving a more stabilized N-acyliminium salt (17).

It is interesting to note that a related unusual dehydration, associated with a hydride transfer, has already been observed in the series of the acenaphto[5,4-b]furan,<sup>7</sup> acenaphto[5,4-b]thiophene<sup>7</sup> and fluorantheno[1,2-b]thiophene.<sup>8</sup> In these cases too, the driving force giving rise to the hydrogen shift was, in part, an additional stabilization of charge by an heteroatom.

From our results it appears that this rearrangement is quite general, and we believe that mechanisms based on this type of hydrogen shift could help to understand the low stability of some condensed nitrogen heterocycles.

In a typical experiment,  $\text{AlCl}_3$  (44.7g, 354 mmol) was added in 3 steps to chloride 1 ( $\text{Ar} = 2\text{-C}_6\text{H}_5\text{Cl}$ ) (32.1g, 118 mmol) in benzene (150 ml). The mixture was refluxed during 30 minutes, stirred 2.5 hours at 20°C, then poured on crushed ice. The aqueous phase was extracted

(CH<sub>2</sub>Cl<sub>2</sub>) and the organic phases were washed with water, dried and evaporated. The residue was fractionated under vacuum ; ketones 6a (5%, bp 195°C (0.2 mmHg), mp 126-127°C (ether-CH<sub>2</sub>Cl<sub>2</sub>) and 10a (31%, bp 218°C (0.1 mmHg)) were obtained as previously described ; 2a lactone 7a crystallized by addition of ether and few drops of CH<sub>2</sub>Cl<sub>2</sub> to the second distillation fraction (bp 179°C (0.2 mmHg)) ; 2% yield, mp 134°C (acetone). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 60 MHz) 2.8-3.7 (sym. m, 4H), 7.1-8.3 (m, 4H), 9.4 (bs, 1H).

Anal. calcd for C<sub>12</sub>H<sub>8</sub>NO<sub>2</sub>Cl : C, 61.69 ; H, 3.45 ; N, 5.99 ; Cl, 15.17.

Found : C, 61.43 ; H, 3.62 ; N, 5.75 ; Cl, 15.11.

#### References and notes :

- (1) S. Yasuda, Y. Yamamoto, S. Yoshida and M. Manaoka, *Chem. Pharm. Bull.*, **36**, 4223 (1988)  
W. J. Gensler and M. W. Hu, *J. Org. Chem.*, **38**, 3848 (1973)  
H. C. Wormser and H. N. Abamson, *J. Pharm. Sci.*, **64**, 1882 (1975)  
F. G. Fang and S. Danishefsky, *Tetrahedron Lett.*, 3621 (1989) T. Otha, T. Kimura, N. Sato and S. Nozoe, *Tetrahedron Lett.*, 4303 (1988).
- (2) a) B. Rigo and N. Kolocouris, *J. Heterocyclic Chem.*, **20**, 893 (1983).  
b) G. S. Lee, Y. S. Cho, S. C. Shim, W. J. Kim, E. Eibler and W. Wiegrebe, *Arch. Pharm. (Weinheim)*, **322**, 607 (1989).  
c) T. F. Buckley and H. Rapoport, *J. Org. Chem.*, **48**, 4222 (1983).



- (3) First reports on the synthesis of ketones 5 by using aluminum chloride as a catalyst are described in references (2a) and (4).
- (4) L. L. Martin, S. J. Scott, M. N. Agnew and L. L. Setescak, *J. Org. Chem.*, 51, 3697 (1986)  
L. L. Martin, S. J. Scott, L. L. Setescak and D. Van Engen, *J. Heterocyclic Chem.*, 24, 1541 (1987).
- (5) B. Rigo, E. Tullier, D. Barbry, D. Couturier, V. Warin, J. Lamiot and F. Baert, *J. Heterocyclic Chem.*, 27, 1383 (1990)  
J. Lamiot, F. Baert, A. Guelzim, D. Barbry, D. Couturier, B. Rigo and E. Tullier, *Acta Cryst. (C)*, to be published.
- (6) It is known that N-acyliminium salts easily isomerise to enamides :  
J. C. Hubert, J. B. P. A. Wijnberg and W. N. Speckamp, *Tetrahedron*, 31, 1437 (1975)  
K. Nyberg, *Synthesis*, 545 (1976)  
H. Horikawa, T. Iwasaki; K. Matsumoto and M. Miyoshi, *J. Org. Chem.*, 43, 335 (1978).
- (7) E. Lee-Ruff and Y-S. Chung, *J. Heterocyclic Chem.*, 23, 1551 (1986).
- (8) E. Lee-Ruff and Y-S. Chung, *J. Heterocyclic Chem.*, 27, 899 (1990).

(Received in UK 11 January, 1991)