BECKMANN FRAGMENTATION IN THE WOLFF-KISHNER REDUCTION OF 6-ARYL-3-HYDROXYIMINO-4-PIPERIDONES

Joan Bosch*, Montserrat Moral, and Mario Rubiralta

Department of Organic Chemistry, Faculty of Pharmacy,

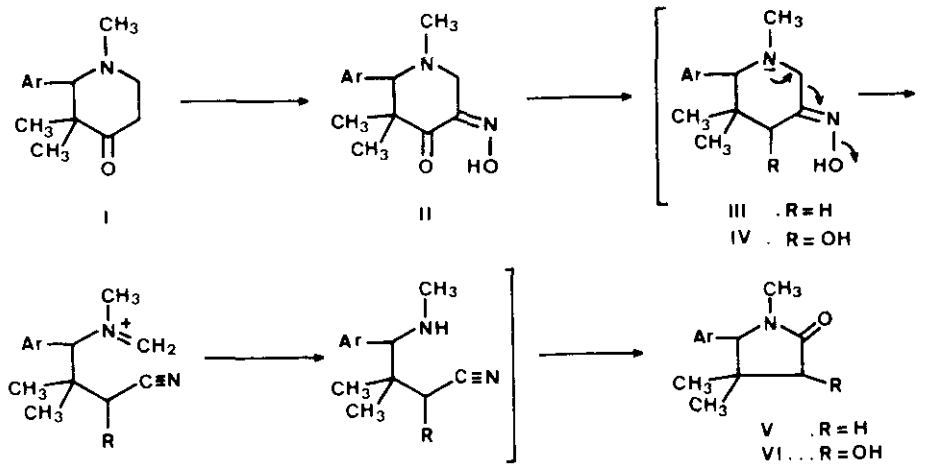
University of Barcelona, Barcelona, Spain

Abstract- Treatment of 6-aryl-3-hydroxyimino-4-piperidones under Wolff-Kishner conditions afforded 5-aryl-2-pyrrolidones by a process that involves a Beckmann fragmentation.

In connection with our previous work about the synthesis[1] and synthetic applications[2] of 2-aryl-4-piperidones we intended to study the transposing of the keto function and the adjacent methylene group in 4-piperidones I. Among the procedures developed for effecting a 1,2-carbonyl migration within ketones[3] we chosed a three step sequence involving formation of a hydroxyimino ketone, Wolff-Kishner reduction, and hydrolysis of the resulting oxime.[4]

The required hydroxyimino ketones II[5] were prepared from piperidones I[1] by nitrosation with isopentyl nitrite and potassium *tert*-butoxide. Treatment of IIa under Wolff-Kishner conditions (excess hydrazine hydrate, potassium hydroxide, 190°C, 3 hours) afforded a mixture of 2-pyrrolidones Va and VIa, which were separated by column chromatography (silica gel, benzene-ether as eluent) and identified by elemental analysis and spectroscopic data.[6]

The above result can be interpreted by considering that piperidine IIIa and piperidinol IVa, the products from the Wolff-Kishner reduction,[7] under the alkaline reaction conditions undergo a Beckmann fragmentation[8] followed by hydrolysis and cyclization to give the isolated 2-pyrrolidones.



Although there are precedents of Beckmann fragmentations from similar α-amino ketoxime derivatives,[8] the subsequent evolution of the primary fragmentation products to 2-pyrrolidone systems have not been described.

In a similar way, the only isolable product from the Wolff-Kishner reduction of hydroxyimino ketone IIb was 3-hydroxy-2-pyrrolidone VIb, which was identified by elemental analysis and spectroscopic data.[9]

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5. (a) All compounds gave elemental analysis consistent with the proposed structures. (b) IIa: mp 188-189°C (acetone-ethanol). Ir (KBr): 3100-3500, 1710, and 1630 cm^{-1}. Nmr ($CDCl_3$): δ 1.02 (s,3H,CH_3eq), 1.27 (s,3H,CH_3ax), 2.15 (s,3H,NCH_3), 3.45 (s,1H,CH), 3.62 (s,2H,CH_2), 6.90 (d,2H,ArH), 7.25 (d,2H,ArH). IIb: mp 190-192°C (acetone-ether). Ir ($CHCl_3$): 3100-3500, 1700, and 1590 cm^{-1}. Nmr (CCl_4):δ 1.05 (s,3H,CH_3eq), 1.25 (s,3H,CH_3ax), 2.20 (s,3H,NCH_3), 3.35 (s,1H,CH), 3.65 (s, 2H,CH_2), 3.70 (s,9H,OCH_3), 6.15 (s,2H,ArH).
6. Va: oil. Ir ($CHCl_3$): 1680 cm^{-1}. Nmr ($CDCl_3$): δ 0.68 (s,3H,CH_3), 1.28 (s,3H,CH_3), 2.29 (s,2H,CH_2), 2.70 (s,3H,NCH_3), 4.10 (s,1H,CH), 7.00 (d,2H,ArH), 7.37 (d,2H, ArH). VIa: mp 179-182°C (ether). Ir ($CHCl_3$): 3100-3600 and 1690 cm^{-1}. Nmr (d_6-DMSO): δ 0.45 (s,3H,CH_3), 1.08 (s,3H,CH_3), 2.53 (s,3H,NCH_3), 3.77 (d,1H,CHOH), 4.18 (s,1H,NCH), 5.63 (d,1H,OH), 7.18 (d,2H,ArH), 7.42 (d,2H,ArH).
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9. VIb: oil. Ir ($CHCl_3$): 3520, 3100-3500, and 1675 cm^{-1}. Nmr ($CDCl_3$): δ 0.70 (s, 3H,CH_3), 1.25 (s,3H,CH_3), 2.75 (s,3H,NCH_3), 3.82 (s,9H,OCH_3), 3.95 and 4.00 (2s, 2H,CH), 6.20 (bs,2H,ArH).

Received, 6th December, 1982