HETEROCYCLES, Vol 20, No 3, 1983

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

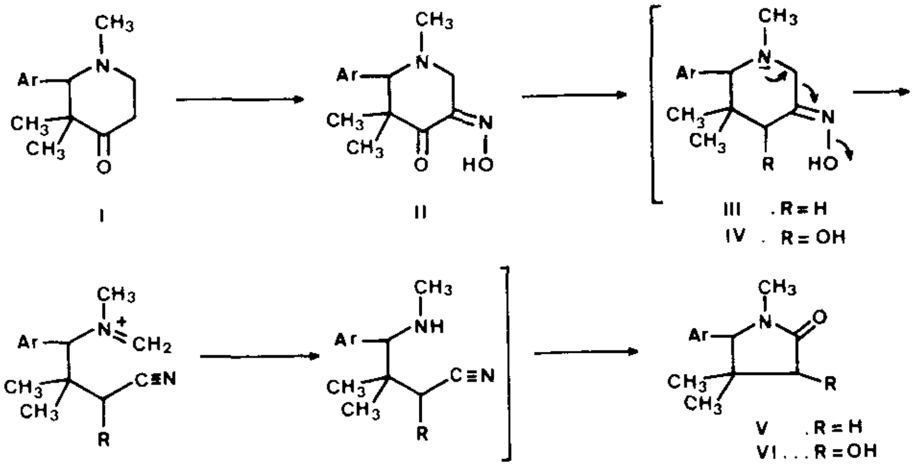
Joan Bosch*, Montserrat Moral, and Mario Rubiralta
Department of Organic Chemistry, Faculty of Pharmacy,
University of Barcelona, Barcelona, Spain

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.



a. Ar = p-Chlorophenyl
b. Ar = 3,4,5-Trimethoxyphenyl

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]

REFERENCES AND NOTES

1. (a) J. Bosch, A.Domingo, F. López, and M. Rubiralta, J. *Heterocyclic Chem.*,1980, *17*, 241. (b) J. Bosch, M. Rubiralta, A. Domingo, and J. Sistaré, *ibid.*,1981, *18*, 47. (c) J. Bosch and M. Rubiralta, *ibid.*, 1981, *18*, 485. (d) J. Bosch and M. Rubiralta, *An. Quím.*, 1982, *78C*, 000. (e) J. Bosch, M. Rubiralta, and M. Moral, *Heterocycles*, 1982, *19*, 473.
2. (a) J. Bosch, M. Rubiralta, M. Moral, and J. Bolós, II Congreso Nacional de la Sociedad Española de Química Terapéutica, Madrid, Spain (1982). (b) J. Bosch, M. Rubiralta, and M. Moral, XIX Reunión Bienal de la Real Sociedad Española de Química, Santander, Spain (1982).
3. W.E. Fristad, T.R. Bailey, and L.A. Paquette, J. *Org. Chem.*, 1980, *45*, 3028; and references cited therein.
4. J. Just and Y.C. Lin, *Chem. Comm.*, 1968, 1350.
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,$C\underline{H}OH$), 4.18 (s,1H,NCH), 5.63 (d,1H,OH), 7.18 (d,2H,ArH), 7.42 (d,2H,ArH).
7. The formation of alcohols is a known secondary process in the Wolff-Kishner reductions: D. Todd, in "Organic Reactions", Vol. 4, R. Adams, Ed., John Wiley and Sons, Inc., New York, N.Y. 1948, p. 378.
8. (a) C.A. Grob and P.W. Schiess, *Angew. Chem., Int. Ed. Engl.*, 1967, *6*, 1. (b) C.A. Grob, *ibid.*, 1969, *8*, 535; and references cited therein.
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