Tetrahedron Letters No.22, pp. 2677-2679, 1968. Pergamon Press. Printed in Great Britain.

ARYL MIGRATION DURING PICTET-GAMS REACTION[1]

A.A. Bindra, M.S. Wadia[2] and N.L. Dutta
National Chemical Laboratory, Poona 8, India

(Received in UK 25 January 1968; accepted for publication 2 March 1968)

Though a number of isoquinolines have been synthesised using the well known Pictet-Gams reaction[3], no rearrangement has so far been reported involving this reaction. The present investigation reports on an aryl migration observed during such reaction.

In the course of our work on the synthesis of some alkaloids of the Berberine group, it became necessary to prepare 1-methyl-3-phenyl isoquinoline. One of the methods[4] for preparing this compound used the Pictet-Gams cyclisation of the hydroxy amide I, and obtained a syrup which was characterised through its picrate. By following the same procedure, we have now isolated a crystalline compound $C_{15}H_{13}N$*, m.p.79°, which is different from 1-methyl-3-phenyl isoquinoline. Other methods[5,6] for the preparation of this compound have been reported to furnish a product m.p. 46-49°. An unambiguous synthesis of 1-methyl-3-phenyl isoquinoline by ammonia treatment of the recently reported[7] pyrilium salt II afforded a product $C_{15}H_{13}N$, m.p. 48° whose UV[8] [245 mμ log ε 4.69 and 288 mμ (log ε 3.15)] and PMR spectra[9] [3 proton singlet at 2.8 δ (aromatic methyl), one proton singlet at 7.66 δ (C-4 proton), two proton quartet at 8.02 δ (J = 2 and 7.5 cps, 2' and 6' proton), and seven proton multiplet at 7.2 - 7.8 δ (other aromatic protons)] - were consistent with its formulation as 1-methyl-3-phenyl isoquinoline III.

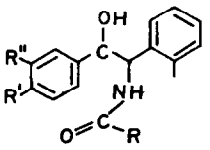
The isomeric compound obtained by us through the Pictet-Gams reaction must therefore be a rearranged product. Since the UV spectrum of this product [219 mμ (log ε 4.97), 280 mμ (log ε 3.98) and 316 mμ (log ε 3.85)] was similar to that of isoquinoline itself[10] [215 mμ (log ε 4.91), 263 mμ (log ε 3.52), 306 mμ (log ε 3.32) and 320 mμ (log ε 3.34)], this compound could be formulated as 1-methyl-4-phenyl isoquinoline (IV); the phenyl group at C-4 causing no change in the UV spectrum as it is twisted out of the plane of the isoquinoline nucleus.

This formulation was supported by the PMR spectrum [three proton singlet at 2.9 δ (aromatic methyl), one proton singlet at 8.25 δ (C-3 proton) two proton multiplet at 7.9 δ (C-6 and C-7 protons), two proton broadened doublet at 7.45 δ (C-5 and C-8 protons) and five proton singlet at 7.4 δ (protons of phenyl nucleus)] and confirmed

---

*The compounds reported in this communication gave satisfactory analysis.

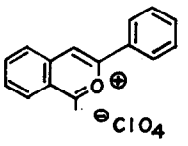
by a syntnesis of 1-methyl-4-phenyl isoquinoline according to the method of



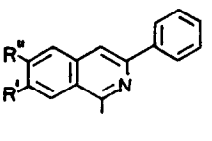
I R=Me, R'=R"=H

V R=R'=R"=H

VII R=Me, R'R"= -O-CH_2-O-

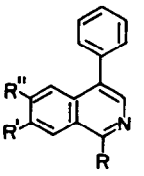


II



III R'=R"=H

VIII R',R"=-O-CH_2-O-



IV R=Me, R'=R"=H

VI R=R'=R"=H

IX R=Me, R'R" = -O-CH_2-O-

Govindachari et al.[11]. The identity of the synthetic compound and the product obtained from I was established by the usual methods (m.p., mixed m.p., m.p. of the picrates, TLC, IR and UV).

In an attempt to understand the mechanism of this phenyl migration cyclisation of the diastereoisomer of I was carried out[12]. As the product isolated was identical with that (IV) obtained earlier, this reaction did not help in establishing the mechanism.

The demonstration that this is a general reaction was furnished by carrying out a cyclisation[12] of the amide (V). The UV spectrum [221 mμ (log ϵ 4.66), 274 mμ (log ϵ 3.62) and 312 mμ (log ϵ 3.54)] together with its properties (m.p.79-80°, picrate m.p. 209°; lit.[13] m.p. 79-80°, picrate m.p. 209°) established that it was the 4-phenyl isomer (VI). The PMR spectrum also confirmed this finding.

Cyclisation of the methylenedioxy derivative of I (VII) had been reported[11] to yield the corresponding 3-phenyl isoquinoline (VIII) m.p. 138°. By following this procedure, a product having the same m.p. was obtained, but its properties were not identical with a sample of the 3-phenyl derivative (VIII) m.p. 151-52° obtained[14] by dehydrogenation of the 3,4-dihydro derivative of VIII. The compound m.p. 138° must therefore be the 4-phenyl derivative (IX). This structure is consistent with its UV spectrum [219 mμ (log ϵ 4.49), 257 mμ (log ϵ 4.77) with shoulder at 288 and 340 mμ]. The PMR spectrum of this compound supports this contention.

Further studies on the scope and mechanism of this reaction are in progress.

Acknowledgement: One of us (A.A.Bindra) is grateful to the CSIR, India, for a fellowship during the tenure of this work.

REFERENCES

1 Communication No.1174 from the National Chemical Laboratory, Poona 8, India.

2 Present address: Dept. of Chemistry, Poona University, Poona 7.

3 W.M. Whaley and T.R. Govindachari, Organic Reactions ed. R. Adams 6, 151 (1951).

4 T. Kametani and K. Ohtsuki, J. Pharm. Soc. Japan 75, 705 (1955); Chem. Abs. 50, 3460 (1956).

5 B. Bhattacharya, Indian J. Chem. 2, 25 (1964).

6 S. Goszczynki, Roznii. Chem. 38, 893 (1964); Chem. Abs. 62, 16187 (1965).

7 G.N. Dorofenko and V.I. Dulenko, J. Gen. Chem. (USSR), 32, 3378 (1962).

8 UV spectra were measured in alcoholic solution.

9 PMR spectra were measured on a Varian A-60 spectrophotometer on 10% solutions. Values are reported in δ units using tetramethylsilane as internal standard.

10 H.H. Jaffe and M.Orchin, Theory and Applications of Ultraviolet Spectroscopy, John Wiley and Sons Inc. New York, 370 (1962).

11 T.R. Govindachari, B.R. Pai and U.R. Rao, Proc. Ind. Acad. Sci. 48A, 111 (1958).

12 W.D. McPhee and E.S. Erickson, J. Amer. Chem. Soc. 68, 624 (1946).

13 G. Berti, Gazz. Chim. Ital. 87, 707 (1957).

14 B.B. Dey and V.S. Ramanathan, Proc. Natl. Inst. Sci. India, 9, 193 (1943).