Tetrahedron Letters No. 30, pp 2821 - 2822, 1973. Pergamon Press. Printed in Great Britain.

BIS-ANIL INTERMEDIATES IN THE CYCLODEHYDRATION OF ANILINOMETHYLENECYCLOHEXANONES TO TETRAHYDROACRIDINES

R. M. Acheson and R. G. Bolton
Department of Biochemistry, University of Oxford,
South Parks Road, Oxford, OX1 3QU.

(Received in UK 25 May 1973; accepted for publication 13 June 1973)

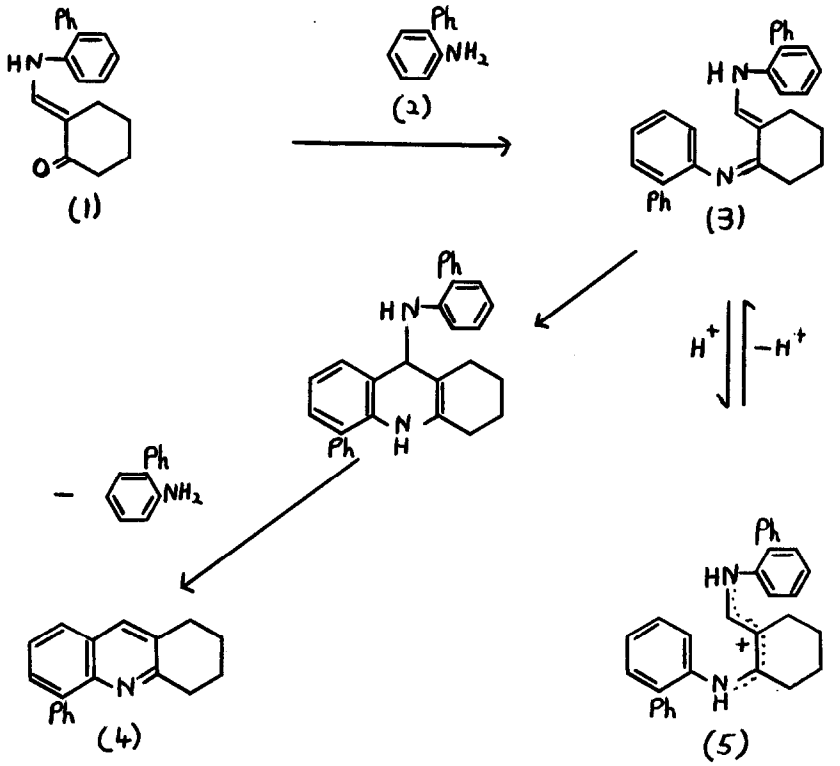
The mechanism of the acid-catalysed cyclodehydration of 2-arylaminomethylene-cyclohexanones (eg 1) to tetrahydroacridines (eg 4) rather than to tetrahydrophenanthridines has long been a source of conjecture.[1,2] Petrow[1] originally suggested the intermediacy of a bis-anil (eg 3) which would allow the exchange of anilino groups. Tilak et al[3,4] have shown that high yields of tetrahydroacridines could be obtained using lactic acid as solvent, and have considered the possibilities of azetines and bis-anils[5] as intermediates.

We have now isolated the bis-anil (3) from (1) with hot lactic acid, thereby showing that acid disproportionation of (1) to (3), probably via hydrolysis to the amine (2), occurs under these conditions. Compound (3) was identical with an authentic specimen prepared from 2-chlorocyclohexenal and 2-aminobiphenyl by the method of Gagan and Lloyd.[6]

The anil (1) (11.5 g) was heated at 100° for 15 hr in lactic acid (40 ml) containing water (1 ml). After the standard work-up,[3] chromatography on alumina yielded only (1) and yellow needles (0.11 g, mp 138 - 140°), eluted with and crystallised from petrol, of N-2-(2 -biphenylaminomethylene)-cyclohexylidine-2-biphenylamine (3) (Found: C, 87.0; H, 6.6; N, 6.6. $C_{30}H_{28}N_2$ requires: C, 86.9; H, 6.6; N, 6.5%) NMR ($CDCl_3$); Ar-H (18) and N-H (1), 2.5 - 3.1m; vinyl-H (1), 3.5d; CH_2, 7.78t; CH_2, 8.20t; 4-CH_2 and 5-CH_2, 8.5 - 8.9m; J vinyl 1H, NH 8.0. Mass spectrum, m/e (% rel. abundance): 428 (100) [M^+], 351 (18) [M - Ph·], 275 (10) [M - PhC_6H_4·], 260 (45) [M - PhC_6H_4NH·], ν_{max} ($CHCl_3$) 1640 cm^{-1} strong (C=N). The UV spectrum of the bis-anil (3) in methanol [212nm ($10^{-4}\varepsilon$, 3.40), 225 infl (2.93), 376 (1.40)] showed a marked bathochromic shift [212 (3.27), 234 (2.25), 392 (2.09)] on addition of 1 drop of 70% perchloric acid, due to the formation of a symmetrical delocalised cation (5). A similar cation is proposed as an intermediate in a new synthesis of tetrahydroacridines from 2-chlorocyclohexene-1-al and arylamines,[6] and is also formed from 2,3-dihydro-1,4-diazepines.[7] The mono-anil (1) [211 (2.20), 225 (1.96), 260 infl (0.70), 369 (2.14)] showed a hypsochromic shift [211 (2.33), 240 infl (1.18), 345 (1.75)] on similar treatment.

The bis-anil (3) with glacial acetic acid at 100° for 1 hr was completely converted to the acridine (4) and 2-aminobiphenyl, while the mono-anil (1) was unchanged under these conditions. The mono-anil (1), however, with anhydrous lactic acid (130°, 20 hr) did give (4) (25%) and the N-(2-diphenyl)lactamide (47%). It is therefore extremely probable that the bis-anil is the key intermediate in the lactic acid, and similar cyclisations of the type (1)→(4) which could take place either by an initial electrocyclic process or by a non-

concerted process involving the alternative N-H tautomer of (3).



REFERENCES

1. V. Petrow, J. Chem. Soc., 693 (1942).
2. G. E. Hall and J. Walker, J. Chem. Soc. (C), 2237 (1968).
3. B. D. Tilak, H. Berde, V. N. Gogte and T. Ravindranathan, Ind.J. Chem., 8, 1 (1970).
4. H. V. Berde, V. N. Gogte, A. G. Namjoshi and B. D. Tilak, Ind.J. Chem., 10, 9 (1972).
5. H. V. Berde, V. N. Gogte and B. D. Tilak, Ind. J. Chem., 10, 332 (1972).
6. J. M. F. Gagan and D. M. Lloyd, J. Chem. Soc. (C), 2488 (1970).
7. A. M. Goringe, D. Lloyd, D. R. Marshall and L. A. Mulligan, Chem. and Ind., 130 (1968).