Tetrahedron Letters No. 6, pp 531 - 534, 1972. Pergamon Press. Printed in Great Britain.

INTRAMOLECULAR REACTIONS OF AMIDO RADICAL

Y. L. CHOW and R. A. PERRY

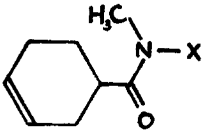
Department of Chemistry, Simon Fraser University

BURNABY 2, B. C., CANADA

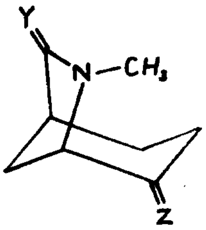
(Received in France 5 January 1972; received in UK for publication 10 January 1972)

In terms of polarity, an amido radical is expected to be somewhere in between a protonated amino (aminium) and an amino radical ; the reactivities of these radicals are therefore expected to follow the same order. Aminium radicals (1-3) have been shown preferentially to add a π- bond rather than to abstract a hydrogen both in inter- and intramolecular (4,5) reactions ; this preference appears to be reversed in a neutral amino radical from the limited information available at present (6-8). Amido radicals have been shown (9-12) to abstract alkyl hydrogen efficiently in competition with other decomposition pathways. Contrary to the expectation of being an electrophilic radical, the N-methylacetamido radical, generated from a photolysis of the corresponding N-nitroso compound (9), fails to add to styrene and preferentially abstracts the allylic hydrogen of 1, 3-pentadiene (13).

We wish to report efficient intramolecular additions initiated by an amido radical. In order to suppress an incursion of the intramolecular hydrogen abstraction (9, 11)(at C-5), N-methyl-3-cyclohexene-1-carboxamido radical was selected as the model ; the generation of which was achieved by photolysis (9) of the corresponding N-nitroso (1) and N-chloro (2) compounds.

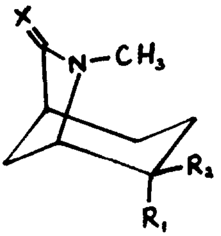


1; X = NO
2; X = Cl



3; Y = Z = O
4; Y = O, Z = N↗OH
5; Y = O, Z = N↘OH
6; Y = H_2, Z = O

Nitrosamine 1 [1725, 1500 cm^{-1}] was synthesized by the known method (13) and was photolysed (>400 nm) as a benzene solution (~0. 05 M) to give, after chromatography on an alumina column, the keto lactam 3 [21 % ; ir(neat) 1735, 1715, and 1645 cm^{-1} ; nmr($CDCl_3$) τ 6.3 (dd, J=5 and 2 Hz, 1 H), 7.15 (s, 3 H) ; m/e 153.0744(M^+), 137, 125, 110 and 97], a mixture of the oximido lactams anti-4 and syn-5 [63 % ; the nmr singlets at 7.18 and 7.10 in the ratio of 1 : 1.9], and the oximes of 5-(N-methylcarboxamido)-2-cyclohexen-1-one [6 % ; ir($CHCl_3$) 1680, 1070 and 1050 cm^{-1} ; nmr($CDCl_3$) τ 2.70 (m, 1 H), 3.25(m, 1H) and 7.23 (s, 3 H) ; m/e 168, 137, 109, 96, 80 and 79]. The mixture of the oximido lactams was readily recrystallized from ethanol to afford anti-4 [mp. 201-203° ; ir($CHCl_3$) 3300, 3100, 1670, 950 and 920 cm^{-1} ; nmr($CDCl_3$) τ5.80 (broad d, J=5 Hz, 1 H), 6.1-6.5 (m, 1 H) and 7.10 (s, 3 H) ; m/e 168.0822 (M^+) 152, 151, 123 and 110] and was deoximated by the bisulfite method (14) to afford keto lactam 3 (76 %). The assignments of the syn-anti geometry follow the correlation of the nmr data and other physical properties in analogy to the previous study (15). Reduction of 3 with lithium aluminium hydride followed by Jones' oxidation led to isolation of the known bicyclic ketone (4,16) 6, whereby the structures were established.



7; X = O, R_1 = H, R_2 = Cl
8; X = O, R_1 = Cl, R_2 = H
9; X = H_2, R_1 = H, R_2 = Cl
10; X = H_2, R_1 = Cl, R_2 = H
11; X = H_2, R_1 R_2 = H

Photolysis of chloramide 2 [3020 and 1660 cm^{-1}] in benzene (0.05 M) was carried out with a Vycor filter to afford a mixture of three vpc components in 8 (the parent amide), 47 and 44 % yields, respectively, in the order of increasing retention times. The two major products were separated by repeated column chromatography to give the more polar isomer, endo-7 [ir(neat) 1690, 765 and 750 cm^{-1} ; nmr τ 5.75 (ddd, J=5, 10 and 1.5 Hz, 1H), 6.14 (d, J=5.5 Hz, 1 H) and 6.95 (s, 3 H) ; M^+ 173.0602] and the less polar one, exo-8 [ir(neat) 1690, 1250 and 815 cm^{-1} ; nmr τ 5.68 (b, $W\frac{1}{2}$ = 8 Hz 1 H), 6.30 (t, J=4.5 Hz, 1 H) and 7.12 (s, 3 H)]. The mass spectral patterns of both isomers are identical, giving peaks at 175 (23 %), 173 (67), 138 (68), 110 (100) and 96 (64).

On treatment with lithium aluminium hydride, the lactam linkage of 7 and 8 was preferentially reduced to give a mixture of endo-aminechloride 9 and exo-aminechloride 10, which was further reduced, the latter more rapidly, to the known bicyclic amine 11 [picrate mp. 255° (dec.) ; reported (17) mp. 250° (dec.)]. A milder LAH reduction however afforded, after chromatography, aminechlorides 9 and 10 ; the former was identified by comparisons of the ir and nmr spectra with those of the authentic sample (18). Aminechloride 10 decomposed on storage.

The results described above demonstrate that the amido radical exclusively adds to the π-bond at 3-position to form the 5-member lactam but scarcely abstracts the allylic hydrogens at the 5-position of the ring. This behaviour is similar to that of aminium radicals (4-6) but just the opposite to the intermolecular reactions of amido radicals. The facile intramolecular addition of the amido radical described above is stereospecific due, probably, to the irreversible process in analogy to the similar additions of aminium radicals (4). However the results show interesting contrasts with the π-route cyclization of a nitrenium ion (18), which apparently undergoes by ionic processes.

Acknowledgment : The authors are grateful to the National Research Council of Canada for the generous financial support of this project. The senior author thanks Professor J. STREITH, Institut des Sciences Exactes et Appliquées, Mulhouse - France, for his hospitality and discussions during the preparation of the manuscript.

References

1) M. P. LAU, A. J. CESSNA, Y. L. CHOW and R. W. YIP, J. Amer. Chem. Soc., **93**, 3808 (1971) and the references cited therein.
2) R. S. NEALE, Synthesis, 1, 1 (1971).
3) F. MINISCI, R. GALLI and M. CECERE, Tetrahedron Lett., 3163 (1966): F.MINISCI and R. GALLI, ibid., 167 (1964) and other papers by the same group.
4) Y. L. CHOW, R. A. PERRY, B. C. Menon and S. C. CHEN, Tetrahedron Lett., 1545 (1971); Y. L. CHOW, R. A. PERRY and B. C. MENON, ibid., 1549 (1971).
5) J. M. SURZUR, L. STELLA and R. NOUGUIR, Tetrahedron Lett. 3107 (1970) : J. M. SURZUR, L. STELLA and P. TORDO, Bull. Soc. Chim. France, 115 (1970).
6) C. J. MICHEJDA and W. P. HOSS, J. Amer. Chem. Soc., **92**, 6298 (1970).
7) A. GOOD and J. C. J. THYNNE, J. Chem. Soc. B, 684 (1967).
8) H. PRAKASH and H. H. SISLER, J. Org. Chem., **35**, 3111 (1970).
9) Y. L. CHOW and J. N. S. TAM, J. Chem. Soc. C, 1138 (1970) ; Y. L. CHOW, J. N. S. TAM and A. C. H. LEE, Can. J. Chem., **41**, 2441 (1969).
10) Y. L. CHOW ant T. C. JOSEPH, Chem. Commun., 490 (1969).

11) L. P. KUHN, C. G. KLEINSPEHN and A. C. DUCKWORTH, J. Amer. Chem. Soc., 89 3858 (1967).

12) R. S. NEALE, N. L. MARCUS and R. G. SCHEPERS, J. Amer. Chem. Soc., 88, 3051 (1966).

13) J. N. S. TAM, Ph. D. THESES, Simon Fraser University, Burnaby, B. C.,Canada 1969.

14) S. H. PINES, J. M. CHERMADA and M. A. KOZLOWSKI, J. Org. Chem., 31, 3446 (1966).

15) Y. L. CHOW and C. J. COLON, J. Org. Chem., 33, 2598 (1968).

16) G. ESPOSITO, R. FURTOSS and B. WAEGELL, Tetrahedron Lett.; 899 (1971).

17) R. FURTOSS, P. TEISSIER and B. WAEGELL, Chem. Commun., 384 (1970).

18) P. G. GASSMAN, Accounts Chem. Res., 3 , 26 (1970) ; P. G. GASSMAN and J. H. ~~DYGOS, Tetrahedron Lett., 4745, (1970). The authors are grateful to Prof.~~ P. G. GASSMAN for the comparisons of the spectra.