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ANRORC-MECHANISM IN THE AMINO-DEOXOGENATION OF OXOHETEROCYCLES WITH PHENYL PHOSPHORODIAMIDATE[1,2]

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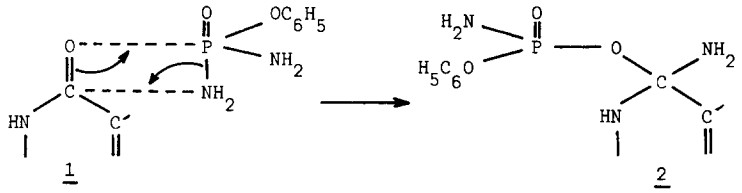
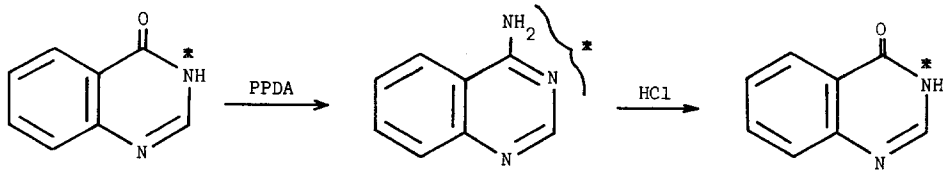
In recent years derivatives of phosphoric acid amides attract considerable attention as potential reagents for converting oxo derivatives of azaheterocycles into the corresponding amino compounds. Examples are the conversion of 1,2-dihydro-2-oxoquinoline into 2-dimethylaminoquinoline[3] by simply heating with hexamethylphosphorotriamide and of 6-methyluracil into 2,4-diamino-6-methylpyrimidine[4] and 3,4-dihydro-4-oxoquinazoline into 4-aminoquinazoline[5] on treatment with phenyl phosphorodiamidate (PPDA). The reactions with PPDA have been proposed[5] to involve the transition states 1 and 2.



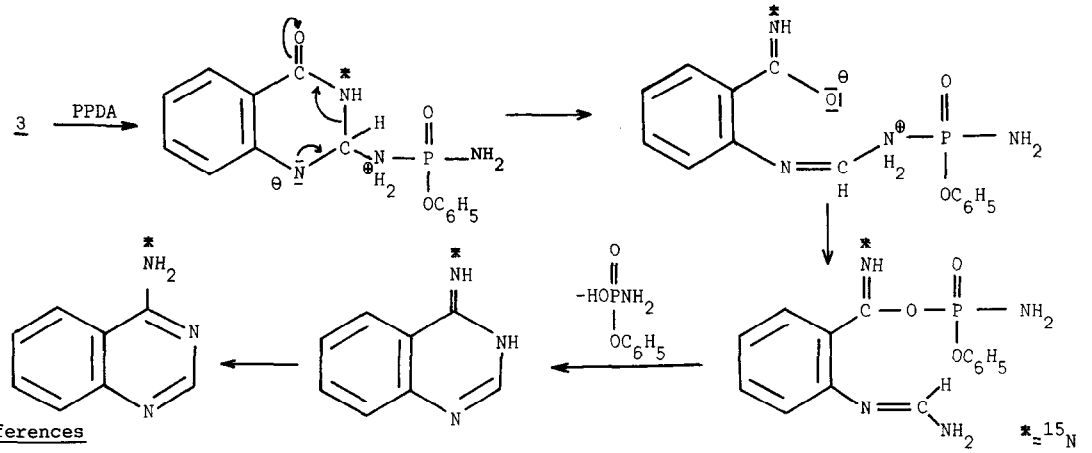
1 2

Due to our current interest on the occurrence of a S_N(ANRORC)-mechanism in the amino-dehalogenation of halogeno diaza-aromatics by nucleophiles[6], this proposal attracted our attention as it could be possible that also in the reaction of PPDA a S_N(ANRORC)-mechanism would be involved. Since we had available the 4-oxo-[3-^{15}N]-quinazoline[7] (3), we decided to investigate the reaction of 3 with PPDA. When melting together 3 (7.9% of ^{15}N)[8] with PPDA at 235°C for 45 min, 4-aminoquinazoline (4)(5.3% of ^{15}N)[8] is obtained. This considerable decrease of ^{15}N strongly indicates that during the reaction a ring opening and ring closure has occurred. By converting 4 with concentrated hydrochloric acid[7] into the 4-oxoquinazoline (5), which was proved to contain 2.3% of ^{15}N, we could establish that in 4 2.3/5.3 x 100% = 45% of the excess is present at N_3 and thus 55% on the exocyclic nitrogen of the amino group[9].



*=^{15}N 3 4 5

It was further observed that on a renewed treatment of 4 with PPDA (235°C, 45 min) ^{15}N exchange occurs since in the 4-aminoquinazoline, recovered after the reaction, 2.8% of ^{15}N is present and in the 4-oxoquinazoline only 1.1% of ^{15}N. This result indicates that at these conditions a ring opening - ring closure sequence can take place with 4. Although the decrease of ^{15}N-content in the conversion 3 → 4 does not allow the definitive conclusion that the amino-deoxogenation takes place via an ANRORC-mechanism (because of the fact that ^{15}N exchange can take place in 4-aminoquinazoline) the available data suggest that a pathway as given below can also operate in the replacement of the oxo-group by the amino-group. Further and more detailed work on the occurrence of an ANRORC-mechanism in amino-deoxogenations is in progress.



References

1. Part XIV on S_N(ANRORC)-mechanism. Previous paper in this series: A.P.Kroon, H.C.van der Plas and G.van Garderen, Recl.Trav.Chim.(Pays-Bas), submitted.
2. Part XLVII on pyrimidines from this laboratory, see for part XLVI ref.1.
3. E.B.Pederson and S.-O.Laweson, Tetrahedron 30, 875 (1974).
4. E.A.Arutyunyan, V.I.Gunar, E.P.Gracheva and S.I.Zavyalov, Izv.Akad.Nauk SSSR, Ser.Khim. 1969, 655; E.A.Arutyunyan, V.I.Gunar and S.I.Zavyalov, ibid. 1970, 904.
5. A.Rosowsky and N.Papathanasopoulos, J.Heterocyclic Chem. 9, 1235 (1972).
6. J.de Valk and H.C.van der Plas, Recl.Trav.Chim. (Pays-Bas) 91, 1414 (1972); P.J.Lont, H.C.van der Plas and A.J.Verbeek, ibid. 91, 949 (1972); A.P.Kroon and H.C.van der Plas, ibid. 93, 111 (1974). For a recent example in the isoquinoline series, see G.M.Sanders, M.van Dijk and H.J. den Hertog, ibid., in press.
7. J.de Valk, H.C.van der Plas, F.Jansen and A.Koudijs, Recl.Trav.Chim. (Pays-Bas) 92, 460 (1973).
8. The excess of ^{15}N in the compounds 3, 4 and 5 was determined by mass spectrometry, measuring the M + 1 and M peaks. The accuracy of the measurements was $\pm$ 0.2%. Mass spectrometric measurements were carried out with an AE MS 902 spectrometer.
9. In a duplicate experiment nearly identical results were found:
   3 (^{15}N, 7.6%) ⟶ 4 (^{15}N, 4.9%) ⟶ 5 (^{15}N, 2.3%).