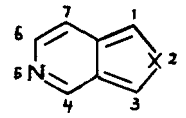
Tetrahedron Letters No. 20, pp 1741 - 1742, 1977. Pergamon Press. Printed in Great Britain.

PREPARATIVE FLASH VACUUM THERMOLYSIS. SYNTHESIS OF FURO[3,4-c]PYRIDINE BY RETRO DIELS-ALDER REACTION.

U.E.Wiersum* and C.D.Eldred
(AKZO Research Laboratories, Corporate Research Department, Arnhem, Holland)
P.Vrijhof and H.C.van der Plas*
(Lab.of Organic Chemistry, Agricultural University, Wageningen, Holland)

(Received in UK 25 March 1977; accepted for publication 4 April 1977)

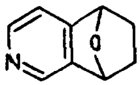


I

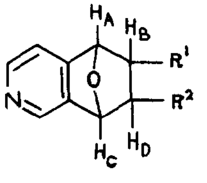
Whereas the highly reactive thienopyridine (I, X=S) is known, furo[3,4-c]pyridine (I, X=0), although given as a textbook excercise to name polyheterocyclic systems[2], has not been described. We now report that parent I, X=0 is quantitatively formed in retro Diels-Alder reaction after flash vacuum thermolysis (FVT) of 5,8-epoxy-5,6,7,8-tetrahydroisoquinoline (II). This compound was obtained after catalytic hydrogenation of 5,8-epoxy-5,8-dihydroisoquinoline [3], being prepared by oxidation of 1-aminotriazolo[4,5-c]pyridine with lead tetraacetate[4] in the presence of furan. Sublimation of II at 65°, at a pressure below 0.1 mmHg, into an unpacked quartz tube (250 mm long, 19 mm diam.), heated between 600 and 650°, gives ethylene and white crystals of I, X=0, which are collected in a liquid nitrogen cooled trap attached to quartz tube. As the trap warmed up under nitrogen, the ethylene readily vaporized and pure crystalline I(X=0) was left. The crystals remained white under nitrogen, but immediately turned reddish brown in contact with air. They melt below room temperature and polymerize to a viscous mass. In solution (5% in CCl_4) the compound is reasonably stable ($t_{\frac{1}{2}}$=50 hrs at 4^o). The nmr spectrum ($CDCl_3$) shows separate signals for each proton at δ9.03 (broadened s, H_4, $J_{4,7}$=1.8Hz, $J_{4,6}$ 1Hz), δ8.20 (splitted d, H_1 or H_3, $J_{1,3}$=1.9Hz), δ7.99 (d, H_3 or H_1), δ7.79 (d, H_6, $J_{6,7}$=6.5Hz) and δ7.13 (splitted d, H_7). The resonances were assigned after spin decoupling experiments and the pattern is similar to that of the sulphur analogue thieno[3,4-c]pyridine[1] (I, X=S).

The structure of I (X=0) is further supported by its high reactivity in the Diels-Alder reaction. When chloroform solutions of equimolar amounts of maleic anhydride or N-phenylmaleimid were added to crystalline I, the adducts IIIa and IIIb were instantaneously formed in quantitative yields. The endo/exo ratios were determined by nmr to be ca.3:1.

The bridgehead H_A and H_C protons show no coupling in the exo-compounds with H_B and H_D, while in the endo-isomers J_{AB} and J_{CD} are about 5Hz. When a CH_2Cl_2 solution of title compound I is titrated with a solution of 1,4-naphthoquinone until the brownish yellow colour of the quinone remains, pure 8-aza-6,11-epoxy-6,11-dihydro-5,12-naphthacene dione IIIc (endo/exo ratio about 10:1), is obtained after evaporation of the solvent. Furo[3,4-c]pyridine opens a simple route to substituted isoquinolines and polycyclic aza-aromatics, by hydrolysis of the oxygen bridge in the adducts III. When 50mg of III_c was boiled for 2h in 10ml of methanol containing 15 drops of concentrated hydrochloric acid, 32mg of the unknown 8-aza-5,12-naphthacene dione IV was obtained as a yellow orange solid. (m.p. 269-273°).



II

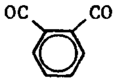


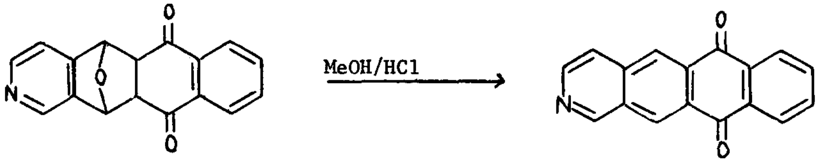
IIIa-c

(a) R^1-R^2 = CO_2CO

(b) R^1-R^2 = CON(Ph)CO

(c) R^1-R^2 = OC CO





III_c

IV

The present formation of furo[3,4-c]pyridine illustrates the versatility of the FVT method for synthesis of reactive isoannelated systems like isobenzfuran[5] and isoindole[6], from structure type II compounds.[7]

REFERENCES

1. L.H.Klemm, W.O.Johnson and D.V.White, J.Heterocyclic Chem., 9,843(1972).
2. J.D.Roberts and M.C.Casserio, Basic Principles in Organic Chemistry, Benjamin Inc. New York, 1965,p.974.
3. M.Malet, F.Marsais,G.Quequiner and P.Pastour,C.R.Acad.Sc.,Paris,t.275,Série C,1439('72).
4. G.W.J.Fleet and J.Fleming, J.Chem.Soc. (C), 1969, 1758
5. (a) U.E.Wiersum and W.J.Mijs, J.C.S.Chem.Comm., 1972,347.
   (b) E.Chako, D.J.Sardella and J.Bornstein, Tetrahedron Letters, 1976,2507.
6. R.Kreher and K.J.Herd, Tetrahedron Letters, 1976, 1661 and references cited.
7. For contrasting results in attempted FVT preparation of the corresponding isobenzofulvenes see R.N.Warrener, K.I.Gell and N.M.Paddon-Row, Tetrahedron Letters, 1977,53.