An Aryne Route to 2-Aminopyrene

ARNE JENSEN and ARNE BERG

Department of Chemistry, University of Aarhus, Aarhus C, Denmark

As a consequence of the pronounced selectivity of pyrene in electrophilic substitution reactions pyrene-2-derivatives (Ring Index numbering) are difficultly accessible. In the few instances,[1-3] where such derivatives are reported, rather tedious procedures were followed.

We have now found a simple route, leading to 2-aminopyrene, in the reaction of the easily available 1-bromopyrene with potassium amide in liquid ammonia. 1-Aminopyrene is formed at the same time. The two isomers can easily be separated by crystallization or by column chromatography, the total yield of purified amines, based on converted bromopyrene, being 60–70 % with an isomer ratio (2-amine/1-amine) of 1.3. 1-Chloropyrene with potassium amide and both of the two 1-halogenopyrenes with sodamide yielded much poorer results, although the reaction was evident in these cases too. 1-Iodopyrene and 1-fluoropyrene could be recovered quantitatively from reaction with potassium amide. Presumably the amine products are formed by an aryne (1,2-pyryne) mechanism. Only a single reference to a 1,2-pyryne intermediate is found in literature in a kinetic study by Huisgen *et al.*[4] on the simultaneous reactions of aryl halides with phenyllithium and lithium piperidide in ether. The 2-aminopyrene may be a key compound for the synthesis of additional 2-derivatives. Thus, 2-fluoro-, 2-chloro-, 2-bromo- and 2-iodopyrene, as well as 2-cyanopyrene have been prepared. Surprisingly, it was found that 2-bromopyrene, now available, did not yield any amine with potassium amide in liquid ammonia. More than half of the 2-bromopyrene was recovered, whereas the remainder was transformed into products not yet identified. The examination of pyryne reactions is being continued.

Experimental. 2-Aminopyrene. 1-Bromopyrene (14 g; 0.05 mole) was added rapidly to a stirred suspension of potassium amide (from 4.0 g (0.1 g. at.) of potassium) in 300 ml of liquid ammonia. The flask was cooled in a dry ice-acetone bath at −50 to −40°. The grayish colour of the suspension immediately turned deep red and this colour remained for at least 24 h. Unchanged potassium amide was destroyed by ammonium chloride, ether (200 ml) was cautiously added and the ammonia allowed to evaporate. After extraction with boiling ether (800 ml in all) and filtration, the solution was saturated with dry hydrogen chloride, and the amine hydrochlorides that precipitated were treated with sodium carbonate solution, yielding 5.1 g of crude amines. Separation was effected on alumina (Merck, standardized, Brockmann). There was obtained 2.2 g (29.7 %) of 1-aminopyrene, m.p. 112–13° (115–116° after recrystallization from cyclohexane) and 2.8 g (37.8 %) of pure 2-aminopyrene, m.p. 221–22°. (Found: C 88.22; H 5.22; N 6.32. Calc. for $C_{16}H_{11}N$: C 88.44; H 5.10; N 6.44). The two amines were identical with authentic samples (m.p., mixed m.p., U.V.-spectrum) prepared after Vollmann *et al.*[1] (Literature values of m.p. for 2-aminopyrene are 207°[1] and 215–216°.[3] We obtained 222–223° for the amine, when prepared after Vollmann.[1] This procedure was modified in the last step: Hydrolysis of 2-acetaminopyrene was effected by introduction of hydrogen chloride gas at 140° into a solution of the acetyl compound in diethylene glycol, thus avoiding the use of an autoclave). From the ethereal mother liquor, 4.4 g (31.4 %) of almost pure 1-bromopyrene was recovered. In two experiments with reaction time 2 and 24 h, respectively, results were almost identical.

2-Halopyrenes (F, Cl, Br, I) and 2-cyanopyrene. These compounds were prepared by conventional procedures. Diazotization (2 g of 2-aminopyrene was used in all experiments) was not followed by filtration[5] as the diazonium salt separated from the solution. For preparation of the bromo-compound diazotization was run in hydrobromic acid. 2-Fluoropyrene was prepared by the procedure described for the 1-fluoro-isomer.[5] The products were all purified by sublimation *in vacuo* or by chromatography before recrystallization.

2-Fluoropyrene. Yield (crude) 72 %. M.p. 151–152° (ethanol). (Found: C 87.20; H 4.14; F 8.51. Calc. for $C_{16}H_9F$: C 87.30; H 4.12; F 8.63).

2-Chloropyrene. Yield (subl.) 33.5 %. M.p. 146–147° (ethyl acetate), (Ref. 3, 143–145°).

2-Bromopyrene. Yield (crude) 48 %. M.p. 135.5–136.5° (ethanol : ethyl acetate, 10:1). (Found: C 68.04; H 3.28; Br 28.60. Calc. for $C_{16}H_9Br$: C 68.30; H 3.22; Br 28.42).

2-Iodopyrene. Yield (crude) 47 %. M.p. 157–158° (ethanol: ethyl acetate, 4:1). (Found:

C 58.41; H 2.95; I 38.75. Calc. for $C_{16}H_9I$: C 58.54; H 2.76; I 38.66).

2-Cyanopyrene. Yield (crude) 15 %. M.p. 201–202° (chlorobenzene), (Ref. 1, 203–204°).

1. Vollmann, H., Becker, H., Corell, M. and Streeck, H. *Ann.* **531** (1937) 1.
2. Berg, A. *Acta Chem. Scand.* **10** (1956) 1362.
3. Bolton, R. *J. Chem. Soc.* **1964** 4637.
4. Huisgen, R., Mack, W., Herbig, K., Ott, N. and Anneser, E. *Chem. Ber.* **93** (1960) 413.
5. Lund, H. and Berg, A. *Kgl. Danske Videnskab. Selskab, Mat.-Fys. Medd.* **22** (1946) No. 15.

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Reaction of Tabun with Fluoride in Aqueous Solution

E. HEILBRONN

Research Institute of National Defense, Department 1, Sundbyberg 4, Sweden

In a previous communication [1] it was shown that fluoride is able to reactivate cholinesterase after the inhibition of this enzyme by methyl-isopropoxy-phosphoryl fluoride (Sarin). Further experiments revealed that cholinesterase inhibited by dimethylamido-ethoxy-phosphoryl cyanide (Tabun) can be reactivated by fluoride.[2] It is possible that fluoride, known to have a striking reactivity towards the phosphoryl group,[3] is able to make a nucleophilic attack at the phosphorus atom of the phosphorylated cholinesterase, followed by reactions finally leading to the reactivation of the enzyme. The affinity of fluoride for the phosphorus atom in organophosphorus compounds can be demonstrated by the ability of fluoride to react with Tabun in aqueous solution as shown by the following experiments:

Upon addition of 7.3×10^{-3} M sodium fluoride to a 1.0×10^{-3} M Tabun solution in 0.1 M potassium chloride at pH 7.4 the pH of the solution immediately rose to 9.2 and continued to rise slowly with time. This observation indicated that a substance with a high pK_a was split off from Tabun without the formation of equimolar amounts of a monobasic phosphorus acid. In further experiments cyanide ion could be demonstrated upon addition of sodium fluoride to freshly prepared Tabun solutions. The cyanide ions were determined according to a method given by Asmus and Garschagen [4] which method was not disturbed by the presence of sodium fluoride. During these experiments the pH of the solution was kept at 7.4 by means of a barbital buffer

Table 1. Amount of CN^- liberated at pH 7.4 and 25°C from 10^{-5} M Tabun in veronal buffer solution after incubation with 10^{-4} M sodium fluoride. The third column shows CN^- formed from a 10^{-4} M Tabun solution only. The figures are corrected for blank values.

Incubation, min	CN^- in % of total amount of Tabun cyanide obtained from	
	10^{-5} M Tabun + 10^{-4} M NaF	10^{-4} M Tabun alone
11	13	4
20	24	5
31	27	7
41	31	9

Table 2. Amount of CN^- liberated at pH 7.4 and 25°C from 10^{-5} M Tabun in veronal buffer after incubation for 33 min with varying amounts of sodium fluoride.

Conc. of NaF M	CN^- in % of total amount of Tabun cyanide obtained from	
	10^{-5} M Tabun + NaF	10^{-4} M Tabun alone
1×10^{-2}	103	15
5×10^{-3}	103	15
1×10^{-3}	101	15
5×10^{-4}	83	15
2×10^{-4}	52	15
1×10^{-4}	36	15
5×10^{-5}	27	15
1×10^{-5}	14	15