BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 40 2363—2365 (1967)

Medium-Sized Cyclophanes. IV. The Halogenation Reactions of [2.2]Metacyclophane[1]

Takeo SATO, Meiko WAKABAYASHI (née FUJIMOTO), Yoshio OKAMURA, Teruo AMADA and Kazuo HATA

Department of Chemistry, Faculty of Science, Tokyo Metropolitan University, Setagaya-ku, Tokyo

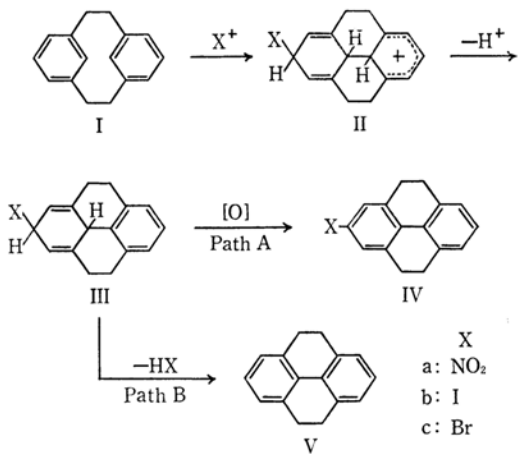
(Received March 22, 1967)

It has been postulated that, with proper control and choice of reaction conditions, the halogenation reactions of [2.2]metacyclophane might be directed in either of two ways: (A) the addition-oxidation path or (B) the addition-elimination path. An attempted iodination (iodine-silver perchlorate or iodine chloride) or bromination (bromine-iron catalyst) of [2.2]-metacyclophane resulted in the formation of 4, 5, 9, 10-tetrahydropyrene according to the path B reaction. On the other hand, iodination reaction in the presence of nitric acid has been shown to afford 2-iodo-4, 5, 9, 10-tetrahydropyrene, after path A. Both the reactions have been explained by assuming a common intermediate, which is formed by the attack of the halogenonium ion on one ring, accompanied by a simultaneous transannular attack of the generated phenonium ion on the second ring.

In a previous paper of this series, it has been reported[1] that the nitration reaction of [2.2]-metacyclophane (I) is accompanied by a transannular reaction of the ten-membered ring and that it gives products with a pyrene structure. Moreover, the reaction has been shown to take different courses, depending on the nature of the nitrating reagent; while dilute nitric acid afforded 2-nitro-4, 5, 9, 10-tetrahydropyrene (IVa) as the sole product, benzoyl nitrate in carbon tetrachloride furnished 4, 5, 9, 10-tetrahydropyrene (V) as an initial product, further reactions of which led to the formation of a complex mixture. An oxidation reaction with nitric acid, and a nitrous acid elimination reaction of a common intermediate IIIa, which resulted *via* IIa with the loss of a proton, were assumed to be responsible for the formation of the nitro compound IVa and the hydrocarbon V respectively.

The question arises as to whether similar dual decay processes, namely, the addition-oxidation (path A) *vs.* the addition-elimination (path B), of the intermediate III, would occur in other electrophilic substitution reactions of I, This paper will record the iodination reaction of I, which proceeded in two ways, in full confirmation of the above scheme.[2]

Compound I in an ether solution was treated with iodine and silver perchlorate, and the reaction mixture was analyzed by column chromatography on alumina. Elution with *n*-hexane afforded the starting material (34.5% recovery)



and then colorless plates, mp 135—137°C, the NMR spectra[3] of which showed only two singlets at δ 6.95 and 2.80 in a ratio of 3 : 4. It was identified as to be 4, 5, 9, 10-tetrahydropyrene (V) by means of the identical infrared spectra and by a mixed-melting-point determination with authentic material, mp 138°C. The yield reached 59%.

It has been shown[1] that the treatment of I with nitric acid, less concentrated than 11 N, dissolved in acetic acid at room temperature, resulted in the complete recovery of the starting material. When, however, the reaction mixture was warmed or when more concentrated nitric acid was used, compound

1) Part III: M. Fujimoto, T. Sato and K. Hata, This Bulletin, **40**, 600 (1967).

2) For the preliminary report see, T. Sato, E. Yamada, Y. Okamura, T. Amada and K. Hata, *ibid.*, **38**, 1049 (1965).

3) NMR spectra were measured on a Varian A-60 spectrometer by Mr. M. Kainosho, Ajinomoto Co., to whom the authors thanks are due. Carbon tetrachloride was used as a solvent and the spectra were expressed in δ value (ppm) from TMS which served as an internal reference.

I was converted to IVa in a high yield. It is assumed that the nitric acid oxidation of the iodinated intermediate IIIb would give rise 2-iodo-4, 5, 9, 10-tetrahydropyrene (IVb). Thus compound I dissolved in acetic acid was treated with dilute nitric acid (6 N) and iodine at room temperature for 24 hr. By chromatography on alumina, there was isolated a halogenated compound, mp 111—112°C, the NMR spectra of which showed three signals; a two-proton singlet at δ 7.36 (aryl), a three-proton AB_2 pattern at 6.99 (aryl), and an eight-proton singlet at 2.82 (methylene). The compound, which was formed in a 10% yield, was identified as IVb. The chemical evidence was obtained by comparing the compound with an authentic material, mp 111—112°C,

VI

which had been prepared from 2-amino-4, 5, 9, 10-tetrahydropyrene (VI)[4] by a diazotization reaction, followed by treatment with potassium iodide. Under the same reaction conditions, V was found to be neither iodinated nor nitrated. It may, therefore, be inferred that IVb was produced by a path A reaction and not by a path B reaction followed by iodination. Due to the extended reaction period, the nitration product IVa was also formed in a 22.8% yield. Moreover, as the first fraction of the chromatography, 31.3% of tetrahydropyrene (V) was isolated, indicating that the path B reaction was also occurring. Thus the two competing reactions could not be cleanly separated in this oxidative iodination reaction. When more reactive iodine chloride was used in place of iodine, the reaction proceeded after path B even in the presence of an oxidant (6 N NHO_3) affording a 80% yield of V. Compound IVb was also detected in a small amount in the reaction mixture resulting from the reaction of V with iodine-silver perchlorate.

The same situation was also encountered in the bromination reaction of I. In an unpublished work, cited in a monograph by Smith,[5] Allinger and his co-workers reported the formation of IVc by the bromination of I. An alternative route, which leads to the formation of V, has now been realized by the treatment of I with bromine in a carbon tetrachloride solution in the presence of iron powder. As a related reaction, though it is different in mechanism, Boekelheide and his co-workers[6] have shown that compound I, under irradiation with bromine, afforded a fully dehydrogenated compound, pyrene.

In conclusion, it has been well established that the reaction of I toward an electrophilic substitution reaction could be directed in either of two ways, addition-oxidation or addition-elimination, with proper control and choice of reaction conditions.

Experimental

Reaction Conditions. For the purpose of comparison, similar halogenation reactions were applied to [2.2]metacyclophane (I) as well as to 4, 5, 9, 10-tetrahydropyrene (V). Since there is good evidence that I is much more reactive than V toward electrophilic substitution reactions, those reaction conditions under which V is largely recoverable were selected.

Reaction with Iodine and Silver Perchlorate. *a) Compound V.* To a solution of 0.88 g (4.3 mmol) of V in 4 m*l* of ether, 0.5 g (5.0 mmol) of calcium carbonate and 1.1 g (5.2 mmol) of silver perchlorate[7,8] were added. Under good stirring, 1.1 g (4.4 mmol) of iodine was then added to the mixture in small portions. After having been kept at room temperature for 2 hr, the reaction mixture was refluxed for another 2 hr. The filtrate was then washed with water, with a sodium thiosulfate solution, and then again with water. The residue was found to be the starting material. In one experiment, IVb was obtained as a minor product.

b) Compound I. Under similar conditions, 424 mg (2.04 mmol) of I was treated with 447 mg (2.15 mmol) of silver perchlorate and 584 mg (2.32 mmol) of iodine. No base was added in this case. Chromatography on alumina, which had been eluted with *n*-hexane, afforded 34.5% of the starting material and then 59% yield of V, mp 135—137°C. Identifications were achieved by means of the IR and NMR spectra and by direct comparison with authentic materials. Further elution with chloroform afforded a small amount of an unidentified material, mp 66—90°C, which gave a positive Beilstein test.

When compound I and silver perchlorate were refluxed in ether, it was found that they form a complex which decomposes at 178°C. The complex is soluble in acetone and is sparingly soluble in water and ether. IR (KBr): 720, 800 and 1113 (broad) cm^{-1}. The treatment of the complex with iodine in dioxane resulted in the recovery of I.

Reaction with Iodine and Nitric Acid. *a) Compound V.* A solution of 204 mg (1 mmol) of V and 630 mg (5 mmol) of iodine in 1 m*l* of acetic acid was treated with 2 m*l* of 16 N nitric acid. After the mixture had been warmed on a water bath for 1 hr at 90°C, it was diluted with water and the precipitate was taken up in an ether solution. The starting material was completely recovered.

Under more forced conditions, in which the mixture was heated at 120°C, an unidentified tarry matter with

4) N. L. Allinger, M. A. Da Rooge and R. B. Hermann, L. A. Singer, *J. Am. Chem. Soc.*, **83**, 1974 (1961).
5) B. H. Smith, "Bridged Aromatic Compounds," Academic Press Inc., New York, N. Y. (1964), p. 211.
6) *Cf.* W. S. Lindsay, P. Stokes, L. G. Humber and V. Boekelheide, *J. Am. Chem. Soc.*, **83**, 943 (1961).
7) A. E. Hill, *ibid.*, **43**, 254 (1921).
8) E. D. Copley and H. Harthey, *J. Chem. Soc.*, **1930**, 2488.

IR spectra indicative of the presence of nitro and carbonyl groups was obtained.

b) Compound I. Since nitric acid more concentrated than 11 N was known to afford a nitration product,[1,4] compound I (104 mg, 0.50 mmol) in 20 m*l* of acetic acid was treated with 1 m*l* of 6 N nitric acid and 38 mg (0.30 mmol) of iodine. After the mixture had been stirred for 24 hr at room temperature, the product was analyzed by column chromatography on alumina. Elution with *n*-hexane afforded a 31.3% yield of V and then, when 5% of chloroform was added, a 10% yield of IVb as a colorless compound, mp 111—112°C. The IR spectra and melting point agreed with those of the authentic material prepared from IVa (see below). Further elution with chloroform furnished a 22.8% yield of IVa.

Attempted Iodination Reaction with Iodine and Yellow Mercuric Oxide. The attempted iodination of I as well as of V with iodine-yellow mercuric oxide[9] in ether, *n*-hexane, or ethanol resulted in the recovery of the starting materials.

2-Iodo-4, 5, 9, 10-tetrahydropyrene (IVb). 2-Amino-4, 5, 9, 10-tetrahydropyrene (VI) was prepared by the catalytic hydrogenation of IVa, which in turn was obtained by the nitration of 1 mmol of I, using 5% palladium-on-charcoal according to the method of Allinger *et al.*[4] Without isolation, it was converted to the hydrochloride by treatment with 0.5 m*l* of concentrated HCl in 6 m*l* of acetic acid and 1 m*l* of water. Under cooling, the hydrochloride suspension was diazotized with 75 mg (0.92 mmol) of sodium nitrate in 2 m*l* of water, and then treated with 180 mg (1.1 mmol) of potassium iodide in a minimum amount of water. Column chromatography on alumina, which had been eluted with *n*-hexane containing 5% ether, afforded IVa as colorless plates, recrystallized from ethanol, mp 111—112°C. The NMR spectra showed three bands, at δ 7.36 (2H), 6.99 (3H), and 2.82 (8H).

Found: C, 57.03; H, 3.96%. Calcd for $C_{16}H_{13}I$: C, 57.25; H, 3.94%.

IR (KBr): 730, 774, 802 and 863 cm^{-1}.

Reaction of Compound I with Iodine Chloride. To a solution of 104 mg (0.5 mmol) of I in 20 m*l* of carbon tetrachloride, 162.5 mg (1.2 mmol) of iodine chloride[10] was added; the mixture was then stirred for 4 hr. By column chromatography on alumina, using *n*-hexane as an eluent, V was isolated in a 34.3% yield.

When a mixture of 104 mg (0.5 mmol) of I, 100 mg (0.6 mmol) of iodine chloride, 20 m*l* of acetic acid, and 1 m*l* of 6 N nitric acid was stirred for 4 hr, V was isolated in a 86.7% yield.

Reaction with Bromine. *a) Compound V.* Neither V nor 4, 5-dihydropyrene was brominated by treatment with bromine in carbon tetrachloride at room temperature. In the presence of an iron catalyst, V afforded dibromo-4, 5, 9, 10-tetrahydropyrene as yellow powder, mp 195—205°C, by a reaction with excess bromine for 6 hr at room temperature. The NMR spectra in carbon disulfide showed two singlets, at δ 7.11 and 2.80, in a ratio of 1 : 2.

Found: C, 51.76; H, 3.34%. Calcd for $C_{16}H_{12}Br_2$: C, 52.78; H, 3.32%.

IR (KBr): 7.31, 796, 835 and 859 cm^{-1}.

b) Compound I. A mixture of 50 mg (0.25 mmol) of I, 50 mg (0.31 mmol) of bromine, and a small amount of iron powder in 10 m*l* of carbon tetrachloride was brought to reflux and then left to stand at room temperature for 15 min. After a few minutes further reflux, the product, which was identified as V (14.5% yield), was isolated by column chromatography on alumina. The rest of the material was found to be the starting material.

When the same reaction mixture was kept at 15—20°C for 24 hr, there was isolated a quantitative yield of V.

The authers wish to express their hearty thanks to the Ministry of Education for a grant-in-aid for fundamental scientific research.

9) W. Minnis, "Organic Syntheses," Coll. Vol. II, p. 357 (1948).

10) G. Brauer, "Handbuch der Präparative Anorganischen Chemie," Ferdinand Enke Verlag, Stuttgart (1954), p. 227.