

Figure 1. The molecule $\text{bipy}(\text{OC})_5\text{ClMoSnCH}_2\text{Cl}_2$ as viewed down the a axis. Standard errors of all specified bond lengths are less than 0.01 \AA , and of the bond angle is 0.3° .

stereochemistry is analogous to that of $\pi\text{-C}_5\text{H}_5(\text{OC})_3\text{-MoCH}_2\text{CH}_3$,³ if the π -cyclopentadienyl group in the latter is regarded as a tridentate ligand. The molybdenum-bonded chlorine, Cl(3), is 2.81 \AA from the tin atom and clearly bridges the two metal atoms. The tin can be regarded as having a distorted trigonal bipyramidal environment, with Cl(1) and Cl(3) as the axial substituents (angle Cl(1)-Sn-Cl(3) = 168°). The axial bond Sn-Cl(1) is significantly longer (2.43 \AA) than the equatorial bond Sn-Cl(2) (2.35 \AA). If the values of 1.39 and 1.61 \AA are taken as the single-bond covalent radii of tin⁴ and molybdenum,⁵ respectively, the lengths of all bonds other than the Mo-Sn and the bridging Sn-Cl are close to expected values. The Mo-Sn bond is 0.25 \AA short, presumably the result of π bonding, since the halogenotin group is considered to be a strong π acceptor.⁸

Although intramolecular halogen-tin coordination may be a rather general phenomenon, it is not viewed as a determinative structural element. It may operate to the extent permitted by the primary structural features, with consequent wide variation. The effect was first observed in (4-bromo-1,2,3,4-tetraphenyl-*cis,cis*-1,3-butadienyl)dimethyltin bromide,⁹ where the coordinating bromine-tin distance was greater and distortion from tetrahedral tin less extensive. In cases where two possible coordination geometries have comparable stability, secondary interactions of this type may be decisive. Further structural studies of related molecules are in progress.

(3) M. J. Bennett and R. Mason, *Proc. Chem. Soc.*, 273 (1963).

(4) Calculated as half the Sn-Sn distance in diphenyltin hexamer, as reported by D. H. Olson and R. E. Rundle, *Inorg. Chem.*, 2, 1310 (1963); this value agrees well with that derived from the C-Sn distance in methyltin compounds.

(5) Although the single-bond radius appropriate for the transition metal in carbonyl derivatives is open to discussion, three starting points give essentially this value: the Mo-CH₂ distance in $\pi\text{-C}_5\text{H}_5(\text{OC})_3\text{-MoCH}_2\text{CH}_3$;³ the Mo-N distance in *cis*-diethylenetriaminemolybdenum tricarbonyl;⁶ and the Mo-Mo distance in $[\pi\text{-C}_5\text{H}_5(\text{OC})_3\text{Mo}]_2$.⁷

(6) F. A. Cotton and D. C. Richardson, *Inorg. Chem.*, 5, 1851 (1966).

(7) F. C. Wilson and D. P. Shoemaker, *J. Chem. Phys.*, 27, 809 (1957); R. J. Doedens and L. F. Dahl, *J. Am. Chem. Soc.*, 87, 2576 (1965), footnote 21.

(8) W. Jetz, P. B. Simons, J. A. J. Thompson, and W. A. G. Graham, *Inorg. Chem.*, 5, 2217 (1966); W. A. G. Graham *ibid.*, 7, 315 (1968).

(9) F. P. Boer, J. J. Flynn, H. H. Freedman, S. V. McKinley, and V. R. Sandel, *J. Am. Chem. Soc.*, 89, 5068 (1967); F. P. Boer and H. H. Freedman, personal communication.

Acknowledgment. We thank the National Research Council of Canada for financial assistance.

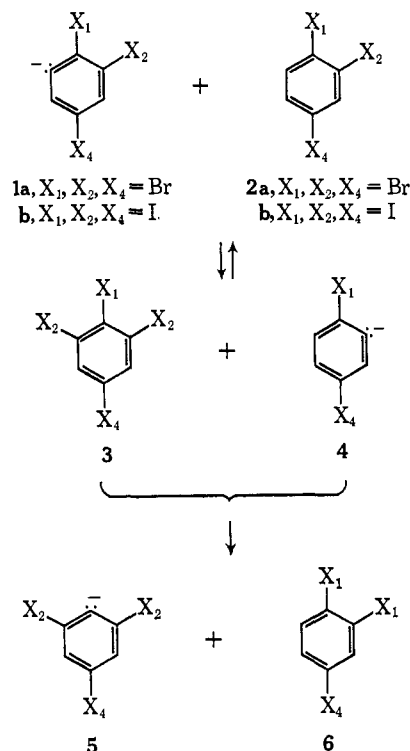
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Received January 26, 1968

Iodine Scrambling Accompanying Base-Catalyzed Isomerization of 1,2,4-Triiodobenzene

Sir:

The base-catalyzed isomerization and disproportionation of oligohalobenzenes was rationalized by Moyer and Bunnett^{1,2} in terms of a sequence of nucleophilic displacements *on halogen*, in which an aryl anion nucleophile displaces an aryl anion leaving group. For example, the isomerization of 1,2,4- to 1,3,5-tribromobenzene, catalyzed by potassium anilide in liquid ammonia, was postulated to involve attack of 6-anion **1a** on the 2-Br of **2a**, forming the product pair **3** and **4** (probably as a complex), quickly followed by attack of anion **4** on X₁ of **3** to form **6** and **5**, which is the conjugate base of the observed isomerization product (Scheme I).

Scheme I



Pathways involving 5-anions from 1,2,4-trihalo-benzenes were also invoked, for instance, to explain transformation of 1-iodo-2,4-dibromobenzene to 1,2,4-tribromobenzene (Scheme II, with **7a** and **8a**).

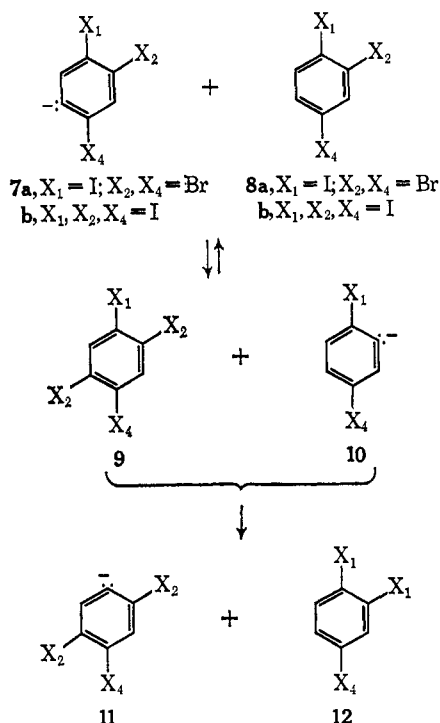
An intriguing observation was that 1,2,4-triiodobenzene afforded very little of its 1,3,5 isomer³ under

(1) C. E. Moyer, Jr., and J. F. Bunnett, *J. Am. Chem. Soc.*, 85, 1891 (1963).

(2) C. E. Moyer, Jr., Ph.D. Thesis, Brown University, 1964; *Dissertation Abstr.*, 25, 4412 (1965).

(3) 1,2,4-Triiodobenzene was initially reported¹ not to isomerize, but subsequently Moyer² obtained a trace of its 1,3,5 isomer from one run. In the present work, under slightly different conditions, yields of the 1,3,5 isomer as high as 5% have been obtained.

Scheme II



conditions which were favorable for isomerization of 1,2,4-tribromobenzene and for isomerization-disproportionation of 1-iodo-2,4-dibromo- and 1-iodo-2-bromo-4-chlorobenzenes.^{1,2} A conceivable explanation² is that the aggregation of three iodines in a 1,2,3 arrangement, as in **3**, is sterically so unfavorable that reaction of **1b** with **2b** is very slow.

Steric compressions should, however, be less serious in an intermediate such as **9** from **7b** and **8b** because only 1,2-diiodo-type arrangements are involved. However, the follow-up attack of **10** on **9** would simply regenerate **7b** and **8b** when all the halogens involved were indistinguishable iodines. Though reaction would have occurred, it would have been invisible.

However, if X₂ in **7b** and **8b** were radiolabeled, the occurrence of reaction could be recognized through redistribution of the radiolabel. Follow-up attack of **10** on X₁ of **9** would afford **11** and thence 1,2,4-triiodobenzene with the label distributed in equal portions in the 1 and 4 positions. (The consequences of follow-up attack of **10** on X₂ or X₄ of **9** must of course also be considered.)

We now report the results of experiments with 1,2,4-triiodobenzene labeled with iodine-131 in the 2 position. Our original preparation (A)⁴ of this substance was refluxed with an equimolar amount of potassium anilide plus a small excess of aniline in liquid ammonia for 8 hr. The 35% recovered 1,2,4-triiodobenzene (B) and the 5% yield of 1,3,5-triiodobenzene (C) were substantially equal in molar activity and probably equal to the original 1,2,4-triiodobenzene.⁶ A portion of B, on

(4) A was prepared from *p*-diiodobenzene and 50 μ Ci of iodine-131 by the method of D. H. Derbyshire and W. A. Waters, *J. Chem. Soc.*, 3694 (1950). Deiodination after the method of Bunnett and Victor⁵ afforded *p*-diiodobenzene of negligible activity.

(5) J. F. Bunnett and R. R. Victor, *J. Am. Chem. Soc.*, **90**, 810 (1968).

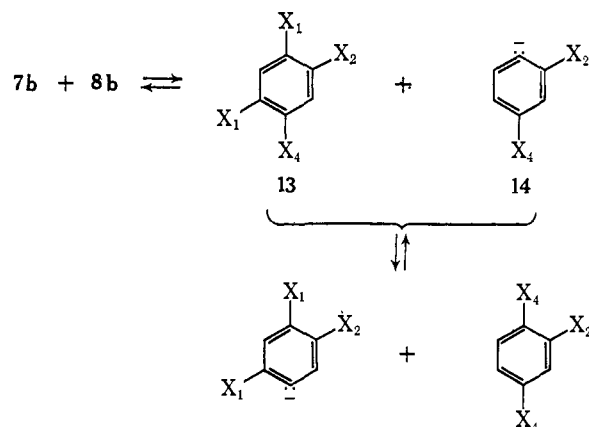
(6) The apparent molar activity of A, as measured, was about 35% greater than that of B or C. A is believed to have been contaminated with a radioactive impurity, possibly elemental iodine. A more highly purified sample (D) of the original 1,2,4-triiodobenzene, on exposure to

treatment with potassium *t*-butoxide in 50% *t*-butyl alcohol-50% dimethyl sulfoxide,⁵ gave in high yield *p*-diiodobenzene containing 68.6% of the molar activity of B. A further portion of B was deiodinated with 1-phenyl-2-benzenesulfonylhydrazide in 2 *M* methanolic sodium methoxide.⁷ This afforded a mixture of diiodobenzenes, and by means of a reverse isotope dilution technique the molar activity of the *meta* isomer⁸ was determined to be 66.4% of that of B. It follows that B had $33.3 \pm 1.5\%$ of its activity in each position.

A more highly purified sample (D) of the original 1,2,4-triiodobenzene preparation was submitted to the same reaction conditions except that reaction was interrupted after 30 min. This reaction afforded (i) no 1,3,5-triiodobenzene and (ii) 1,2,4-triiodobenzene of molar activity equal to that of D but with an uneven distribution of label: 30.2% in the 1 position, 46.4% in the 2 position, and 23.4% in the 4 position.

The mechanism of Scheme II accounts for the statistical redistribution of label during 8-hr reaction time, but it cannot fully account for the results after 30 min because it calls for the label to appear in exactly equal amounts at the 1 and 4 positions. However, the alternative mechanism of Scheme III, involving attack by 5-anion **7b** on X₁ of **8b**, etc., allows the 1 position to gain label faster than the 4 position. Scheme III as written is incomplete; in addition to follow-up attack of **14** on X₄ of **13**, as shown, it should include attack on X₂ of **13** and on the X₁ groups *ortho* to X₂ and X₄. When all possibilities are taken into account, Scheme III calls for the 1 position initially to gain label from the 2 position twice as fast as the 4 position.

Scheme III



A full discussion of the implications of this type of mechanism would take account of the further transformations of the 1- and 4-labeled 1,2,4-triiodobenzene molecules formed according to Scheme II or III. Their over-all consequence, of course, is to approach ever more closely a statistical distribution of label.

Actually, it is not necessary to invoke the mechanism of Scheme II to account for the statistical redistribution within 8 hr, but, because of the known positional effects of fluorine and bromine on the stability of phenyl anions⁹ and of analogy with orientation in the above *t*-potassium anilide in ammonia for 30 min, suffered partial scrambling but no loss of activity (see below).

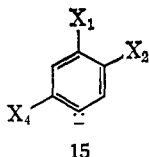
(7) J. F. Bunnett and C. C. Wamser, *ibid.*, **89**, 6712 (1967).

(8) Formed in 23% yield (glpc on 5% SE-30 plus 5% Bentone-34 on Chromosorb P).

(9) G. E. Hall, R. Piccolini, and J. D. Roberts, *J. Am. Chem. Soc.*, **77**, 4540 (1955); R. Huisgen, W. Mack, K. Herbig, N. Ott, and E. Anneser, *Chem. Ber.*, **93**, 412 (1960).

butoxide-*t*-butyl alcohol-dimethyl sulfoxide deiodination, which probably involves nucleophilic displacement on iodine as a key step,⁵ redistribution according to Scheme II is believed to proceed faster than by Scheme III. Schemes involving attack by the 3-anion of 1,2,4-triiodobenzene or by **1b** or **7b** on X_4 in **2b** or **8b** are unlikely because the products of such steps would be highly energetic.

Our experiments do not rule out mechanisms involving 1,2 shifts of iodine atoms, e.g., **7b** \rightarrow **15**, but



such shifts are disfavored because they cannot account for halogen transfer between rings.^{1,2}

Acknowledgment. This research was supported in part by the National Science Foundation.

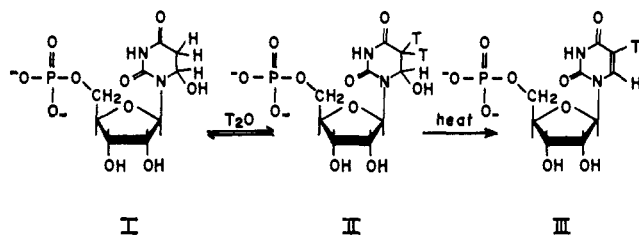
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Synthesis of Tritiouridine 5'-Phosphate via the Photohydrate of Uridylic Acid

Sir:

During some nmr studies on the photohydrate of uridine 5'-phosphate (I) we observed that deuterium was incorporated into the pyrimidine ring. After the exchange was complete, the solution was heated to convert the photohydrate to deuteriouridine 5'-phosphate. The nmr spectrum¹ showed no signal at δ 6.50 ppm where the H-5 doublet is found in the uridine 5'-phosphate (U5'P) spectrum. The H-6 doublet at 8.63 ppm seen in the U5'P spectrum was replaced by a singlet in the deuterated compound. Thus, the deuterium is attached to the 5 position in deuterated U5'P.

These results suggested a simple method for detecting uridyate photohydrates in RNA by incorporation of tritium. The synthesis of tritiouridine 5'-phosphate (III) described in this communication establishes the feasibility of this scheme.



A mechanically stirred, aqueous solution of disodium uridine 5'-phosphate (6 μ mol in 3.5 ml) was irradiated² at 254 nm in a stoppered 1-cm quartz spectro-

(1) Nmr was measured with a Varian A-60A spectrophotometer using D_2O as a solvent. The spectra were calibrated externally with TMS in a capillary tube.

(2) Irradiation was performed with a low-pressure mercury lamp (Mineralight, 9 W) equipped with the low-wavelength filter (model SL 2537) and a piece of Vycor glass (2 mm thick) between the filter and the cell.

photometer cell until the absorbance dropped to 0.15 (6 hr). The solution was evaporated to dryness under reduced pressure at room temperature.³ The residue (invisible) was transferred to a 1.5-ml ampoule with three 50- μ l portions of water. The solution was lyophilized and the residue taken up in 0.1 ml of tritiated water (3.6 μ Ci/ μ mol). The ampoule was sealed and allowed to stand for 17 hr at room temperature. The sealed ampoule was heated in a 70° water bath for 2.5 hr and cooled. The ampoule was opened at the tip and the condensation washed down the wall with several small portions (totaling 0.1 ml) of water. The solution was evaporated to dryness in a vacuum desiccator over P_2O_5 under reduced pressure (water pump). The residue was dissolved in 25 μ l of H_2O and transferred to a 4.5 \times 22.5 cm strip of Whatman 3 MM paper that had been washed with distilled water and air dried just before use. Electrophoresis was carried out at 1000 V for 2 hr at pH 3.5 (0.02 M ammonium citrate).

The electropherogram was scanned with a Nuclear Chicago Actigraph III (windowless). A small amount of radioactivity remained at the origin. A trace of activity was found in a minor uv-absorbing spot with a mobility 0.47 that of U5'P. The major activity was found in the U5'P spot. The U5'P spot was cut out and eluted with 2 ml of 0.1 M sodium phosphate buffer, pH 7.0 (3.8 μ mol, 63% recovery).⁴ A 0.2-ml aliquot was counted in Bray's solution⁵ in a Nuclear Chicago Mark I scintillation spectrophotometer. The specific activity of the U5'P was 5.8×10^5 cpm/ μ mol. Since our counting efficiency was 22%, this corresponds to 1.2 μ Ci/ μ mol. After three recrystallizations from aqueous methanol in the presence of unlabeled U5'P (20 mg), the specific activity was 1.0 μ Ci/ μ mol. This demonstrates unequivocally that the tritium is bound to U5'P and is non-exchangeable. If the original exchange and reversal had been quantitative, the specific activity should have been 3.6 μ Ci/ μ mol. The reason for this discrepancy is not clear. However, the observed specific activity of 1 μ Ci/ μ mol is adequate to detect a single photohydrate in transfer RNA.

A more detailed account of the kinetics of the exchange and dehydration reactions as well as the application of this labeling technique to photochemical studies on transfer RNA will be reported subsequently.^{5a}

Acknowledgments. The expert technical assistance of Mrs. Lelde V. Riekstins and Mrs. Irene Rosenberg

(3) A neutral, aqueous solution of the photohydrate I can be evaporated to dryness under reduced pressure at room temperature without appreciable conversion to III.

(4) Estimated from absorbance measurements. A large and variable blank makes this correction difficult. Therefore 63% represents the minimum recovery.

(5) G. A. Bray, *Anal. Biochem.*, 1, 279 (1960).

(5a) NOTE ADDED IN PROOF. It should be pointed out that the formation of 5-deuterio- (or tritio-) uridine 5'-phosphate constitutes strong evidence that the photohydrate of uridine 5'-phosphate has structure I. This is in agreement with recent chemical evidence of Miller and Cerutti on the structure of the uridine photohydrate.⁶ In addition, we have studied the uridine 5'-phosphate photohydrate directly by nmr. A multiplet at δ 3.47 ppm disappears slowly in D_2O . Concurrently, another multiplet centered at δ 6.21 ppm changes to two single proton peaks located at δ 6.16 and 6.26 ppm, respectively. These latter two peaks are assigned to the H-6 protons in the two diastereoisomers of I. Therefore, the multiplet at δ 3.47 ppm is assigned to H-5. This provides direct evidence for assignment of structure I to the photohydrate of uridine 5'-phosphate. It does not rule out the possibility that the "hydrate" may not be a water addition product, but a phosphodiester formed by photoaddition of the 5'-phosphate to the 5,6-double bond.

(6) S. I. Miller and R. U. Cerutti, *Proc. Natl. Acad. Sci. U. S.*, 59, 34 (1968).