A Mechanistic Study of the Photoreactions of Deoxy Iodo Sugars[1]

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Quantum yields of 0.31, 3.7, and 1.1 have been determined for the photochemical disappearance in heptane of 6-deoxy-6-iodo-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (1), 3-deoxy-3-iodo-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (2), and 3-deoxy-3-iodo-1,2:3,4-di-*O*-isopropylidene-α-D-glucofuranose (3), respectively. The major reaction for compounds 2 and 3 is epimerization at C-3, a reaction not observable for compound 1. Photochemical epimerization takes place in at least two ways. First, carbon–iodine bond homolysis followed by recombination of the radicals produced either regenerates the starting iodide or gives its C-3 epimer. Second, a chain reaction takes place in which the propagation step involves transfer of an iodine atom from the deoxy iodo sugar (2 or 3) to the carbon radical produced by carbon–iodine bond homolysis. In the presence of oxygen a new set of photoproducts is formed. These include enol esters, alcohols, and carbonyl compounds.

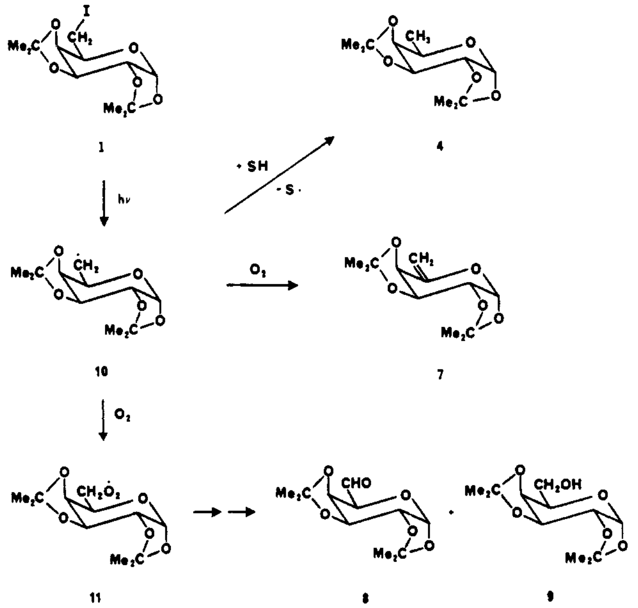
Introduction

Photolysis of compounds which contain carbon to iodine bonds is a topic which has been of interest to chemists for nearly fifty years.[2] During the past decade photochemical study of iodides has intensified, partly because this reaction can lead to formation of carbocations[3] but also because it has synthetic potential. Irradiation of iodobenzenes, for example, produces biphenyls.[4] The most promising synthetic application to date, however, is in carbohydrate chemistry where iodide (deoxy iodo sugar) photolysis leads to the formation of deoxy sugars.[5] Characteristics of the photochemical reaction of deoxy iodo sugars are high product yields, mild reaction conditions, and short reaction times. Actual quantitative information about efficiency is not available, however, since no quantum yields for deoxy iodo sugar photolysis have been reported.[6]

There has been considerable mechanistic work done on the photochemical reactions of alkyl iodides; however, it would be unwise to extrapolate the findings to reactions of deoxy iodo sugars since the basic photochemistry of these two systems appears to be different. These is no evidence from the photolysis of deoxy iodo sugars that cationic intermediates are formed; yet, this is a major process in the solution phase photolysis of simple alkyl iodides and bicyclic iodo compounds.[3]

A mechanism which adequately explains the existing information on the photochemistry of deoxy iodo sugars is that photolysis homolytically cleaves the carbon–iodine bond and hydrogen abstraction from the solvent by the resulting carbon radical gives the deoxy sugar (Scheme I). Some unanswered questions about this mechanism: Is it consistent with the quantum yields for deoxy iodo sugar reaction? Are any of the proposed reaction steps reversible? Why are cationic intermediates not formed? Although we have been interested primarily in the synthetic aspects of iodide photolysis,[7,8] we have attempted to answer these questions because improved mechanistic understanding might be translated into more effective use of this process.

Scheme I



Results and Discussion

A. Selection of a Photolysis Solvent. Most irradiations of deoxy iodo sugars have been conducted in either methanol or 2-propanol. Neither of these solvents was acceptable for quantum yield determinations because irradiations in each (under nitrogen) rapidly produced a material which absorbed a considerable amount of the incident light even at low conversions. Since the absorbing materials may have been carbonyl compounds, a hydrocarbon solvent (heptane) was selected. Irradiations in heptane were free from these absorbing materials.

B. Quantum Yield Determinations. 1. 6-Deoxy-6-iodo-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (1). The quantum yield for disappearance of 1 during photolysis under nitrogen in heptane was found to be 0.31, a value which was independent of the amount of starting material reacted. The quantum yield was determined from an average of three irradiations, all of which were run to less than 15% conversion. The only product detected (95% yield, based on starting material reacted) was 6-

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(1) Taken from the Ph.D. dissertation of Richard C. Roth, Cleveland State University, 1983.

(2) Reviews which have been published: (a) Majer, J. R.; Simons, J. P. *Adv. Photochem.* **1964**, *2*, 137. (b) Calvert, J. G.; Pitts, J. N. Jr. "Photochemistry"; John Wiley and Sons, Inc.: New York, 1967; p 521. (c) Sammes, P. G. In "Chemistry of the Carbon-Halogen Bond"; Patai, S., Ed; Wiley: New York, 1973; Chapter 11. (d) Kropp, P. J. *Acc. Chem. Res.* **1984**, *17*, 131.

(3) Kropp, P. J.; Poindexter, G. S.; Pienta, N. J.; Hamilton, D. C. *J. Am. Chem. Soc.* **1976**, *98*, 8135.

(4) Kharasch, N.; Wolf, W. *Angew. Chem.* **1962**, *26*, 284.

(5) Binkley, R. W. *Adv. Carbohydr. Chem. Biochem.* **1981**, *38*, 105.

(6) A proposal has een made (Lemmes, R.; von Sonntag, C. *Carbohydr. Res.* **1982**, *105*, 276), based upon δ-radiolysis of deoxy iodo sugars in 2-propanol, that deoxy sugar formation from UV photolysis occurs via a chain reaction.

(7) Binkley, R. W.; Hehemann, D. G. *Carbohydr. Res.* **1979**, *74*, 337.

(8) Binkley, R. W.; Binkley, W. W. *Carbohydr. Res.* **1968**, *8*, 370; *Carbohydr. Res.* **1969**, *11*, 1.

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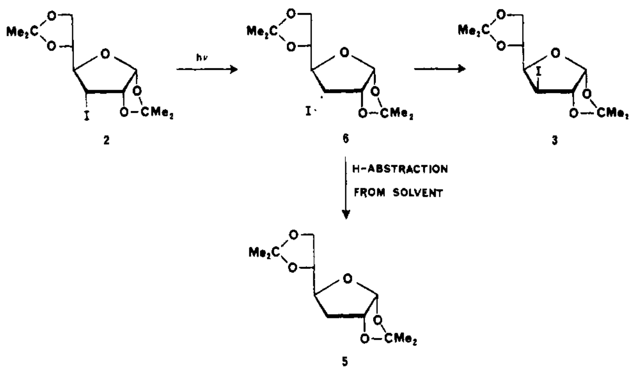
Scheme II



deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (4) (Scheme I), the same compound formed from photolysis of 1 in 2-propanol[7] and methanol.[8] (The procedure for quantum yield determination, product identification, and product quantitation is given in the Experimental Section.)

2. 3-Deoxy-3-iodo-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (2). The quantum yield for disappearance of 2 was found to be larger than unity and dependent upon the extent of reaction. Extrapolation of the quantum yield data to 0% conversion gave a value of 3.7. Analysis of a typical reaction mixture showed that, in addition to unreacted starting material (2), two other compounds were present. The major product (94% yield) was a 3-deoxy-3-iodo-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (3), the C-3 epimer of the starting material (2). The minor product (2%) was 3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranose (5).

Although several mechanistic possibilities exist for conversion of the iodide 2 into its epimer 3, those reactions involving radical intermediates satisfy best the existing information. Even though carbocation formation could lead to epimerization at C-3 in compound 2, it is unlikely that cations are involved in this process because the characteristic carbocation reactions of rearrangement and elimination are not observed. The epimerization at C-3 may be arising in part by recombination of the radical 6 and its associated iodine atom to give 3 (Scheme II). This radical recombination reaction could have a maximum quantum yield of unity; therefore, another process, one with a quantum yield greater than one, also must be operative.

There are three basic chain reactions which involve either the radical 6 or an iodine atom interacting with a molecule of the allo iodide 2 to convert it into the gluco iodide 3. The propagation steps for these three are given in eq 1–4 (R· = the radical 6, R_A–I = compound 2, R_G–I = compound 3). The effect of added molecular iodine on

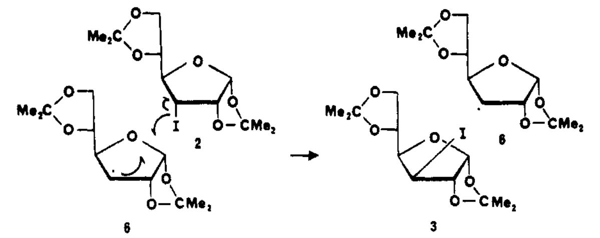
$$R\cdot + R_A\text{-}I \xrightarrow[\text{BY } R\cdot]{\text{IODINE ABSTRACTION}} R_G\text{-}I + R\cdot \qquad (1)$$

$$I\cdot + R_A\text{-}I \xrightarrow[\text{BY } I\cdot]{\text{IODINE ABSTRACTION}} R\cdot + I_2 \qquad (2)$$

$$R\cdot + I_2 \xrightarrow{\qquad} R_G\text{-}I + I\cdot \qquad (3)$$

$$R_A\text{-}I + I\cdot \xrightarrow[\text{BY } I\cdot]{\text{IODINE DISPLACEMENT}} R_G\text{-}I + I\cdot \qquad (4)$$

Scheme III



the photochemical epimerization of 2 should differentiate between the propagation step shown in eq 1 and those indicated by eq 2–4. Addition of I_2 to the reaction mixture should reduce or terminate a chain reaction dependent upon the propagation step shown in eq 1 because the radical 6 (R·) would react with I_2. The presence of added I_2 should not adversely effect processes shown in eq 2–4, however, since iodine atoms are essential to propagation of these reactions. When molecular iodine was included as a reactant in the photolysis of 2, the quantum yield, corrected for a small amount of light absorption by iodine, was reduced to 1.0 and was no longer dependent upon the extent of conversion. This result favored the process shown in eq 1.

In a related experiment, iodine again was added to the reaction mixture but this time irradiation was conducted with a sun lamp. Under these conditions compound 2 did not absorb light but I_2 did; therefore, iodine atoms were being generated. If either of the processes described by eq 2–4 were operative during this photolysis, epimerization should have occurred. No reaction was observed. We conclude from this experiment and from the others described above that the mechanism shown in Scheme III best explains the intermolecular conversion of 2 into 3.

3. 3-Deoxy-3-iodo-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (3). If the mechanism pictured in Scheme III is correct, then iodine transfer should be reversible; that is, photolysis of the gluco iodide 3 should produce the allo epimer 2. When compound 3 was irradiated, it did, in fact, give 2 as essentially the only product. (A trace of the deoxy sugar 5 was formed.) The quantum yield for disappearance of 3 was 1.1, a result which indicated that chain reaction was less important in the epimerization of the gluco iodide 3 than the allo iodide 2. This difference in reactivity can be explained on stereochemical grounds.

A leaving group at C-3 is displaced more easily from the 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose system than from the corresponding gluco epimer,[9–11] due primarily to steric hinderance at the side of the molecule bearing the 1,2-*O*-isopropylidene group. Similar steric differences should exist for formation of the allo iodide 2 from the radical 6. A reaction involving formation of 3 in its propagation step, therefore, should have a lower activation energy and a higher quantum yield than a similar reaction for formation of 2.

C. Irradiations in the Presence of Oxygen. Since molecular oxygen is an effective radical scavenger as well as an efficient triplet-state quencher, photolysis of the iodides 1–3 in the presence of oxygen is a potential source of information about the intermediates produced in these reactions. When the galacto iodide 1 was irradiated in heptane in an oxygen atmosphere, the yield of the deoxy sugar 4 was reduced to 3% and a new set of photoproducts

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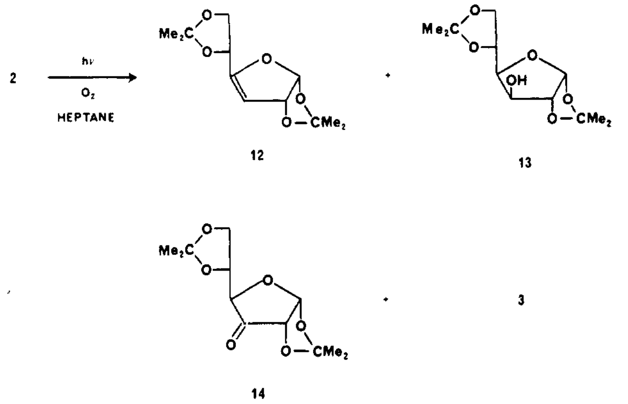
(9) Nayak, W. G.; Whistler, R. L. *J. Org. Chem.* **1969**, *34*, 3819.

(10) Foster, A. B.; Hems, R.; Webber, J. M. *Carbohydr. Res.* **1967**, *5*, 292.

(11) Buck, K. W.; Foster, A. B.; Hems, R.; Webber, J. M. *Carbohydr. Res.* **1966**, *3*, 137.

was formed. The new compounds were 1,2:3,4-di-*O*-isopropylidene-L-*arabino*-hex-5-enopyranose (**7**, 17%), 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose (**8**, 43%), and 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**9**, 37%). A proposed mechanism for the formation of these compounds is given in Scheme I. According to this mechanism, compound **7** would result from abstraction by oxygen of the hydrogen attached to C-5 while compounds **8** and **9** could arise from combination of oxygen with the radical **10**. Autoxidation of organic compounds produces peroxy radicals which form alcohols and carbonyl compounds through a complex set of reactions.[12] Compounds **8** and **9** may be formed from the peroxy radical **11** through a similar series of transformations.

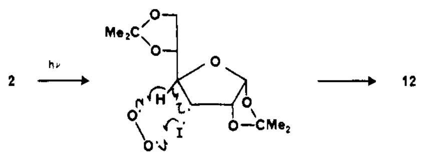
A new group of products also was formed when the allo iodide **2** was irradiated in the presence of oxygen. The new compounds were 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hex-3-enofuranose (**12**, 44%), 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**13**, 17%), and 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexulofuranose (**14**, 12%). These products presumably were generated in a manner similar to the formation of compounds **7**–**9**. A significant amount (18%) of the gluco iodide **3** also was produced in this reaction. Formation of **3**, under conditions where intermolecular reaction such as that shown in Scheme III would be prevented by reaction of the radical **6** with oxygen, supports the proposal that some C-3 epimerization takes place by radical recombination after the initial photochemical bond homolysis in **2**.



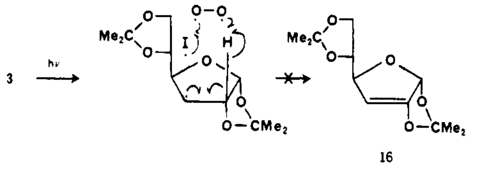
Radical recombination was nearly the exclusive pathway when the gluco iodide **3** was irradiated in the presence of oxygen. The epimeric iodide **2** was formed in 90% yield along with a small amount (5%) of 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (**15**). It appears that for oxygen to react at C-3 in compounds **2** and **3**, it must approach the furanose ring from the side opposite the departing iodine. The greater steric requirements for approach to the side of the ring bearing the 1,2-isopropylidene group should make reaction of oxygen at C-3 more difficult when the gluco iodide **3** is irradiated.

If oxygen approaches compound **2** or **3** from the same side as a departing iodine, it is prevented by iodine from interacting with C-3 but it can react with the departing iodine and a neighboring hydrogen in a syn elimination process. The enol ether **12**, a compound formed only from **2**, appears to result from this type of reaction (Scheme IV). A similar reaction of **3** to give **16** would not be expected since it would produce a highly strained molecule (Scheme V).

Scheme IV



Scheme V



D. Possible Formation of Carbocations. The possible involvement of carbocations in the reactions of compounds **1**–**3** needs to be considered further. Although some of the photoproducts might be formed from radicals or cations, cationic intermediates are not required to explain the results. We believe that, in general, the best evidence for the intermediacy of cations is the formation of products arising from rearrangement and/or capture of nucleophiles (usually solvent molecules); however, even apparent nucleophile capture can take place without a carbocation being involved.[13] Neither reaction was observed here, although solvent capture was not a real possibility. While formation of unsaturated compounds is a criterion for carbocation intermediates, care must be exercised in using this criterion since unsaturated compounds can be produced in radical reactions. For the sugars studied, formation of unsaturated compounds is observed only when oxygen is present; therefore, simple electron transfer between carbon and iodine atoms to produce carbocations does not take place.

Why are carbocations generated by photolysis of some iodides and not others? The answer to this question is not known; however, at least two factors may be important in the apparent lack of carbocation formation from compounds **1**–**3**. First, carbohydrates form carbocations with difficulty except at the anomeric carbon. The large number of electron-withdrawing oxygen atoms in these molecules discourages development of a positive charge unless the charge can be directly stabilized (as it can at the anomeric carbon) by interaction with a lone pair of electrons on oxygen. The electron transfer, which is postulated to follow photochemical carbon–iodine bond homolysis,[3] may be energetically too unfavorable in typical carbohydrates. The nature of the reaction medium also may influence the electron-transfer process. The generation of carbocations may be dependent to some extent upon the polarity of the reaction solvent. The solvent used in this study (heptane) is among the least effective in stabilizing cations. Compounds **1**–**3** previously have been irradiated in 2-propanol, however, to give only the corresponding deoxy sugars **4** and **5**;[7] thus, the solvent is not determining the course of reaction for these compounds.

E. Possible Formation of Divalent Intermediates. Recently it has been reported that irradiation of alkyl iodides can generate carbenes as well as carbocations.[14] These divalent intermediates, which usually are formed

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(12) Lowry, R. H.; Richardson, K. S. "Mechanism and Theory in Organic Chemistry"; Harper and Row: New York, 1976; p 499.

(13) Apparent capture of a nucleophile does not always require a carbocation intermediate. Photolysis of (iodomethyl)naphthalene in methanol (Slocum, G. H.; Kaufmann, K.; Schuster, G. B. *J. Am. Chem. Soc.* **1981**, *103*, 4625) follows a different pathway.

(14) Kropp, P. J.; Sawyer, J. A.; Snyder, J. J. *J. Org. Chem.*, **1984**, *49*, 1583.

(15) Beckett, A.; Porter, G. *Trans. Faraday Soc.* **1963**, *59*, 2039.

Table I. Quantum Yield Determination for Compounds 1–3[a]

no.	irradn time, min	quantum yield	atm
1	30	0.31	N_2
1[b]	30	0.29	N_2
2	5–20	3.7[c]	N_2
2[b]	8	1.0	N_2
2	8	1.0	O_2
3	8–30	1.2	N_2
3[b]	8	1.0	N_2

[a] Determined by disappearance of starting material. [b] 6.6 × 10^{-3} M concentration of iodine present at initiation of photolysis. [c] Value obtained by extrapolation to 0% conversion.

in minor but significant amounts along with carbocations, rearrange to alkenes. As with carbocations, the intermediacy of carbenes in the photolysis of compounds **1–3** seems unlikely since the characteristic reaction of these species does not take place. The reason for the lack of carbene formation from irradiation of **1–3** probably parallels that for the absence of carbocations; that is, generation of electron deficient intermediates in molecules containing many electronegative atoms is energetically too difficult.

F. Summary. Photolysis of the deoxy iodo sugars **1–3** results in an efficient homolytic cleavage of the carbon–iodine bond and subsequent reactions characteristic of radical intermediates. The most important of these reactions (observable only for compounds **2** and **3**) is inversion of configuration at the chiral center where iodine is attached. This epimerization process takes place both by cage recombination of the radicals produced by photolysis and by intermolecular transfer of iodine. The other reaction observed from photolysis of compounds **1–3** under nitrogen is the previously reported[7,8] deoxy sugar formation.

Experimental Section

Quantum Yield Determinations. Irradiations were conducted with a Rayonet photochemical reactor which was equipped with a RPR-2537 Å lamp and contained a merry-go-round assembly. The merry-go-round apparatus held two photolysis cells (3 mL each), one for the deoxy iodo sugar and the other for the actinometer (benzophenone in ethanol, quantum yield = 1.0[15]). This apparatus was constructed so that each cell was rotating past the lamp and each cell was purged independently during photolysis. The actinometer cell was always purged with ethanol saturated nitrogen while the identity of the heptane saturated gas (nitrogen or oxygen) passing through the sample cell was determined by the particular experiment. The photolysis cells were purged with the appropriate gas for 1 h prior to irradiation. Photolyses were conducted on 6.6 × 10^{-3} M solutions for periods of time ranging from 5–30 min (see Table I). Under these conditions, essentially all the light entering the photolysis cells was absorbed. The maximum percent conversion for any run was 16% for the deoxy iodo sugars and 20% for the actinometer. Each determination was repeated twice and the average of the three values was taken as the quantum yield (see Table I).

Immediately after irradiation, the reaction mixture was transferred to a 5-mL volumetric flask and diluted to volume with heptane. This solution was analyzed by HPLC with Altex equipment: a Model 110A pump, a Model 153 analytical UV detector, and an 8-μL analytical UV optical unit. Two Whatman Partisil PX5 10/25 columns, connected in sequence and eluted at 1.0 mL/min with 4:1 hexane–ethyl acetate, were used for separation.

The results from various quantum yield determinations are summarized in Table I. (Conrol runs, in which the light was not turned on, showed no reaction; also, reaction mixtures after photolysis did not show further reaction.)

Table II. Preparative Irradiations of Compounds 1–3[a]

no.	products (% yield)	atm
1	4 (95%)	N_2
1[b]	4 (95%)	N_2
1	4 (3%), 7 (17%), 8 (43%), 9 (37%)	O_2
2	5 (2%), 3 (98%)	N_2
2[b]	3 (100%)	N_2
2	3 (18%), 12 (44%), 13 (17%), 14 (12%)	O_2
3	5 (3%), 2 (97%)	N_2
3[b]	5 (1%), 2 (99%)	N_2
3	15 (5%), 2 (90%)	O_2

[a] Iodoheptanes were present in reaction mixtures conducted under nitrogen but no effort was made to quantitate them. [b] 6.6 × 10^{-3} M concentration of iodine present at initiation of photolysis.

Product Identification. A series of extended photolyses (see Table II for reaction times) was conducted with the same apparatus used for the quantum yield determinations. These reaction mixtures were analyzed by gas chromatography/mass spectrometry. Chemical-ionization mass spectra were obtained from a Finnigan 1015-D mass spectrometer with methane as the reagent gas at a pressure of 1 torr and an ionizing voltage of 110 eV. Separation of compounds was accomplished by a 140 × 0.5 cm column of 3% OV-101 on 80–120 mesh Chromosorb W, attached to the spectrometer. Temperature programming was set with an initial temperature of 50 °C and an increase of 4 °C/min to 200 °C. Compounds were identified by comparison of their mass spectra (and retention times) with those of independently prepared samples. The starting materials and photoproducts were stable under the GC conditions. Quantitative analysis of reaction mixtures was conducted using a Hewlett-Packard 5400A gas chromatograph equipped with a flame-ionization detector. The conditions were the same as those used for the GC/MS analysis. The detector response to the various photoproducts was determined from known samples (see below).

Preparation of Deoxy Iodo Sugars 1–3. The starting materials were synthesized according to a procedure developed in our laboratory.[16]

Synthesis of Photoproducts 4, 5, 7–9, and 14. All photoproducts except **13** and **15** were independently synthesized by known procedures. The retention times and mass spectra of these known compounds were used to establish photoproduct structure. These samples also were used for calibration purposes in quantitative analysis of photolysis mixtures. References to procedures used for preparation of these compounds: **4**,[7] **5**,[7] **7**,[17] **8**,[18] **9**,[19] **12**,[20] and **14**.[18] Compounds **13** and **15** were purchased from Pfanstiehl Laboratories, Inc., Waukegan, IL.

Photolysis of Compounds 1–3 in the Presence of Iodine with Visible Light. Visible light photolyses in the presence of added 6.6 × 10^{-3} M iodine were conducted for 1 h with a 275-W General Electric sun lamp. The light was passed through a dose lime glass plate (to remove any UV light) before reaching the sample. No reaction was observed for compounds **1–3**.

Acknowledgment. We wish to thank the Standard Oil Company (Ohio) for support of this work.

Registry No. **1**, 4026-28-2; **2**, 67337-61-5; **3**, 14260-27-6; **4**, 4026-27-1; **5**, 4613-62-1; **7**, 22618-03-7; **8**, 4933-77-1; **9**, 4064-06-6; **12**, 2774-28-9; **13**, 582-52-5; **14**, 2847-00-9; **15**, 2595-05-3.

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(16) Binkley, R. W.; Ambrose, M. G.; Hehemann, D. G. *J. Org. Chem.* **1980**, *45*, 4387.

(17) Freudenberg, K.; Raschig, K. *Ber. Dtsch. Chem. Ges.* **1929**, *62*, 373.

(18) Binkley, R. W. *J. Org. Chem.* **1977**, *42*, 1216.

(19) Raymond, A. L.; Schroeder, E. F. *J. Am. Chem. Soc.* **1948**, *70*, 2785.

(20) Weygand, F.; Wolz, H. *Chem. Ber.* **1952**, *85*, 256.