A New Process for Alkene Formation. Photolysis of *o*-Iodobiphenylyl Ethers[1]

Roger W. Binkley* and Dolores J. Koholic

Department of Chemistry, Cleveland State University, Cleveland, Ohio 44115

Received February 6, 1979

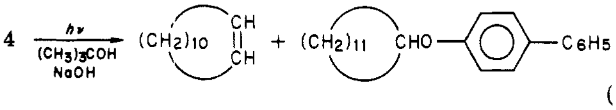
The *o*-iodobiphenylyl ethers **4**, **5**, **9**, and **18** from cyclododecanol, 1-dodecanol, 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose, and 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose, respectively, were synthesized by tosylate (compounds **4**, **5**, and **9**) or triflate (compounds **9** and **18**) displacement by the anion of 2-iodo-4-phenylphenol. Alkene formation, which always was accompanied by formation of the unsubstituted biphenylyl ether (iodine replaced by hydrogen), resulted from photolysis of compounds **4**, **5**, and **9** in 2-methyl-2-propanol. Irradiation of **18** produced only the unsubstituted biphenylyl ether **19**.

During the past several years we have been studying photochemical reactions of carbohydrates in an effort to add to the useful synthetic transformations of these compounds.[2] One goal for this work has been to find an effective photochemical process for the often difficult task of introducing carbon-to-carbon unsaturation into carbohydrates.[3] The results presented here describe an attempt to achieve this goal.

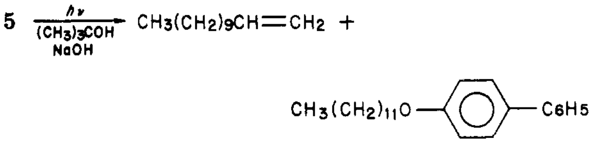
One possible method for generating an alkene involves an elimination reaction in which the loss of a stabilized radical is the final step (Scheme I). Such a process depends upon creating an intermediate with a radical center on a carbon atom adjacent to a carbon bearing an effective leaving group. The phenoxy-substituted radical **1** (Scheme I) is a potential candidate for such an intermediate. One pathway to this intermediate (**1**) could be to generate a radical center at the ortho position of a benzene ring (as in **2**) in anticipation of a hydrogen transfer in a six-membered-ring process. Since photolysis of an *o*-iodophenyl ether should produce the intermediate **2**, irradiation of compounds with the general structure **3** could begin the process of alkene formation.

Results and Discussion

To test the sequence proposed in Scheme I, we converted a secondary alcohol (cyclododecanol) and a primary alcohol (1-dodecanol) each to the corresponding 2-iodobiphenylyl ethers (**4** and **5**, respectively) according to the reactions outlined in Scheme II. The 2-iodobiphenylyl chromophore was selected over the more readily available 2-iodophenyl one because it has a sufficiently longer wavelength UV absorption to allow Pyrex-filtered irradiation. Irradiation of **4** under nitrogen in 2-methyl-2-propanol containing sodium hydroxide (eq 1) produced cyclododecene (88% yield) and biphenylyl cyclododecyl ether (10% yield). (Omission of a base from the reaction mixture caused it to become acidic during irradiation.) Irradiation of **5** (eq 2) resulted in formation of 1-dodecene in 54% yield and biphenylyl 1-dodecyl ether in 33% yield; thus, alkene formation was the major reaction pathway in the two "test systems" selected.



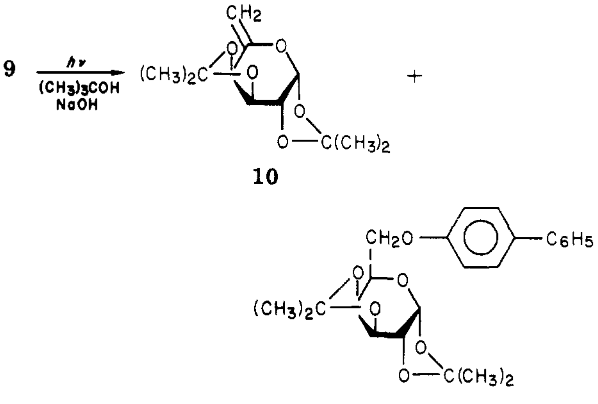
(1)



(2)

The results from irradiation of compounds **4** and **5** seemed sufficiently promising to merit application of this process to a partially protected carbohydrate. Conversion of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**7**) into its 6-*O*-tosyl derivative followed by tosylate displacement with the sodium salt of 2-iodo-4-phenylphenol (3-iodo-4-biphenylol) in refluxing dimethylformamide resulted in formation of 1,2:3,4-di-*O*-isopropylidene-6-*O*-(2-iodobiphenylyl)-α-D-galactopyranose (**9**). Alternatively, compound **9** was synthesized under much milder conditions (25 °C) by displacement of the trifluoromethanesulfonyl (triflyl) group from **8**.

Once the likelihood of a mild ether synthesis existed, a detailed study of **9** was undertaken. The results from this study, which are given in Table I, reveal several interesting features of this reaction. First, the photochemical reaction (eq 3) can be directed away from alkene (**10**) formation entirely by irradiation in 2-propanol (run 1, Table I). Clearly, the intramolecular, alkene-forming reaction only competes effectively with the intermolecular process when good hydrogen donors are excluded from the reaction mixture.



10

11

(3)

As can be seen from a comparison of runs 2 and 3 in Table I, the photochemical reaction took place much more rapidly when the Pyrex filter (280-nm cutoff) was replaced by a Corex filter (260-nm cutoff). This change caused a modest reduction in alkene yield and a considerable increase in darkening of the reaction mixture. At the close of every irradiation in 2-methyl-2-propanol, insoluble material was suspended in the yellow reaction mixture. A

---

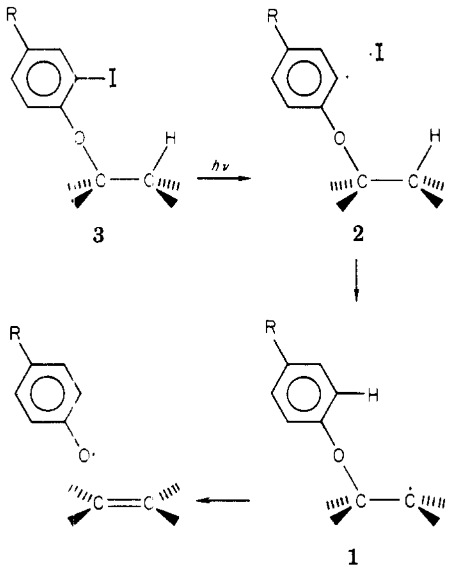
[1] A preliminary report of this research was made at the IXth International Symposium on Carbohydrate Chemistry, April 1978; see Abstract B 26.

[2] (a) R. W. Binkley, *J. Org. Chem.*, **42**, 1216–21 (1977); (b) R. W. Binkley, D. G. Hehemann, and W. W. Binkley, *ibid.*, **43**, 2573–76 (1978); (c) R. W. Binkley, *Carbohydr. Res.*, **48**, C1–C4 (1976); (d) R. W. Binkley, *ibid.*, **58**, C10–C12 (1977).

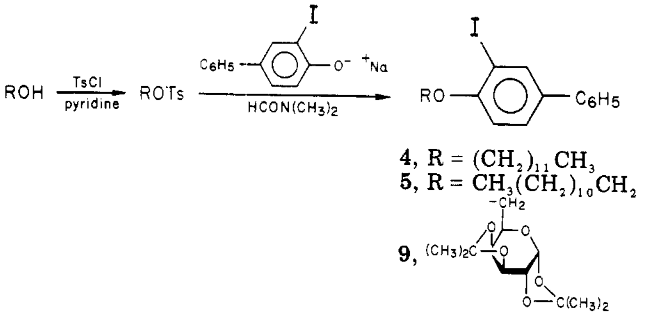
[3] W. A. Szarek, *Adv. Carbohydr. Chem. Biochem.*, **28**, 225–306 (1973).

0022-3263/79/1944-3357$01.00/0

Scheme I



Scheme II



4, R = $(CH_2)_{11}CH_3$
5, R = $CH_3(CH_2)_{10}CH_2$

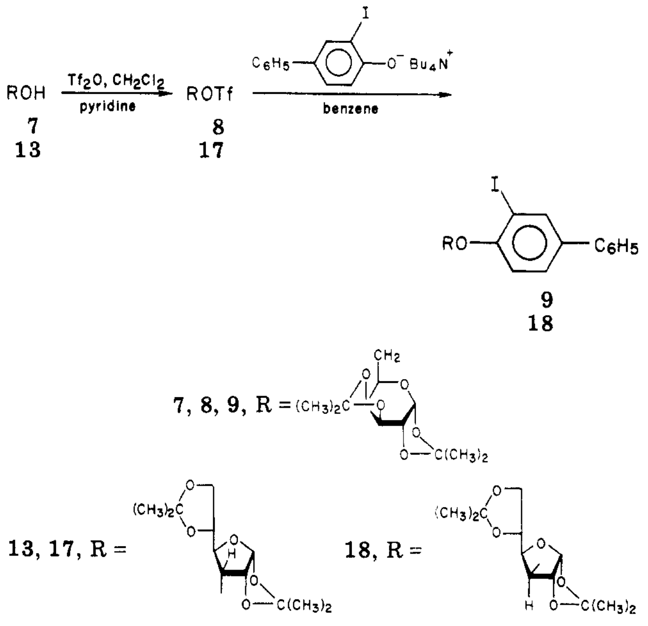
Table I. Irradiations of 9

run	filter	irradiation time, h	solvent	base	% yield of products 10	% yield of products 11
1	Pyrex	9	$(CH_3)_2CHOH$	$NaHCO_3$ or NaOH	0	94
2	Pyrex	18	$(CH_3)_3COH$	NaOH	80	14
3	Corex	3	$(CH_3)_3COH$	NaOH	65	17
4	Pyrex	18	$(CH_3)_3COH$	ion-exchange resin	47	23

combination of distillation and column chromatography was used to isolate both the alkene 10 and the ether 11 in pure form. If only the alkene was to be isolated, it was easily separated by distillation from the residue remaining after solvent removal.

Since much of the insoluble material formed during photolysis of 9 was soluble in aqueous base, an irradiation was conducted in the presence of a basic ion-exchange resin. The hope was that the acidic material would react with the polymer and be removed from solution as it formed. Irradiation in the presence of the ion-exchange resin did eliminate the formation of insoluble material during reaction but it also reduced the amount of alkene formation and increased the biphenylyl ether (11) produced (run 4, Table I). Repeated washing of the resin with 2-methyl-2-propanol prior to irradiation did not improve the yield of the alkene 10. If the resin were releasing small amounts of amines, they would provide effective sources from which hydrogen abstraction could occur. With this fact in mind, it is noteworthy that thoroughly washed and dried resin gradually developed an "amine-like" odor on standing.

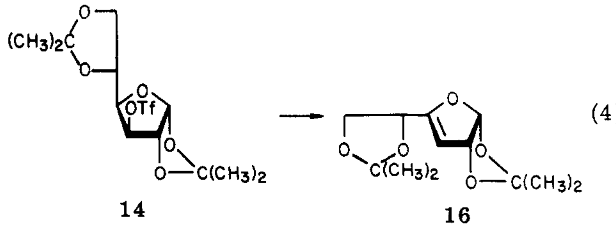
Scheme III



Tf = CF_3SO_2

After completing the study of various reaction conditions on the photolysis of 9, we selected two additional carbohydrates, 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (12) and 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (13), for study. Compound 12 was converted to the corresponding triflate (14), a compound which was unreactive when stirred with the tetrabutylammonium salt of 2-iodo-4-phenylphenol (15). Refluxing these reactants in benzene for 18 h resulted in quantitative conversion to a new carbohydrate, one which contained no aromatic group. This product was identified as 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hex-3-enofuranose (16); thus, elimination occurred under relatively mild conditions. This reaction of the triflate 14 stands in contrast to its reaction with iodide ion where exclusive substitution is observed.[4] The phenoxide ion 15 is considerably more basic and less nucleophilic than iodide. These differences presumably are responsible for favoring the elimination pathway when the phenoxide is present.

Displacement reactions at the 3 position of the 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose system are known to be difficult;[5] however, substitution at the 3 position can occur in compounds with the allo configuration where the corresponding gluco compound experiences elimination.[6] Thus, even though elimination was observed from the gluco triflate 14, substitution of the epimeric allotriflate 17 was attempted. Reaction of the



(4)

14 16

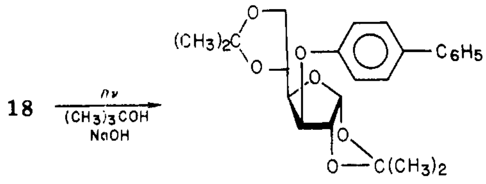
---

[4] R. W. Binkley and D. G. Hehemann, *J. Org. Chem.*, **43**, 3244–5 (1978).

[5] U. G. Nayak and R. L. Whistler, *J. Org. Chem.*, **34**, 3819–22 (1969).

[6] (a) A. B. Foster, R. Hems, and J. M. Webber, *Carbohydr. Res.*, **5**, 292–301 (1967); (b) K. W. Buck, A. B. Foster, R. Hems, and J. M. Webber, *ibid.*, **3**, 137–8 (1966).

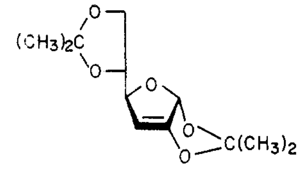
triflate **17** with the phenoxide **15** in benzene for 18 h resulted in formation of the corresponding 2-iodobiphenylyl ether (**18**). Photolysis of **18** in 2-methyl-2-propanol (eq 5) resulted in a dark reaction mixture (similar to that arising from photolysis of **9**); however, chromatography of the reaction mixture resulted in isolation only of the biphenylyl ether **19** (no alkene). Attempted distillation of the crude reaction mixture yielded no volatile material. (The alkenes **10** and **16** readily distilled under the conditions used.) IR analysis of the crude reaction mixture gave no indication of alkene formation. In short, photolysis of **18** did not produce a detectable unsaturated compound.



(5)

19

The reason for the failure of **18** to produce an unsaturated carbohydrate upon photolysis is not clear. A possibility is that an intramolecular, alkene-forming reaction similar to that proposed in Scheme I would require the formation of the strained alkene **20**; thus, even if internal hydrogen abstraction were to occur, loss of the substituted phenoxy radical may be sufficiently endothermic to be prevented from occurring.



20

Since the primary goal of this research was to test a new process for alkene formation, it is appropriate to evaluate this sequence on the basis of the five compounds studied. First, since this process is sufficiently difficult to conduct, other methods for alkene formation normally would be preferred; however, the relatively mild conditions for *o*-iodobiphenylyl ether synthesis and photolysis could be useful in introducing unsaturation into relatively unstable systems decomposed by other methods. Second, although alkene formation was the major reaction pathway in three of the four molecules irradiated, photolysis of the fourth (**18**) indicates that this process has limitations. We are currently investigating other photochemical methods for introducing unsaturation into carbohydrates with the hope of finding a more effective and useful process than *o*-iodobiphenylyl ether synthesis and photolysis.

Experimental Section

General Procedures. Synthesis and irradiation procedures are described below in general form. ^{1}H NMR spectra were obtained (CCl_4, $(CH_3)_4Si$, 0 ppm) from a Varian T-60 spectrometer (coupling constants, *J*, are given in hertz; s, d, t, and m indicate singlet, doublet, triplet, and multiplet, respectively). Mass spectra were measured on a Finnigan 1015-D mass spectrometer, using both electron impact (ionizing voltage of 70 eV) and chemical ionization with methane as the reagent gas at a pressure of 1.00 torr and an ionizing voltage of 110 eV.

Synthesis of 2-Iodobiphenylyl Ethers. Procedure A. 2-Iodo-4-phenylphenol[7] (3-iodo-4-biphenylol, 1.9 g, 6.5 mmol) and sodium hydroxide (0.26 g, 6.5 mmol) were dissolved in 125 mL of dry dimethylformamide at 25 °C. The appropriate tosylate (5.0 mmol) was added to this solution and nitrogen purging begun. The reaction mixture was raised to reflux temperature and maintained there for 1.0 h. The cooled solution was mixed with 300 mL of ethyl ether and washed with 250-mL portions of water, 5% sodium hydroxide, and water (twice). The ether solution was dried over sodium sulfate, and the ether was distilled.

Procedure B. 2-Iodo-4-phenylphenol[7] (1.75 g, 8.0 mmol) and 2.08 g (8.0 mmol) of tetrabutylammonium hydroxide[8] were added to 100 mL of benzene, and the water was removed by azeotropic distillation. The appropriate triflate in 150 mL of benzene was added and the solution stirred at 25 °C for 16 h. The reaction mixture was then washed with 100-mL portions of water, 5% sodium hydroxide, and water. The benzene solution was dried over sodium sulfate, and the benzene was distilled.

Irradiation of 2-Iodobiphenylyl Ethers and Isolation of Photoproducts. Procedure I (Irradiation in 2-Methyl-2-propanol). The 2-iodobiphenylyl ether (0.5 g) and 2 equiv of sodium hydroxide were added to 350 mL of 2-methyl-2-propanol, and the mixture was purged with nitrogen for 2 h. (The 2-methyl-2-propanol had been reacted with sodium, distilled, and recrystallized prior to use.) The nitrogen purge was continued during 18 h of Pyrex-filtered irradiation with a 450-W medium-pressure Hanovia mercury lamp.

Simple distillation of the irradiation solvent after photolysis resulted in loss of volatile materials. This loss was avoided by adopting the following procedure. After photolysis, the reaction mixture was combined with 350 mL of pentane, and the resulting solution was extracted with six 250-mL portions of water. (These extractions removed the 2-methyl-2-propanol from the organic layer without the loss of photoproducts.) The pentane solution was dried and the pentane removed by fractional distillation. The alkene was separated from the biphenylyl ether by distillation at 1 torr with the alkene being collected in a flask cooled in dry ice. The distilling flask was maintained at room temperatue during distillation of cyclododecene and 1-dodecene. For 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hex-3-enofuranose (**16**) the temperature was maintained below 50 °C. The residue after distillation was chromatographed on a 2.5 × 8.0 cm column of TLC grade silica gel, using 500 mL of pentane as the developer. The eluent contained the biphenylyl ether.

Procedure II. The irradiation procedure described above (procedure I) was used except that distilled 2-propanol was the irradiation solvent and sodium bicarbonate replaced sodium hydroxide. Since volatile photoproducts were not formed under these conditions, the 2-propanol was distilled in vacuo after irradiation and the residue extracted with two 100-mL portions of ethyl ether. Evaporation of the ether left a single photoproduct in each case.

Synthesis of Cyclododecyl 2-Iodobiphenylyl Ether (4). Cyclododecyl 2-iodobiphenylyl ether (**4**) was synthesized from cyclododecyl tosylate[9] according to procedure A. After all volatile materials were removed under reduced pressure, it crystallized. Repeated recrystallization from hexane gave 1 g of material, mp 87–89 °C. This product had aromatic ^{1}H NMR absorptions at δ 7.90 (1 H, d, *J* = 2 Hz), 7.50–7.11 (6 H, m), and 6.57 (1 H, d, *J* = 9 Hz). The appearance of these absorptions was indistinguishable from the pattern exhibited by the aromatic portions in 2-iodo-4-phenylphenol. The nonaromatic ^{1}H NMR absorptions in the reaction product were at δ 4.64–4.22 (1 H, m) and 2.08–1.00 (22 H, m). The spectrum for these hydrogens had the appearance of that for the nonaromatic hydrogens in cyclododecyl tosylate. The ^{1}H NMR spectrum indicated clearly that cyclododecyl 2-iodobiphenylyl ether (**4**) was the reaction product. This assignment was confirmed by the elemental analysis and the electron impact mass spectrum which exhibited the following peaks (relative abundances in parentheses): *m/e* 462 (1.51), 296 (100.0), 170 (28.3), 168 (26.8), 141 (2.58), 139 (80.8), 115 (25.8). (The molecular weight of **4** is 462.)

Anal. Calcd for $C_{24}H_{31}IO$: C, 62.34; H, 6.76. Found: C, 62.52; H, 6.78.

---

[7] J. C. Colbert, H. W. Houghton, H. R. Schmidt, and J. L. Abernethy, *J. Am. Chem. Soc.*, 66, 122–4 (1944).

[8] Aldrich Chemical Co., Inc.

[9] R. O. Hutchins, D. Hoke, J. Keogh, and D. Koharski, *Tetrahedron Lett.*, 3495–8 (1969).

Irradiation of 4 in 2-Propanol. Irradiation of 4 and photoproduct isolation according to procedure II resulted in isolation of biphenylyl cyclododecyl ether in 91% yield. This material was identical with a sample synthesized from cyclododecyl tosylate when procedure A was used and 4-biphenylol was substituted for 3-iodo-4-biphenylol.

Irradiation of 4 in 2-Methyl-2-propanol. Irradiation of 4 and subsequent workup following procedure I produced cyclododecene[8] (88%), identified by comparison with an authentic sample, and biphenylyl cyclododecyl ether (6, 10%).

Synthesis of Dodecyl 2-Iodobiphenylyl Ether (5). Dodecyl 2-iodobiphenylyl ether (5) was synthesized from dodecyl tosylate[10] according to procedure A. TLC analysis of the product, a liquid, indicated it to be a single compound. It had ^{1}H NMR absorptions at δ 7.80 (1 H, d, J = 2 Hz), 7.55–7.15 (6 H, m), 6.54 (1 H, d, J = 9 Hz), 3.81 (2 H, t, J = 5 Hz), and 1.90–0.56 (23 H, m). The ^{1}H NMR spectrum, particularly when compared with that of 4, clearly suggested the assignment of structure 5 to the reaction product. Further strengthening this assignment was the electron impact mass spectrum with its parent peak at m/e 464 and the photochemical conversion of this material to biphenylyl 1-dodecyl ether by photolysis in 2-propanol (see below).

Irradiation of 5 in 2-Propanol. Irradiation of 5 and photoproduct isolation according to procedure II resulted in isolation of biphenylyl 1-dodecyl ether in 93% yield. The identity of the photoproduct was established by comparison with a sample synthesized from dodecyl tosylate,[10] using procedure A and substituting 4-biphenylol for 3-iodo-4-biphenylol.

Irradiation of 5 in 2-Methyl-2-propanol. Irradiation of 5 and product isolation following procedure I produced 1-dodecene[8] in 54% yield, identified by comparison with a known sample, and biphenylyl 1-dodecyl ether in 33% yield.

Synthesis of 1,2:3,4-Di-*O*-isopropylidene-6-*O*-(2-iodobiphenylyl)-α-D-galactopyranose (9). Compound 9 was synthesized from 1,2:3,4-di-*O*-isopropylidene-6-*O*-tosyl-α-D-galactopyranose[11] according to procedure A and from 1,2:3,4-di-*O*-isopropylidene-6-*O*-triflyl-α-D-galactopyranose[4] (8) according to procedure B. The analysis of each reaction mixture after workup indicated the presence of a single component. The same product, a liquid, was obtained from each procedure. This material, which had the same aromatic ^{1}H NMR absorption pattern as the other 2-iodobiphenylyl ethers, had ^{1}H NMR absorptions at δ 7.97 (1 H, d, J = 2 Hz), 7.63–7.13 (6 H, m), 6.88 (1 H, d, J = 8 Hz), 5.28 (H_1, d, J_{12} = 5 Hz), 4.75–3.97 (H_2, H_3, H_4, H_5, H_6, $H_{6'}$, m), 1.55 (3 H, s), 1.40 (3 H, s), and 1.30 (6 H, s). This material gave a positive Beilstein test for iodine; unfortunately, it was not sufficiently volatile for mass spectral analysis. This information, when combined with conversion of the reaction product into 1,2:3,4-di-*O*-isopropylidene-6-*O*-biphenylyl-α-D-galactopyranose upon photolysis (see below), allowed the assignment of structure 9 to this compound.

Irradiation of 9 in 2-Propanol. Irradiation of 9 and treatment as described in procedure II resulted in isolation of 6-*O*-biphenylyl-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (11) in 94% yield. Comparison of the photoproduct with an independently synthesized sample (procedure A using 8 and 4-biphenylol) confirmed its structure.

Irradiation of 9 in 2-Methyl-2-propanol in the Presence of Sodium Hydroxide. Irradiation of 9 and product isolation as described in procedure I produced 6-deoxy-1,2:3,4-di-*O*-isopropylidene-β-L-*arabino*-hex-5-enopyranose[12] (10) in 80% yield and 11 in 14% yield.

Irradiation of 9 in 2-Methyl-2-propanol in the Presence of an Ion-Exchange Resin. Irradiation of 9 and product isolation were conducted as described in procedure I except that the sodium hydroxide was replaced with 1 g of IONAC ion-exchange resin ANGA-542 (strong base, polystyrene alkyl quaternary amine).[13] Product yields were 57% for 10 and 23% for 11.

Reaction of 1,2:5,6-Di-*O*-isopropylidene-3-*O*-triflyl-α-D-glucofuranose[14] (14) with the Tetrabutylammonium Salt of 2-Iodo-4-phenylphenol (15). An attempt to react compounds 14 and 15 was first tried according to the conditions described in procedure B. There was no reaction. The attempt was repeated under the same conditions except that the benzene was refluxed for 16 h. A single product was isolated from the reaction mixture following workup and was identified as 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hex-3-enofuranose[15] (16) by comparison with an authentic sample.

Synthesis of 1,2:5,6-Di-*O*-isopropylidene-3-*O*-(2-iodobiphenylyl)-α-D-glucofuranose (18). Compound 18 was synthesized from 1,2:5,6-di-*O*-isopropylidene-3-*O*-triflyl-α-D-allofuranose[14] (17) according to procedure B. TLC analysis of the reaction mixture after workup indicated a single compound, a liquid, to be present. This material, which had aromatic absorptions in the ^{1}H NMR spectrum characteristic of the 2-iodobiphenylyl ether substituent, had ^{1}H NMR absorptions at δ 7.93 (1 H, d, J = 2 Hz), 7.63–7.10 (6 H, m), 6.93 (1 H, d, J = 9 Hz), 5.82 (1 H, d, J_{12} = 4 Hz), 4.83–3.83 (H_2, H_3, H_4, H_5, H_6, H_6', m), 1.33 (3 H, s), 1.22 (3 H, s), and 1.12 (6 H, s). The reaction product gave a positive Beilstein test for iodine but was not sufficiently volatile for mass spectral analysis. The reaction product was converted into 3-*O*-biphenylyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (19) upon photolysis in 2-propanol (see below). This spectral and chemical evidence allowed the assignment of the structure 18 to the product from reaction of 15 and 17.

Irradiation of 18 in 2-Propanol. Irradiation of 18 and treatment as described in procedure II resulted in isolation of 3-*O*-biphenylyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (19) in 96% yield. Comparison of the photoproduct with a sample synthesized independently by procedure B (4-phenylphenol was used rather than 2-iodo-4-phenylphenol) confirmed its structure.

Irradiation of 18 in 2-Methyl-2-propanol. Irradiation of 18 and product isolation as described in procedure I produced 19 in 51% yield. No volatile material was formed and no other products could be isolated by chromatography.

Registry No. 4, 71001-06-4; 5, 71001-07-5; 6, 71001-08-6; 7, 4064-06-6; 7 tosylate, 4478-43-7; 8, 71001-09-7; 9, 71001-10-0; 10, 22618-03-7; 11, 71001-11-1; 12, 582-52-5; 13, 2595-05-3; 14, 55951-93-4; 15, 71001-13-3; 16, 2774-28-9; 17, 55951-90-1; 18, 71001-14-4; 19, 71001-15-5; 2-iodo-4-phenylphenol, 71031-48-6; tetrabutylammonium hydroxide, 2052-49-5; cyclododecanol, 1724-39-6; tosyl chloride, 98-59-9; 1-dodecanol, 112-53-8; cyclododecyl tosylate, 27092-44-0; biphenylyl cyclododecyl ether, 71001-08-6; cyclododecene, 1501-82-2; 1-dodecene, 112-41-4.

---

[10] V. C. Sekera and C. S. Marvel, *J. Am. Chem. Soc.*, **55**, 345–9 (1933).

[11] A. L. Raymond and E. F. Schroeder, *J. Am. Chem. Soc.*, 70, 2785–91 (1948).

[12] K. Freudenberg and K. Rashig, *Ber. Dtsch. Chem. Ges.*, **62**, 373–83 (1929).

[13] J. T. Baker Chemical Co.

[14] (a) L. D. Hall and D. C. Miller, *Carbohydr. Res.*, **40**, C1–C2 (1975); (b) *ibid.*, **47**, 285–97 (1976).

[15] F. Weygand and H. Wolz, *Chem. Ber.*, **85**, 256–60 (1952).