Addition Reactions of Glycals. IV.[1] The Free-Radical Addition of Thiolacetic Acid to D-Glucal Triacetate[2]

K. Igarashi and T. Honma

Shionogi Research Laboratory, Shionogi & Company., Ltd., Fukushima-ku, Osaka, Japan

Received March 18, 1969

The free-radical addition of thiolacetic acid to D-glucal triacetate using cumene hydroperoxide, with or without ferrous sulfate as an initiator, has been investigated. The addition gave 3,4,6-tri-*O*-acetyl-2-*S*-acetyl-1,5-anhydro-2-thio-D-mannitol (SAc group axial) and -D-glucitol (SAc group equatorial) in *ca.* 70 and 30% yields. It was found that oxygen also initiated the reaction and in this case several by-products were also obtained. The structures of three of these were proved to be 4,6-di-*O*-acetyl-3-*S*-acetyl-3-thio-D-allal and 4,6-di-*O*-acetyl-1-*S*-acetyl-2,3-dideoxy-α- and -β-D-*erythro*-hex-2-enopyranoses. Changing the initial concentrations of the reactants showed almost no effect on the ratio of the products formed.

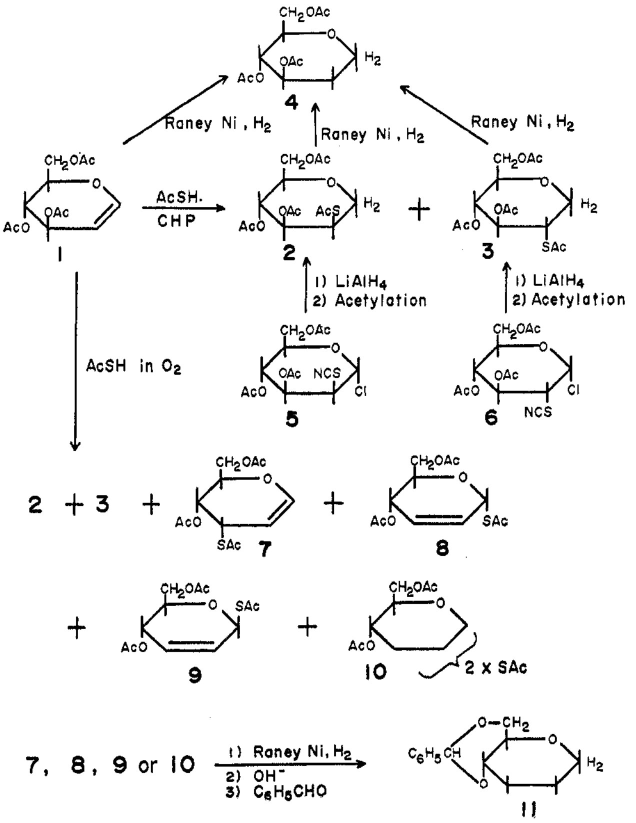
Although the free-radical additions of thiols to cyclohexene derivatives are not stereospecific in contrast with the free-radical addition of hydrogen bromide,[3] stereoselective *trans*-diaxial additions have been observed.[4] In at least one case,[5] the result was explained by assuming an unsymmetrically bridged thiyl radical.

In the sugar field, addition reactions of glycals *via* ionic process have been investigated rather extensively,[6] but little attention has been paid to the free-radical addition reaction. Bailey, Barker, and Stacey[7] reported that γ irradiation of D-glucal in aqueous solution in the presence of barium carbonate *in vacuo* gave D-glucose, D-mannose, D-arabinose, 1,5-anhydro-D-glucitol, and 2-deoxy-D-glucose in a ratio of 1:0.85:0.5:0.84:1.5. In this reaction, 1,5-anhydro-D-mannitol was not detected, although it would be expected to be present. We wish to report herein the free-radical addition of thiolacetic acid to D-glucal triacetate.

Results and Discussion

It is well known that cumene hydroperoxide (CHP) with or without ferrous sulfate, initiates the free-radical addition of thiol or thiol acid to olefin,[8,9] and that oxygen sometimes initiates the reaction.[10] The free-radical addition of thiolacetic acid to D-glucal triacetate (**1**) was studied using these reagents. The reaction did not proceed when a mixture of **1** and thiolacetic acid was allowed to stand at room temperature for 24 hr in an argon atmosphere in the dark[11] or in the light.[12] When CHP with or without ferrous sulfate was added as the initiator to the mixture in air or in an argon atmosphere, the reaction smoothly occurred and two crystalline compounds, **2** and **3**, were obtained in 61.3 and 25.3% yields, respectively (Scheme I).

Scheme I



Both compounds did not reduce Fehling's solution and gave 3,4,5-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hexitol (D-hydroglucal triacetate, **4**)[13] by reduction with Raney nickel. When 3,4,6-tri-*O*-acetyl-2-deoxy-2-thiocyanato-α-D-mannopyranosyl chloride (**5**) and -α-D-glucopyranosyl chloride[6c] (**6**) were reduced with lithium aluminum hydride,[14] and the products were acetylated, **2** and **3** were obtained, respectively. From these results **2** and **3** were proved to be 3,4,6-tri-*O*-acetyl-2-*S*-acetyl-1,5-anhydro-2-thio-D-mannitol and -D-glucitol, respectively.

As mentioned above, it is found that oxygen sometimes initiates the free-radical reaction of thiols. Mik-

---

[1] Part III of this series: K. Igarashi and T. Honma, *Tetrahedron Lett.*, 755 (1968).

[2] A preliminary report of part of this work has been given: K. Igarashi and T. Honma, *ibid.*, 751 (1968).

[3] P. D. Readio and P. S. Skell, *J. Org. Chem.*, **31**, 753 (1966).

[4] (a) H. L. Goering, D. I. Relyea, and D. W. Larsen, *J. Amer. Chem. Soc.*, **78**, 348 (1956); (b) F. G. Bordwell, P. S. Landis, and G. S. Whitney, *J. Org. Chem.*, **30**, 3764 (1965); (c) E. S. Huyser, H. Benson, and H. J. Sinninge *ibid.*, **32**, 622 (1967); (d) N. A. LeBel and A. DeBoer, *J. Amer. Chem. Soc.*, **89**, 2784 (1967).

[5] P. D. Readio and P. S. Skell, *J. Org. Chem.*, **31**, 759 (1966).

[6] See, *e.g.*, (a) R. U. Lemieux and B. Fraser-Reid, *Can. J. Chem.*, **43**, 1460 (1965); (b) P. W. Kent, F. O. Robson, and V. A. Welch, *J. Chem. Soc.*, 3273 (1963); (c) K. Igarashi and T. Honma, *J. Org. Chem.*, **32**, 2521 (1967).

[7] A. J. Bailey, S. A. Barker, and M. Stacey, *J. Chem. Soc.*, 1663 (1963).

[8] M. S. Kharasch, A. Fono, and W. Nudenberg, *J. Org. Chem.*, **15**, 763 (1950).

[9] M. S. Kharasch, A. T. Read, and F. R. Mayo, *Chem. Ind.* (London), **57**, 752 (1938); F. R. Mayo and C. Walling, *Chem. Rev.*, **27**, 351 (1940).

[10] M. S. Kharasch, W. Nudenberg, and G. J. Mantell, *J. Org. Chem.*, **16**, 524 (1951).

[11] The reaction was performed in a foil-covered flask.

[12] The reaction was performed in a usual glass flask without special irradiation.

[13] E. Fischer, *Chem. Ber.*, **47**, 196 (1914).

[14] R. K. Ness, H. G. Fletcher, Jr., and C. S. Hudson, *J. Amer. Chem. Soc.*, **73**, 3742 (1951).

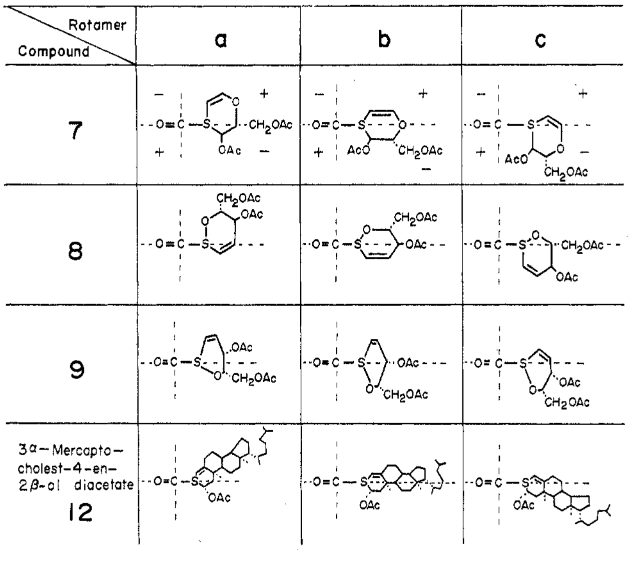
hailov and Blokhina[15] and Beckwith[16] reported that the free-radical addition of thiolacetic acid to anthracene derivatives gave 9,10-dihydro-9,10-diacetylthioanthracenes and 9-acetylthioanthracenes. When **1** was dissolved in thiolacetic acid in oxygen atmosphere and the solution was allowed to stand at room temperature for 24 hr, **2** and **3**, together with several by-products from which three crystalline compounds, **7–9**, and a syrup (**10**) were isolated, were obtained. The nmr and infrared spectra and thin layer chromatography (tlc) of this syrup show that it is a mixture of at least three compounds having two *S*-acetyl groups in each molecule. Compounds **7–10** afforded 1,5-anhydro-4,6-*O*-benzylidene-2,3-dideoxy-D-*erythro*-hexitol (**11**)[17] by Raney nickel reduction, deacetylation, and benzylidation in good yield. The infrared spectra of **7–9** reveal the presence of *O*-acetates, an *S*-acetate, and a double bond in each compound. The double bond of **7** appeared at 1638 cm^{-1} (strong), while the double bonds of **8** and **9** appeared at 1658 and 1657 cm^{-1} (weak), respectively. These facts apparently indicate that **7** has the double bond between C_1 and C_2 and the *S*-acetyl group at C_3, and **8** and **9** should be anomers having the double bond between C_2 and C_3 and the *S*-acetyl group at C_1.

The 100-MHz nmr spectrum of **7**, measured in chloroform-*d*, was well resolved. The large $J_{4,5}$ value (9.5 Hz) supports the conclusion that **7** adopts the H1 conformation, with C_4 above and C_5 below the plane of the ring oxygen and C_1–C_3. Calculation of the dihedral angle (ψ) between C_2–H_2 and C_3–H_3 bonds from the $J_{2,3}$ value (5.8 Hz) using the equation $J = 6.6 \cos^2\psi + 2.6 \sin^2\psi$[18] (for $0° \leqq \psi \leqq 90°$) shows that the dihedral angle is *ca.* 30°. This means that the orientation of H_3 is quasiequatorial, *i.e.*, that of the *S*-acetyl group is quasiaxial. Furthermore, therotation value of **7**, $[\alpha]^{23}D$ +264.5° (in $CHCl_3$), resembles the values of allal derivatives reported,[19] which are over +200°, but differs from that of triacetyl D-glucal, $[\alpha]^{26}D$ −24.9° (in $CHCl_3$). These results support the conclusion that the structure of **7** is 4,6-di-*O*-acetyl-3-*S*-acetyl-3-thio-D-allal (4,6-di-*O*-acetyl-3-*S*-acetyl-1,2-dideoxy-3-thio-D-*ribo*-hex-1-enopyranose). Compound **8** was proved to be identical with 4,6-di-*O*-acetyl-1-*S*-acetyl-2,3-dideoxy-1-thio-α-D-*erythro*-hex-2-enopyranose, reported by Maki, Nakamura, Tejima, and Akagi,[20] by comparison of their infrared and nmr spectra and by mixture melting point determination. They assigned the α configuration from its large dextrorotation value. The nmr spectra of **8** at 100 MHz and even at 220 MHz[21] could not confirm the anomeric configuration. It was shown, however, that **8** had the *H1* conformation with the ring oxygen above, and C_5 below, the plane of C_1–C_4, from the large coupling constant (9 Hz) between H_4 and H_5.

The nmr spectra of **9** at 60 and 100 MHz in chloroform-*d* resembled those of **8**. The $J_{4,5}$ value ($J_{4,5}$ = 6.8 Hz) would show the axial–quasiaxial disposition of the H_4 and H_5 with some flattening of the ring, and therefore the H1 conformation, of **9**. However, the anomeric configuration could not be assigned either.

Kuriyama, Komeno, and Takeda[22] investigated the optical rotatory dispersion and circular dichroism of steroidal thiolacetates and reported an empirical rule by applying the lactone sector rule.[23] They considered that only a few rotameric conformers would be permissible to the stable conformation of the thiolacetate, owing to the steric requirements and from the assumption that the thiolacetate, $H_3C(C{=}O)SC$, would be plannar and exist in the *S-trans* conformation.[24] When the molecule is viewed from the methyl group of the thiolacetate along the bisectrix of the -SCO- angle, the atoms lying in the back upper right and lower left sectors make a positive contribution to the n → π* Cotton effect of the thiolacetate, which appears near 270 mμ, and the atoms in the back upper left and lower right sectors make a negative contribution. The large value, $[\theta]_{270}$ +8580 (in CH_3OH), obtained in 2β-acetoxy-3α-thioacetylcholest-4-ene (**12**) was attributed to the large positive contribution of the double bond at C_4 in its conformers, as in the case of β,γ-unsaturated ketone.[25] The projections of the most probable conformers of **7–9**, according to this view, are shown in Scheme II. In compound **7**, the large positive value, $[\theta]_{270}$ +12,000 (in CH_3OH), is rationalized by the large positive contribution of the double bond in the projections of the three possible conformers. If the structure of **7** is 4,6-di-*O*-acetyl-3-*S*-acetyl-3-thio-D-glucal, a large negative value is expected. Negative and positive values are expected from the pro-

SCHEME II



---

[15] B. M. Mikhailov and A. N. Blokhina, *Dokl. Akad. Nauk. SSSR*, **80**, 373 (1951); *Chem. Abstr.*, **40**, 5025 (1952); **50**, 16735 (1956).

[16] A. L. J. Beckwith and L. B. See, *J. Chem. Soc.*, 1304 (1961).

[17] M. Bergmann and W. Breuers, *Justus Liebigs Ann. Chem.*, **470**, 51 (1929).

[18] E. W. Garbisch, *J. Amer. Chem. Soc.*, **86**, 5561 (1964).

[19] R. J. Ferrier, *Advan. Carbohyd. Chem.*, **20**, 72 (1965).

[20] T. Maki, H. Nakamura, S. Tejima, and M. Akagi, *Chem. Pharm. Bull.* (Tokyo), **13**, 764 (1966).

[21] C. V. Holland, D. Horton, M. J. Miller, and N. S. Bhacca, *J. Org. Chem.*, **32**, 3077 (1967).

[22] K. Kuriyama, T. Komeno, and K. Takeda, *Ann. Rep. Shionogi, Res. Lab.*, **17**, 66 (1967).

[23] J. P. Jennings, W. Klyne, and P. M. Scopes, *J. Chem. Soc.*, 7211, 7229 (1965); C. G. De Grazia, W. Klyne, P. M. Scopes, D. R. Sparrow, and W. B. Whalley, *ibid.*, 896 (1966).

[24] *Cf.* J. P. Jennings, W. P. Mose, and P. M. Scopes, *ibid.*, 1102 (1967). In the studies of the optical rotatory dispersion curves of a large number of steroid acetates, they considered that the preferred conformation of the acetate in solution is that in which the carbonyl oxygen of the acetoxy group and the hydrogen attached to the same carbon atom are in the eclipsing positions.

[25] A. Moscowitz, K. Misloco, M. A. W. Glass, and C. Djerassi, *J. Amer. Chem. Soc.*, **84**, 1945 (1962).

TABLE I[a]

Run	Molar ratio[b]	CHP[c]	$FeSO_4$	Time, hr	Conditions[d]	Product distribution, %: 2	Product distribution, %: 3	2/3	Total yield, %[e]
1	38	...	...	24	Argon	...	...	...	...
2	1.5	0.147	...	1/2	Argon	74.8	25.2	2.9	...
3	5.0	0.147	...	1/2	Argon	72.4	27.6	2.6	90.1
4	10	0.147	...	1/2	Argon	70.3	29.7	2.4	92.5
5	18.4	0.147	...	1/2	Argon	70.9	29.1	2.4	92.4
6	38	0.147	...	1/2	Argon	70.8	29.2	2.4	96.5
7	38	0.15	0.14	2/3	Air	69.2	30.8	2.2	94
8	38	...	...	24	Oxygen	68.7	31.3	2.2	43
9	38	...	...	24	Oxygen	68.3	31.7	2.2	66.5

[a] Each experiment was repeated twice. [b] AcSH/**1**. [c] Purified cumene hydroperoxide. The amounts of CHP and ferrous sulfate are molar equivalent to **1**. [d] At 25°. Most reactions were carried out in the usual manner without special irradiation except run 1, in which the reaction was carried out both in the usual manner and in a foil-covered flask, and run 9, in which the reaction was carried out in a foil-covered flask. [e] Based on **1** used.

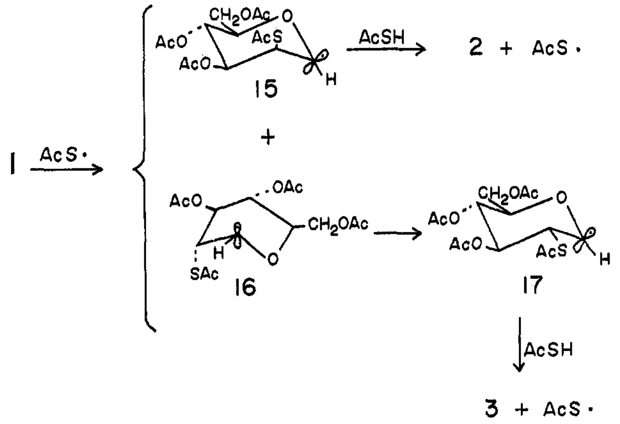
jections of the conformers of 4,6-di-*O*-acetyl-1-*S*-acetyl-2,3-dideoxy-1-thio-α- and -β-D-*erythro*-hex-2-enopyranoses, respectively, by the large contribution of the double bond. Actually, **8** and **9** showed a large negative value, $[\theta]_{270}$ −6130 (in CH_3OH), and a positive value, $[\theta]_{265}$ +2090 (in CH_3OH), respectively.

From the results obtained in the nmr and circular-dichroism studies, the anomeric configuration of **8** is proved to be α, as Tejima, *et al.*, assigned it, and that of **9** is β. Furthermore, in comparison of the absolute values of the maxima near 270 mμ in **8** and **9**, the smaller absolute value of **9** would support the quasi-equatorial orientation of the *S*-acetyl group, that is, that **9** also adopts the *H1* conformation, with the ring oxygen above, and C_5 below, the plane of C_1–C_4, since a Dreiding-model inspection shows that the overlapping between the π orbitals of the double bond and the quasiequatorial *S*-acetyl group of **9** in the *H1* conformation is much less than that between the π orbitals of the double bond and the quasiaxial *S*-acetyl group of **8**. If the orientation of the *S*-acetyl group of **9** is quasiaxial, that is, if **9** has an alternative *1H* conformation or a boat form, the absolute value of the maximum near 270 mμ in **9** should be similar to that in **8**, since the spatial correlation between the double bond and the *S*-acetyl group in **8** and **9** is in a mirror image.

Ferrier and Sankey[26] reported that 1,2,4,6-tetra-*O*-acetyl-3-deoxy-α-D-*erythro*-hex-2-enopyranose (**13**) and its β anomer (**14**), which were obtained by the allylic rearrangement of **1** with acid, adopted the *H1* and *1H* conformations, respectively, in which the acetoxy groups at C_1 of both compounds occupied the quasiaxial orientation. In the present study, the reason that **9** adopts the *H1* conformation with the quasi-equatorial orientation of the *S*-acetyl group at C_1 as the preferred conformation would be attributed to the facts that the anomeric effect of sulfur is less than that of oxygen[27] and the eclipsing interaction between the *S*-acetyl group and H_2 of **9** would be less than that between the acetoxy groups at C_1 and C_2 of **14** in the *H1* conformation.[26,28,29]

Stereochemistry of the Free-Radical Addition.— The results of the quantitative analyses of **2** and **3** using glpc are summarized in Table I. The addition of ferrous sulfate and the use of air instead of argon (run 7) showed no effect on the formation of **2** and **3**. Although the reactions initiated by oxygen (runs **8** and **9**) were very sensitive to the conditions used and the yields of the products varied with each run, the product ratio of **2**/**3** was found to remain constant. In the reactions initiated by CHP, changing the initial concentrations of **1** and thiolacetic acid showed almost no effect for the **2**/**3** product ratio. This fact indicates that **2** and **3** correspond to the kinetically controlled products. The fact that the attack of AcS· radical occurred only at the C_2 position but not at the C_1 position is reasonable, since a thiyl radical is known to be electrophilic[30] and an alkoxy radical is stabilized by resonance in the radical involved ($-\dot{C}HO- \leftrightarrow -C^{-}H\dot{O}^{+}-$), which is found to be small.[31] The preferential formation of **2**, in which the thioacetyl group is axial, over **3**, in which the thioacetyl group is equatorial, is consistent with the results obtained in the free-radical additions of thiols to cyclohexene derivatives.[4,5] Attack of AcS· radical to the double bond of **1** from directions perpendicular to the π orbitals gave intermediate radicals, **15** and **16** (Scheme III), in which **15** is more favored than **16** since to form **15** there is no remarkable steric hindrance and **15** has a chair conformation,[32] probably with some flattening of the

SCHEME III



---

[26] R. J. Ferrier and G. H. Sankey, *J. Chem. Soc.*, 2345 (1966).

[27] P. L. Durette and D. Horton, Abstracts, 155th National Meeting of the American Chemical Society, San Francisco, Calif, April 1968, No. 22C.

[28] R. J. Ferrier and N. Prasad, *J. Chem. Soc., C*, 1417 (1967).

[29] F. Johnson and S. K. Malhotra, *J. Amer. Chem. Soc.*, **87**, 5492 (1965); S. K. Malhotra, D. F. Moakley, and F. Johnson, *Chem. Commun.*, 448 (1967).

[30] W. A. Pryor, "Mechanisms of Sulfur Reactions," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 85.

[31] C. Walling, "Free Radicals in Solution," John Wiley & Sons, Inc., New York, N. Y., 1957, p 117; C. Walling and W. Helmerich, *J. Amer. Chem. Soc.*, **81**, 1144 (1959).

[32] W. T. Dixon and R. O. C. Norman [*J. Chem. Soc.*, 4850 (1964)] reported in the esr study that a radical obtained by a hydrogen-atom abstraction from *p*-dioxane had a chair conformation.

ring caused by the participation of the lone-pair electrons of the ring oxygen, whereas **16** has an unfavorable twist–boat conformation. Abstraction of a hydrogen atom from thiolacetic acid by the radical **15** gave **2**. It would be more likely to consider[4b–d] that the radical **16** has to isomerize to a radical **17** with a chair conformation with some flattening of the ring similar to **15** before abstraction of a hydrogen atom from thiolacetic acid. Abstraction of a hydrogen atom by the radical **17** gave **3**. The formation of **7–9**, however, in the reaction initiated by oxygen was rather unexpected and could not be explained clearly. If the elimination of acetoxy group at the C_3 position occurred by a radical process, carbon dioxide should be produced. However, a very small amount of carbon dioxide was detected in the reaction product. The formation of **10** would be interpreted by the combined radical and ionic processes, as Beckwith[16] postulated in the addition of thiolacetic acid to anthracene derivatives.

Experimental Section

Melting points were measured on a Monoscope (H. Boch, Frankfurt am Main, Germany) and were uncorrected. The nmr spectra were obtained, unless otherwise stated, in chloroform-*d* with Varian A-60 and HA-100 spectrometers using tetramethylsilane as an internal reference. The infrared spectra were measured using a Koken Model D.S.-301 infrared double-monochromatic spectrophotometer. The rotations were measured using a Perkin-Elmer Model 141 polarimeter, and the circular dichroisms were measured using a Jasco Model ORD/UV-5 (Japan Spectroscopic Co., Ltd.). The solvents were evaporated under reduced pressure below 40° using a rotatory evaporator.

Materials.—Thiolacetic acid was purified by distillation, once at atmospheric pressure, bp 89–91°, once under nitrogen at reduced pressure, bp 34–36° (100 mm), and just prior to use under nitrogen at reduced pressure after degassing by a freeze–thaw method. Thiolacetic acid thus obtained is a colorless liquid, $n^{23.7}_{\mathrm{D}}$ 1.4562 (lit.[33] n^{25}_{D} 1.4630). Cumene hydroperoxide was purified through the sodium salt and distillation of the freed hydroperoxide: bp 62° (0.1 mm); purity 99.1% by Barnard's method[34] and 99.7% by Wagner's method;[35] mp 54–54.5°; $[\alpha]^{28}_{\mathrm{D}}$ $-14.1 \pm 0.5°$ (*c* 1.050, EtOH); $[\alpha]^{26}_{\mathrm{D}}$ $-24.9 \pm 2°$ ($CHCl_3$) [lit. mp 54–55°;[36,37] $[\alpha]^{19}_{\mathrm{D}}$ $-15.7°$ (EtOH).

Reaction of D-Glucal Triacetate with Thiolacetic Acid.—An appropriate amount of D-glucal triacetate (**1**) was accurately weighed in a flask. Air in the flask was replaced by argon by flushing with an argon stream dried with sulfuric acid. An appropriate amount of thiolacetic acid, which was purified by redistillation under an argon atmosphere after degassing by a freeze–thaw method just prior to use, was added with flushing argon. To the stirred, cold solution, purified CHP (and ferrous sulfate) was added using a glass pipet with flushing argon. The flask was closed by a glass stopper and the solution was stirred at 25° for 30 min. Ice was added and the mixture was extracted with dichloromethane. The dichloromethane solution was washed with cold water, cold sodium carbonate solution, and cold water, dried over sodium sulfate, and evaporated. The residue was fractionated by tlc. For glpc, an appropriate amount of methyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside as the internal standard was added to the reaction mixture before the extraction, the residue was dissolved in carbon disulfide, and the solution was analyzed. Analyses were carried out with a Yanagimoto gas chromatograph GCG-550F with a flame ionization detector using a 2.25 m × 3 mm i.d. stainless steel column packed with 1.5% diethylene glycol succinate on Gaschrom Q (80–100 mesh) under the following conditions: column temperature, 191°; injection temperature, 293°; carrier gas, nitrogen (13.5 ml/min, 1.7 kg/cm^2); hydrogen (25 ml/min). Areas were determined by the half-height width method. The retention times in minutes follow: **2**, 13.92; **3**, 12.25; internal standard, 5.88. Calibration curves for **2** and **3** were linear and the lines crossed their origins. Preliminary experiments with mixtures of known amounts of **2** and **3** showed a reproducibility of 1% in the absolute value of the per cent of a given component in a given sample for the mixture compositions. To establish identity by gas–liquid chromatographic analysis, comparisons were made both by retention times and by simultaneous injection of a standard with the mixture to observe peak enhancement.

In the reaction initiated by oxygen, air in the flask was exchanged by flushing with an oxygen stream dried with sulfuric acid, the flask was closed, and the solution was allowed to stand at room temperature for 24 hr.

Product Isolation. A. Initiated by CHP.—The residue, which was obtained from 340 mg of **1**, 5 ml of thiolacetic acid, and 30 mg of CHP, was fractionated by preparative tlc on silica gel using benzene–ether (1:1) as the developer.

From the upper zone (R_f 0.55), 113 mg of a colorless syrup was obtained. Recrystallization from ether–petroleum ether (bp 30–45°) gave 90 mg (20.7%) of **3** as prisms: mp 59–61°; $[\alpha]^{20}_{\mathrm{D}}$ $+7.8 \pm 0.3°$ (*c* 0.941, $CHCl_3$); $\lambda_{\max}^{\mathrm{Nujol}}$ 1738 (*O*-acetates) and 1693 cm^{-1} (*S*-acetate); $\lambda_{\max}^{\mathrm{CCl_4}}$ 1761 and 1708 cm^{-1}; CD max $[\theta]_{268}$ $-2630°$ ($CHCl_3$), $[\theta]_{268}$ $-2300°$ and $[\theta]_{223}$ $-6780°$ (CH_3OH); nmr τ 7.67 (three-proton singlet, SAc) and 7.91 and 7.98 (three- and six-proton singlets, OAc).

Anal. Calcd for $C_{14}H_{20}O_8S$: C, 48.27; H, 5.79; S, 9.20. Found: C, 48.52; H, 5.79; S, 9.24.

The nmr and ir spectra of the mother liquor (20 mg, 4.6%) were identical with those of the pure sample.

From the lower zone (R_f 0.49), 296 mg of a colorless syrup was obtained. Recrystallization from ether–petroleum ether gave 220 mg (50.2%) of **2** as prisms: mp 65.5–67°; $[\alpha]^{22}_{\mathrm{D}}$ $-10.0 \pm 2°$ (*c* 1.046 $CHCl_3$); $\lambda_{\max}^{\mathrm{Nujol}}$ 1739 (*O*-acetates) and 1693 cm^{-1} (*S*-acetate); $\lambda_{\max}^{\mathrm{CCl_4}}$ 1754 and 1701 cm^{-1}; CD $[\theta]_{265}$ $-3180°$ ($CHCl_3$), $[\theta]_{265}$ $-3810°$ and $[\theta]_{229}$ $+12{,}900°$ (CH_3OH); nmr τ 7.62 (three-proton singlet, SAc) and 7.89, 7.95, and 8.01 (three-proton singlets, OAc).

Anal. Calcd for $C_{14}H_{20}O_8S$: C, 48.27; H, 5.79; S, 9.20. Found: C, 48.39; H, 5.83; S, 9.11.

The nmr and ir spectra of the mother liquor (48.7 mg, 11.1%) were identical with those of the pure sample. Compounds **2** and **3** did not reduce Fehling's solution, even when heat was applied.

B. Initiated by Oxygen.—The residue (3.5 g), which was obtained from 2.5 g of **1** and 20 ml of thiolacetic acid in an oxygen atmosphere, was fractionated by preparative tlc on silica gel using benzene–ether (1:1) as a developer. From the lower and middle zones (R_f 0.49 and 0.55), **2** and **3** were obtained, respectively. The upper zone (R_f 0.61–0.64) was a mixture of at least three components.

A syrup obtained from the upper zone was further fractionated using a mixture of *n*-hexane and ethyl acetate.

A syrup obtained from the upper zone (R_f 0.5) was recrystallized from ether–petroleum ether, giving **7** as prisms: mp 49–50.5°; $[\alpha]^{23}_{\mathrm{D}}$ $+264.5 \pm 3°$ (*c* 0.999, $CHCl_3$); $\lambda_{\max}^{\mathrm{Nujol}}$ 1752 and 1744 (*O*-acetates), 1702 (*S*-acetate), and 1644 cm^{-1} (OC=C); $\lambda_{\max}^{\mathrm{CHCl_3}}$ 1744, 1694, and 1648 cm^{-1}; CD max $[\theta]_{271}$ $+14{,}700°$ ($CHCl_3$), $[\theta]_{270}$ $+12{,}000°$, $[\theta]_{237}$ $-1820°$, and $[\theta]_{213}$ $+67{,}700°$ (CH_3OH); nmr (100 MHz) τ 3.58 (one-proton quartet, $J_{1,2} = 5.8$ and $J_{1,3} = 1$ Hz, H_1), 4.63 (one-proton quartet, $J_{3,4} = 4.5$ and $J_{4,5} = 9.5$ Hz, H_4), 5.20 (one-proton triplet, $J_{2,3} = 5.8$ Hz, H_2), 5.52 (one-protou octet, H_3), 5.59 (one-proton quartet, $J_{6,6'} = 12$ Hz, H_6), 5.75 (one-proton quartet, $H_{6'}$), and 5.90 (one-proton octet, H_5).

Anal. Calcd for $C_{12}H_{16}O_6S$: C, 49.99; H, 5.59; S, 11.12. Found: C, 50.26; H, 5.68; S, 11.10.

From the middle zone (R_f 0.44), a syrup was obtained. Repeated fractional recrystallization of the syrup from ether–petroleum ether gave two crystalline compounds. One (**8**) was obtained as needles: mp 107–108°; $[\alpha]^{23}_{\mathrm{D}}$ $+170.1 \pm 2.2°$ (*c* 0.959, $CHCl_3$); $\lambda_{\max}^{\mathrm{Nujol}}$ 1738 (*O*-acetates), 1694 (*S*-acetate), and 1658 cm^{-1} (C=C, weak); CD max $[\theta]_{270}$ $-7870°$ ($CHCl_3$), $[\theta]_{270}$ -6130, $[\theta]_{225}$ $+21{,}000°$, and $[\theta]_{210}$ $-15{,}200°$ (CH_3OH).

Anal. Calcd for $C_{12}H_{16}O_6S$: C, 49.99; H, 5.59; S, 11.12. Found: C, 50.13; H, 5.66; S, 11.38.

This compound was identical with 4,6-di-*O*-acetyl-1-*S*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranose prepared by the

---

(33) E. K. Ellingboe, *Org. Syn.*, **31**, 105 (1951).

(34) D. Barnard and K. R. Hargrave, *Anal. Chim. Acta*, **5**, 476 (1951).

(35) C. D. Wagner, R. H. Smith, and E. D. Peters, *Anal. Chem.*, **19**, 976 (1947).

(36) B. Helferich, E. N. Mulcahy, and H. Ziegler, *Chem. Ber.*, **87**, 233 (1954).

(37) E. Fischer, *ibid.*, **47**, 196 (1914).

method of Tejima, *et al.*,[20] by comparison of rotation value and infrared spectrum and by mixture melting point determination.

Another crystalline compound (9) was obtained as fine needles: mp 78–79°; $[\alpha]^{24}\mathrm{D}$ +89.5 ± 1.3° (*c* 0.966, $CHCl_3$); $\lambda_{\max}^{\mathrm{Nujol}}$ 1734 (*O*-acetates), 1691 (*S*-acetate), and 1657 cm^{-1} (C=C, weak); CD max $[\theta]_{265}$ +2090°, $[\theta]_{228}$ −6760°, and $[\theta]_{210}$ +26,100° (CH_3OH); nmr (100 MHz) τ 3.84(one-proton multiplet, H_1), 4.08 (two-proton singlet with satellites, H_2 and H_3), 4.73 (one-proton doublet of quartets, $J_{4,5} = 6.8$ Hz, H_4), 5.79 (two-proton multiplet, 2 H_6), 6.02 (one-proton multiplet, $J_{5,6} = 4$ Hz, $J_{5,6'} = 5.5$ Hz), 7.63 (three-proton singlet, SAc), and 7.93 (six-proton singlet, 2 OAc).

Anal. Calcd for $C_{12}H_{16}O_6S$: C, 49.99; H, 5.59; S, 11.12. Found: C, 50.21; H, 5.60; S, 11.14.

1,5-Anhydro-4,6-*O*-benzylidene-2,3-dideoxy-D-*erythro*-hexitol[17] was obtained from **7**, **8**, and **9** by Raney nickel reduction and hydrolysis followed by benzylidation.

Desulfurization of 2 and 3 with Raney Nickel.—To a solution of 348 mg (1 mmol) of **2** dissolved in 4 ml of methanol was added 2.2 ml of freshly prepared Raney nickel[38] and the mixture was refluxed for 20 min. The catalyst was filtered off and the filtrate was evaporated to dryness. The residue was dissolved in ether and the ethereal solution was treated with charcoal to remove the insoluble material. The filtrate showed one spot on a thin layer plate. The solvent was evaporated and the residue (85.5% yield) was partially crystallized when it was dried over phosphorous pentoxide at room temperature under reduced pressure (0.1 mm) for several days. Crystallization was completed by scratching it after addition of small amounts of *n*-hexane and ether. Recrystallization from the same solvent mixture gave the pure **4** as colorless prisms in 60% yield: mp 41–42.5°; $[\alpha]^{24}\mathrm{D}$ +34.5 ± 0.7° (*c* 0.985, ethanol), $[\alpha]^{24}\mathrm{D}$ +27.7 ± 0.7° (*c* 1.011, $CHCl_3$).

Anal. Calcd for $C_{12}H_{18}O_7$: C, 52.55; H, 6.62. Found: C, 52.72; H, 6.66.

This compound was hydrolyzed with methanolic ammonia, and the product was recrystallized from acetone–ethyl acetate, giving 1,5-anhydro-2-deoxy-D-*arabino*-hexitol (dihydro-D-glucal), mp 87–88°, $[\alpha]^{24}\mathrm{D}$ +16.2 ± 0.4° (*c* 1.004, water). Reduction of **1** with platinum black in glacial acetic acid[37,39] followed by fractionation by preparative tlc on silica gel using *n*-hexane–ethyl acetate (7:3) as the developer gave 4,6-di-*O*-acetyl-1,5-anhydro-2,3-dideoxy-D-*erythro*-hexitol (2%) as a syrup and 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hexitol (dihydro-D-glucal triacetate) (93.3%), mp 41–42.5°, $[\alpha]^{23}\mathrm{D}$ +34.5 ± 0.4° (*c* 1.080, ethanol). The latter compound was found to be identical with **4** by comparison of their ir spectra and by mixture melting point determination. Fischer[13] reported **4** as a syrup, $[\alpha]^{24}\mathrm{D}$ +34.5° (EtOH). The former was characterized by converting it into a crystalline 1,5-anhydro-4,6-*O*-benzylidene-2,3-dideoxy-D-*erythro*-hexitol, mp 141.5–142° (lit.[17] mp 137°), $[\alpha]^{25}\mathrm{D}$ −4.0 ± 0.8° (*c* 1.032, $CHCl_3$).

Desulfurization of **3** in a similar manner also gave crystalline **4**.

Lithium Aluminum Hydride Reductions of 3,4,6-Tri-*O*-acetyl-2-deoxy-2-thiocyanato-α-D-mannopyranosyl Chloride (5) and -α-D-glucopyranosyl Chloride (6).—To a suspension of 200 mg of lithium aluminum hydride in 4 ml of anhydrous ether was added dropwise a solution of 358 mg of **5**,[6c] $[\alpha]^{23}\mathrm{D}$ +98.4°, in 8 ml of anhydrous ether under cooling with ice, and the mixture was stirred for 30 min. Water was added to decompose the excess of lithium aluminum hydride, and the mixture was filtered to remove a precipitate. The precipitate was washed with water. The combined filtrate and washings were evaporated to dryness. The residue was acetylated with 10 ml of pyridine and 5 ml of acetic anhydride. The product was fractionated by preparative tlc on silica gel using benzene–ether (1:1) as the developer. From the upper zone, 218 mg (63.8%) of a syrup was obtained. The syrup was recrystallized from ether–petroleum ether, giving 146 mg (42.8%) of prisms, mp 65–67°, $[\alpha]^{24}\mathrm{D}$ −10.4 ± 0.4° (*c* 1.048, $CHCl_3$), which were identical with **2**.

Reduction of **6**[6c] with lithium aluminum hydride in a similar manner gave prisms, mp 59–61°, $[\alpha]^{24}\mathrm{D}$ +8.4 ± 0.4° (*c* 0.995, $CHCl_3$) (18.6% yield), which were identical with **3**.

Registry No.—**1**, 2873-29-2; **2**, 20746-41-2; **3**, 20746-42-3; **4**, 13035-12-6; **7**, 22931-86-8; **8**, 4631-35-0; **9**, 23025-38-9; thiolacetic acid, 507-90-5.

Acknowledgment.—The authors wish to acknowledge Dr. K. Kuriyama for the interpretation of the CD data.

---

[38] R. Mozingo, *Org. Syn.*, **21**, 15 (1941).

[39] *Cf.* G. R. Gray and R. Barker, *J. Org. Chem.*, **32**, 2764 (1967).

Addition Reactions of Glycals. V.[1]
Solvent Effects in the Chlorine Addition to D-Glucal Triacetate[2]

K. IGARASHI, T. HONMA, AND T. IMAGAWA

Shionogi Research Laboratory, Shionogi and Company, Ltd., Fukushima-ku, Osaka, Japan

Received March 18, 1969

The four possible isomers of D-glucal triacetate dichloride were obtained in crystalline form by the heterolytic addition of chlorine to D-glucal triacetate (**1**) in various solvents. The structure of the dichlorides were clarified from their nmr spectra and chemical reactions. The proportions of the dichlorides were dependent upon the polarity of the solvent used. In nonpolar solvents such as carbon tetrachloride, diethyl ether, chloroform, dichloromethane, and 1,2-dichloroethane, *cis*-addition products, 3,4,6-tri-*O*-acetyl-2-chloro-2-deoxy-α-D-glucopyranosyl chloride (**2**) and -β-D-mannopyranosyl chloride (**3**), were predominantly obtained. In polar solvents, such as nitromethane and propylene carbonate, *trans*-addition products, 3,4,6-tri-*O*-acetyl-2-chloro-2-deoxy-β-D-glucopyranosyl chloride (**15**) and -α-D-mannopyranosyl chloride (**4**), were predominantly obtained. The logarithms of the ratios of (**2** + **15**)/(**3** + **4**) were linearly related to the dielectric constants ϵ, $(\epsilon - 1)/(2\epsilon + 1)$, and the Et values of the solvents.

It has been reported that the polar addition of chlorine to olefins, such as *cis*- and *trans*-2-butene,[3,4] 1-butene,[4b] *cis*- and *trans*-di-*t*-butylethylene,[5a] cyclohexene,[5b] and pentenes,[5c] proceeded in the *trans* sense. However, since Cristol, Stermitz, and Ramey[6] found that the addition of chlorine to acenaphthylene in nonpolar solvents unexpectedly gave only *cis*-dichloroacenaphthane, several examples of *cis* addition of chlorine were reported. Summerbell and Lunk[7] reported that the addition of chlorine to *p*-dioxene in carbon tetrachloride gave *cis*-2,3-dichloro-*p*-dioxane

[1] Part IV: K. Igarashi and T. Honma, *J. Org. Chem.*, **35**, 606 (1970).

[2] Preliminary communications on portions of this work have appeared: K. Igarashi and T. Honma, *Tetrahedron Lett.*, 755 (1968); Abstracts, the 155th National Meeting of the American Chemical Society, San Francisco, Calif., April 1968, No. 27C.

[3] H. J. Lucas and C. W. Gould, *J. Amer. Chem. Soc.*, **63**, 2541 (1941).

[4] (a) R. C. Fahey and C. Schubert, *ibid.*, **87**, 5172 (1965); (b) M. L. Poutsma, *ibid.*, **87**, 2172 (1965).

[5] (a) R. C. Fahey, *ibid.*, **88**, 4681 (1966); (b) M. L. Poutsma, *ibid.*, **87**, 2161 (1965); (c) M. L. Poutsma and J. L. Kartch, *ibid.*, **89**, 6595 (1967).

[6] S. J. Cristol, F. R. Stermitz, and P. S. Ramey, *ibid.*, **78**, 4939 (1956).

[7] R. K. Summerbell and H. E. Lunk, *ibid.*, **79**, 4802 (1957).