88303-86-0; **5** (isomer 2), 88335-41-5; **5** (isomer 2, Me_3Si derivative), 88335-50-6; **5** (isomer 3), 88335-42-6; **5** (isomer 3, Me_3Si derivative), 88335-49-3; **5** (isomer 4), 88335-43-7; **5** (isomer 4, Me_3Si derivative), 88335-51-7; **6**, 88303-80-4; **6** (Me_3Si derivative), 88303-87-1; **7**, 88303-81-5; **7** (Me_3Si derivative), 88303-88-2; **8**, 88303-82-6; **8** (bis Me_3Si derivative), 88303-89-3; **9**, 88303-83-7; **9** (bis Me_3Si derivative), 88303-90-6; **10**, 63024-87-3; **11**, 88303-84-8; (9*S*,12*S*,13*S*)-*threo*-**11**, 88335-45-9; **12**, 88335-46-0; (9*R*,12*S*,13*S*)-*threo*-**12**, 88335-47-1; **13**, 84107-41-5; **14**, 84107-40-4; **15**, 88335-48-2; linoleic acid, 60-33-3; [1-^{14}C]linoleic acid, 3131-66-6.

Oxidative Decarboxylation of Propiolic Acids

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The combination of iodine and iodine pentoxide in methanol was used to convert phenylpropiolic acid and 2-hexynoic acid to the corresponding ketal esters of one less carbon. In both cases, iodoacetylenic compounds were shown to be intermediates. In the case of the phenylpropiolic acid, a diiodoalkene was isolated and shown to be a second intermediate.

The oxidations of diphenylacetylene by I^{7+} and I^{5+} compounds in methanol have been reported to afford ketals of benzil.[1] It was shown that the active species in these oxidations were not any of the several oxides of iodine. Rather, these oxides in combination with molecular iodine lead to iodonium-like species, which could attack the triple bond to form a vinyl cation, captured subsequently by the solvent. Another such attack on the resulting olefins could lead to iodo ketals, the precursors of the observed ketals or diones. Gebeyehu, in a preliminary effort, extended such oxidations to propiolic acids, such as phenylpropiolic acid, and noted the formation of esters rather than keto acids or ketal acids.[2] The subjects of this report resulted from further investigations of these initial observations. The principal findings were that two representative alkynoic acids were converted to decarboxylated products and that iodine-containing intermediates were isolated.

Results and Discussion

The oxidations of phenylpropiolic acid (**1**) were carried out initially by I_2O_5 in refluxing methanol.[2] This system was replaced with iodine and I_2O_5 in methanol at room temperature. The methanol was dried with and distilled over $CaSO_4$ under nitrogen and stored over molecular sieves to minimize water content. Previous studies with diphenylacetylene had demonstrated that more ketones than ketals are formed in untreated methanol.[1] Several products could be isolated depending upon the reactant ratios. If the oxidants were in excess, the principal product was the methyl ketal of methyl phenylglyoxylate (**2**). For example, phenylpropiolic acid (10 mmol) was converted to the ketal ester (**2**) in 82% yield after reaction with iodine pentoxide (5 mmol) and iodine (60 mmol). When the alkynoic acid was the excess reagent, the principal products were 2-iodo-1-phenylethyne (**3**) and (2,2-diiodo-1-methoxyethenyl)benzene (**4**). Thus, a ratio of acid to iodine to oxide of 10:1:5 afforded a yield of the iodoalkyne (**3**) of 73% and the diiodoalkene (**4**) of 27% on a 30% conversion of acid. The latter two compounds are the major intermediates on an oxidation pathway from the acid **1** to ketal ester **2**, as shown in Scheme I. The triiodo precursor **5** was not isolated.

Scheme I

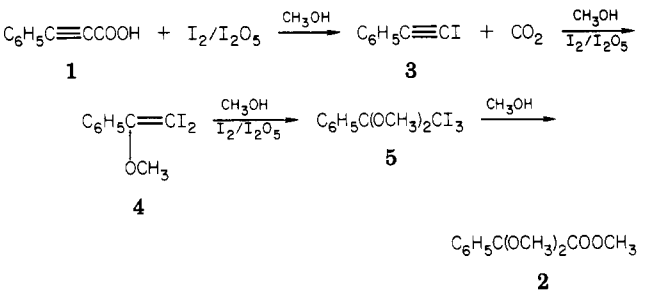

Table I. Oxidation of Phenylpropiolic Acid with I_2 and I_2O_5[a]

I_2, mmol	I_2O_5, mmol	conversion, %	% yield of products 3	4	2
1	5	30	73	27	
5	5	56	52	37	11
10	5	84	7	59	34
20	5	100		19	57
60	5	88			82
10	0.5	65	64	32	4
10	50	100			71

[a] Conditions: 10 mmol of acid **1** in dry methanol (100–150 mL) at room temperature under N_2 for 24 h.

The product **2** was identified by comparison with the known compound prepared from acidic methanol with the methyl ester of phenylglyoxylic acid.[3] The methyl phenylglyoxylate was prepared from the acid and diazomethane. The route via the acid chloride and methanol was not used because decarbonylation of phenylglyoxylyl chloride took place to yield methyl benzoate. The known iodoalkyne **3** was prepared by the treatment of phenylethyne with a Grignard reagent and iodine. The diiodoalkene **4** was identified by ^{1}H NMR, MS, and elemental analysis. Its NMR absorptions at 3.35 (s, 3 H) and 7.31 (s, 5 H) ppm were similar to that reported for the corresponding dichloro compound (3.45 and 7.46 ppm).[4]

(1) Gebeyehu, G.; McNelis, E. *J. Org. Chem.* **1980**, *45*, 4280.
(2) Gebeyehu, G. Thesis, New York University, 1980.
(3) Posner, T.; Aschermann, G. *Chem. Ber.* **1920**, *53B*, 1925.

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The intermediacies of the iodoalkyne **3** and the diiodoalkene **4** were demonstrated by subjecting them to oxidation. When the iodoalkyne **3** (10 mmol) was stirred with iodine (20 mmol) and I_2O_5 (5 mmol) in 100 mL of dry methanol for 34 h at room temperature, it was converted to the diiodoalkene **4** in 41% yield and the ketal ester **2** in 48% yield. The diiodoalkene **4** (10 mmol) with iodine (40 mmol) and I_2O_5 (5 mmol) in methanol was converted to the ketal ester **2** in 96% yield. The results of variations in reactants' concentrations are given in n Table I. An increase in either part of the oxidizing combination leads to an increase in the ketal ester **2**. The progression of intermediates to product, **3** to **4** to **2**, is clear and consonant with the reaction scheme.

The effectiveness of the combination of iodine and iodine pentoxide was shown by examining the reactions of phenylpropiolic acid with each reagent by itself in dry methanol at room temperature. With the acid (10 mmol) and I_2O_5 (5 mmol), no neutral materials were isolated, and 98% of the starting acid was recovered. With the acid (10 mmol) and iodine (20 mmol), the small neutral fraction contained methyl phenylpropiolate (16% yield). If the reactants were acid (10 mmol), I_2 (20 mmol), and I_2O_5 (5 mmol) under the same conditions, there was no recovery of acid. The principal products were the ketal ester **2** (57%) and the enol ether **4** (19%).

The iodine-promoted esterification of the acid in the control reaction was noted also in the case of 2-hexynoic acid. An alkanoic acid, octanoic acid, behaved similarly. Thus, this artifactual product was observed in detectable but not isolable quantities in the oxidative reactions. There are three other products observed in these oxidations—methyl phenylglyoxylate, α,β,β-triiodostyrene, and α,β-diiodocinnamic acid.

The methyl phenylglyoxylate formed whenever the solvent methanol was not dried. This keto acid ester with carbonyl absorptions in the IR at 1755 and 1705 cm^{-1} and methyl protonic absorptions in the NMR at 3.98 ppm was usually observed in small quantities but could reach half the quantity of the kettal ester **2** if no effort were made to dry the methanol. It was also a significant product (29%) when excess iodine pentoxide was used.

The triiodostyrene was the principal product of the I_2/I_2O_5 oxidation of phenylpropiolic acid when chloroform and not methanol was the solvent for the reaction. In the methanol it appeared in variable amounts in the chromatographic fractions of 2-iodo-1-phenylethyne. The maximum yield was 20% of neutral substances formed in a reaction involving phenylpropiolic acid (40 mmol), iodine (5 mmol), and iodine pentoxide (10 mmol).

The diiodocinnamic acid was mixed with phenylpropiolic acid recovered from reactions that had higher ratios of iodine to pentoxide, such as 4:1, and low conversion. It was detected by melting point and mass spectra.

Similar oxidative decarboxylations were observed for 2-hexynoic acid with iodine pentoxide or its admixture with iodine. Refluxing temperatures were necessary as before to effectuate oxidations with the oxide in methanol. At a molar ratio of acid to oxidant of 2:1, the principal products at a conversion of 75% were methyl 2,2-dimethoxy-pentanoate (**6**) and 1-iodo-1-pentyne (**7**) in yields of 43 and 32%, respectively. With the room temperature reaction with iodine (60 mmol) and iodine pentoxide (15 mmol), the hexynoic acid (30 mmol) was oxidized at a 93% conversion to the ketal ester **6** in 96% yield. The enol ether corresponding to **4** was not isolated, but its presence and that of methyl 2-oxopentanoate might be inferred from ^1H NMR spectra and mass spectra of column chromatographic fractions.

The iodopentyne was identified by comparison with material prepared from 1-pentyne via the Grignard reagent and iodine. It in turn was subjected to oxidation by I_2/I_2O_5 in the same ratio as above and was converted to ketal ester **6** in 84% yield. As in the aromatic case, there is the same pattern of an attack by an iodonium species, a decarboxylation to a neutral compound, subsequently converted further to polyiodinated compounds, the precursors to esters.

These oxidative decarboxylations of propiolic acid have precedent in the works of Berliner's group with aqueous halogens. They noted with bromine the formation of bromoalkyne, tribromostyrene, and products of solvent capture, such as dibromoacetophenone.[5] Lesser amounts of decarboxylation were observed with aqueous iodine and iodide.[6] At low iodide concentrations, three unidentified keto acids were formed. On the basis of our findings of phenylglyoxylate esters in methanol, one might suggest one of these acids to be phenylglyoxylic acid.

It is noteworthy that the I_2/I_2O_5 treatment of *trans*-cinnamic acid did not lead to decarboxylation. The products of this reaction are still under study, but a principal one among the exclusively acidic products is iodomethoxylated. This finding lends further support to the proposed reaction path in that it renders iodomethoxylation less likely prior to decarboxylation.

Experimental Section

Materials and Instruments. Phenylpropiolic acid and 2-hexynoic were obtained from the Farchan Division of Albany International Corp. Iodine pentoxide was supplied by Alpha Ventron Chemical Co. *trans*-Cinnamic acid, solvents, and inorganic reagents were reagent grade materials from the J. T. Baker Chemical Co. Spectral determinations were as follows: infrared, Perkin-Elmer Model 137 and Beckman IR-18; nuclear magnetic resonance, Hitachi Perkin-Elmer R-20; mass spectra, Dupont 21-492; GC/MS, Hewlett Packard 5992. Elemental analyses were performed by Schwarzkopf Microanalytical Laboratories, Woodside, NY. Melting points were determined on a Thomas-Hoover Unimelt apparatus, checked periodically with standards supplied by A. H. Thomas Co.

Methyl phenylglyoxylate was prepared from benzoylformic acid and diazomethane: bp 256 °C (760 torr) (lit.[3] bp 255 °C); IR (neat) 1755 (s), 1705 (s), 1600 (m), 1450 (m), 1325 (m), 1205 (s), 1170 (s), 1000 (s) cm^{-1}; ^1H NMR (CCl_4) δ 3.88 (s, 3 H), 7.20–7.55 (m, 3 H), 7.85–8.0 (m, 2 H); MS, *m/e* (relative intensity) 164 (M^+), 135, 117, 105 (100).

The phenylglyoxylate (0.60 g, 3.6 mmol) was dissolved in dried methanol (300 mL) containing *p*-toluenesulfonic acid (0.04 g). The solution was heated to reflux for 30 h, cooled, mixed with CH_2Cl_2 (150 mL), and washed with a 5% bicarbonate solution. Distillation at 14 mm followed drying over $MgSO_4$ and solvent removal. A yellow liquid, **2** (0.38 g), was obtained: bp 260 °C (760 torr) (lit.[7] bp 257 °C); IR (neat) 1765 (s), 1460 (m), 1270 (s), 1250 (s), 1190 (m), 1120 (s), 1075 (s), 1020 (m) cm^{-1}; ^1H NMR δ 3.15 (s, 6 H), 3.52 (s, 3 H), 7.15–7.35 (m, 3 H), 7.40–7.63 (m, 2 H); MS, *m/e* (relative intensity) 179 ($M^+ - OCH_3$), 151 (100, $M^+ - COOCH_3$), 105.

General Oxidation Procedures. All oxidations, unless otherwise noted, were carried out in methanol that had been dried over anhydrous $CaSO_4$, distilled under nitrogen, and collected over molecular sieves (3A). Reactions were kept under a nitrogen atmosphere and were shielded from light with aluminum foil. Workups started by quenching with an equal to double volume

(4) De Renzi, A.; Fischer, E. O. *Inorg. Chim. Acta* **1974**, *8*, 185.

(5) Ehrlich, S. J.; Berliner, E. *J. Am. Chem. Soc.* **1978**, *100*, 1525.
(6) Wilson, M. E.; Berliner, E. *J. Am. Chem. Soc.* **1971**, *93*, 208.
(7) Kohler, E. P.; Corson, B. B. *J. Am. Chem. Soc.* **1923**, *45*, 1975.

of water to the volume of methanol and continued with extraction with several portions of CH_2Cl_2. The CH_2Cl_2 layer was washed with a 10% $Na_2S_2O_3$ solution, a 5% $NaHCO_3$ solution, and water. The CH_2Cl_2 layer was then dried over anhydrous $MgSO_4$. The CH_2Cl_2 was evaporated to neutral residues. The bicarbonate layer was acidified and extracted with ether in order to recover unreacted acids and/or acidic products. Yields of mixed products were approximated by ^1H NMR integrations of reaction mixtures after components had been separated by column chromatography or synthesized. These values agreed within 5% with yields obtained by column chromatographies.

Oxidation of Phenylpropiolic Acid. (a) Preparation of Ketal Ester 2. Phenylpropiolic acid (1.46 g, 10 mmol) and iodine (15.24 g, 60 mmol) were dissolved in dry methanol (100 mL). Iodine pentoxide (1.67 g, 5 mmol) was added. The whole was stirred under nitrogen for 1 day and worked up as in the general procedure. Some starting acid (0.175 g) was recovered in addition to a small amount (0.034 g) of impure α,β-diiodocinnamic acid.[6] The neutral portion (1.51 g, 82%) was the ketal ester: IR (neat) 1770 (s), 1460 (m), 1270 (s), 1250 (s), 1200 (m), 1180 (m), 1120 (s), 1075 (s), 1030 (m) cm^{-1}; ^1H NMR (CCl_4) δ 3.15 (s, 6 H), 3.55 (s, 3 H), 7.15–7.60 (m, 5 H); MS, *m/e* (relative intensity) 179 (68), 151 (100), 105 (59).

(b) Preparation of Enol Ether 4. A similar reaction of acid (1.46 g, 10 mmol), iodine (2.54 g, 10 mmol), and iodine pentoxide (1.67 g, 5 mmol) in dry methanol (100 mL) afforded neutral oils (2.87 g). A portion (1.96 g) was separated into two fractions by means of dry-column chromatography (silica gel) with hexane–CH_2Cl_2 (5:3) as eluant. The first fraction (1.38 g, 59% yield of **4**) was further purified on an alumina dry column with hexane as eluant to pale yellow crystals melting at 104.5–106.0 °C: IR (CCl_4) 2975 (m), 1590 (m), 1495 (m), 1450 (m), 1260 (s), 1095 (s), 980 (s) cm^{-1}; ^1H NMR δ 3.30 (s, 3 H), 7.25 (s, 5 H); MS, *m/e* (relative intensity) 386 (M^+, 100), 228 (37). Anal. Calcd for $C_9H_8I_2O$: C, 28.15; H, 2.15; I, 65.87. Found: C, 28.01; H, 2.09; I, 65.76. The second fraction (0.47 g) was a yellow oil identified as **2** (34% yield).

(c) Preparation of α,β,β-Triiodostyrene. Phenylpropiolic acid (1.46 g, 10 mmol), iodine (2.54 g, 10 mmol), and iodine pentoxide were combined in refluxing chloroform (250 mL) under nirogen for 34 h. Workup was as before. The recovered acid weighed 0.41 g. A yellow solid (1.67 g) was obtained from the neutral fraction and melted at 108–109 °C (lit.[8,9,6] mp 108, 112, and 110–111 °C): IR (CCl_4) 3080 (m), 2940 (m), 1495 (s), 1450 (s), 1265 (m), 1200 (m), 1070 (m), 1035 (s); ^1H NMR (CCl_4) δ 7.14.

Oxidation of 2-Iodo-1-phenylethyne. Phenylacetylene (5.51 g, 54 mmol) was added to ethylmagnesium bromide (25 mL of a 2.5 M solution in THF) in THF (30 mL) at 4 °C. The mixture was heated to reflux for 2 h. After the mixture was cooled, I_2 (13.5 g, 53 mmol) in THF was added slowly, and the mixture was stirred overnight. A pale yellow oil, **3**, was collected after the usual workup (10.53 g): bp 83.5 °C (2.5 mm) [lit.[10] bp 82–83 °C (1.7 mm)]; IR (neat) 3100 (m), 2170 (w), 1610 (s), 1580 (m), 1490 (s), 1450 (s), 1070 (m), 1025 (m), 915 (m), 755 (s), 685 (s); ^1H NMR (CCl_4) δ 7.05–7.45 (m).

Compound **3** (2.28 g, 10 mmol) was treated for 34 h at room temperature with I_2 (5.08 g, 20 mmol) and I_2O_5 (1.67 g, 5 mmol) in dried methanol (100 mL). A pale red oil [3.07 g; a mixture of **2** (58%) and **4** (42%)] was obtained: IR (CCl_4) 1775, 1460, 1270, 1240, 1200, 1120, 1075, 1050, 1035 cm^{-1}; ^1H NMR (CCl_4) δ 3.15 (s, 8 H), 3.35 (s, 3 H), 3.52 (s, 4 H), 7.15–7.65 (m, 12 H).

Oxidation of (2,2-Diiodo-1-methoxyethenyl)benzene (4). Compound **4** (3.86 g, 10 mmol), prepared as indicated previously, was added to dry methanol (200 mL) containing I_2 (10.16 g, 40 mmol) and I_2O_5 (1.67 g, 5 mmol). The mixture was stirred under nitrogen at room temperature overnight with protection from light. After the usual workup, a pale yellow liquid (2.02 g, 96% yield of **2**) was obtained: IR (neat) 1770, 1460, 1270, 1200, 1120, 1075, 1020 cm^{-1}; ^1H NMR (CCl_4) δ 3.15 (s, 6 H), 3.55 (s, 3 H), 7.15–7.60 (m, 5 H).

Oxidation of Cinnamic Acid. *trans*-Cinnamic acid (1.48 g, 10 mmol) in dry methanol (110 mL) was reacted under the usual conditions with iodine (2.54 g, 10 mmol) and iodine pentoxide (1.67 g, 5 mmol) for 31 h. The workup was identical with that for phenylpropiolic acid oxidations. No neutral products were found. A white solid (1.71 g) was obtained by acidification of the bicarbonate solution: IR (CCl_4) 3100–2920 (br), 1700 (s), 1640 (m), 1460 (m), 1420 (m), 1330 (w), 1315 (m), 1290 (m), 1220 (m), 1100 (w) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.22 (s, 3 H), 4.45 (d, 1 H, J = 3 Hz), 6.45 (d, 2 H, J = 17 Hz), 7.25–7.6 (m, 19 H), 7.75 (d, 2 H, J = 17 Hz), 11.05 (s, 3 H). The δ 6.45 and 7.75 peaks are due to unreacted cinnamic acid. The singlet at δ 3.22 and the apparent doublet at δ 4.45 were due to α-iodo-β-methoxyphenylpropionic acid prepared by repeating the above experiment with doubled quantities of oxidants: yield 2.96 g (97%); crude mp 168 °C; crystallized from methanol; mp 171.5–172.5 °C (lit.[13] mp 168–169 °C); IR (Nujol) 1670 (s), 1260 (s), 1210 (m), 1200 (m), 1180 (m), 1130 (m), 1080 (s), 890 (s) cm^{-1}; MS, *m/e* (relative intensity) 306 (M^+), 256, 148, 121 (100); ^1H NMR ($CDCl_3$) δ 3.23 (s, 3 H), 4.30 (d, 1 H, J = 10 Hz), 4.53 (d, 1 H, J = 10 Hz), 7.30 (s, 5 H).[14]

Oxidation of 2-Hexynoic Acid. (a) With I_2 and I_2O_5. 2-Hexynoic acid (3.36 g, 30 mmol), iodine (15.24 g, 60 mmol), and I_2O_5 (4.8 g, 15 mmol) were stirred together in dry methanol (150 mL) under nitrogen at room temperature for 2 days. The usual workup followed. Some starting material (0.23 g) was recovered from the bicarbonate wash. The neutral fraction (4.75 g) was a golden liquid with the spectral properties of the ketal ester **6**: IR (neat) 2990 (s), 1760 (vs), 1460 (s), 1440 (s), 1235 (m), 1215 (m), 1145 (s), 1115 (m) cm^{-1}; ^1H NMR (CCl_4) δ 0.85–0.95 (t, 3 H), 1.2–1.35 (m, 2 H), 1.6–1.7 (m, 2 H), 3.67 (s, 3 H).

(b) I_2 Control. 2-Hexynoic acid (3.36 g, 30 mmol) and I_2 (7.62 g, 30 mmol) were dissolved in dry methanol (100 mL) and treated as in part a. Starting acid (2.75 g) was recovered. A yellow liquid (0.57 g) in the neutral fraction had the spectra of methyl 2-hexynoate: IR (neat) 2995, 2220, 1725, 1445, 1260, 1080 cm^{-1}; ^1H NMR (CCl_4) δ 0.9–2.5 (m, 7 H), 3.77 (s, 3 H).

(c) I_2O_5 Control. 2-Hexynoic acid (3.36 g, 30 mmol) was dissolved in dry methanol (100 mL) as in part a and stirred with I_2O_5 (10.02 g, 30 mmol). Most of the acid (3.21 g) was recovered from the bicarbonate layer. There were no neutral products.

(d) With I_2O_5 in Refluxing Methanol. 2-Hexynoic acid (3.36 g, 30 mmol) was dissolved in dry methanol (150 mL). To this solution was added I_2O_5 (4.8 g, 15 mmol), and the temperature was raised to bring about refluxing under nitrogen. After 1 day, the mixture was worked up in the usual manner. Starting acid (0.83 g) was recovered from the bicarbonate wash. The neutral portion was a yellow oil (2.72 g): IR (neat) 2940, 2270, 1770, 1460, 1440, 1250, 1140, 1050 cm^{-1}; ^1H NMR (CCl_4) δ 0.9–1.8 (m, 28 H), 2.2–2.8 (m, 8 H), 3.15 (s, 10 H), 3.58 (s, 5 H), 3.68 (s, 3 H). A portion (1.64 g) of this mixture of ketal ester **7** and other products was chromatographed on silica gel with hexane as eluant. A first fraction (0.38 g) had no carbonyl absorptions in the IR and neither methyl ketal nor methyl ester proton absorbances in the ^1H NMR. The mass spectrum had peaks at 448 (M^+ of C–C–C–Ci=CI_2), 321 (448 - I), 292 ($C_3H_2I_2^+$), 194 (100, C–C–C–C≡CI), 165 ($C_3H_2I^+$). The ^1H NMR absorbances at δ 0.9–1.9 (m, 9 H) and 2.22–2.73 (m, 2 H) (the latter present in 1-iodopentyne but not 1,1,2-triiodo-1-pentene) were used to estimate that this fraction was 55% of the iodopentyne **7** and 45% of the triiodopentene. Intermediate fractions (0.082 g) were mixtures of **6** and **7**. A later fraction (0.77 g) had the spectral properties of **6**: IR (neat) 2980, 1765, 1470, 1330, 1280, 1220, 1140, 1070, 1055 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.9–2.1 (m, 7 H), 3.28 (s, 6 H), 3.8 (s, 3 H) [lit.[11] NMR (CCl_4) δ 0.95 (t, 3 H), 1.27 (m, 2 H), 1.77 (t, 2 H), 3.2 (s, 6 H), 3.7 (s, 3 H)]; MS, *m/e* (relative intensity) 145 ($M^+ - OCH_3$), 117 (100, $M^+ - COOCH_3$).

Oxidation of 1-Iodo-1-pentyne (7). (a) Preparation of 7. Butylmagnesium bromide (25 mL of a 2.5 M solution in THF) was reacted with 1-pentyne (3.62 g, 53 mmol). After the solution was refluxed for 2 h, iodine (13.5 g) in ether (250 mL) was added,

(8) Liebermann, C.; Sachse, H. *Chem. Ber.* **1891**, *24*, 4112.
(9) Franzen, V. *Chem. Ber.* **1954**, *87*, 1148.
(10) Grindley, B.; Johnson, K. F.; Katritzky, A. R.; Keogh, H. J.; Thirkettle, C.; Topsom, R. D. *J. Chem. Soc., Perkin Trans. 2* **1974**, 282.
(11) Trost, B. M.; Massiot, G. S. *J. Am. Chem. Soc.* **1977**, *99*, 4405.
(12) Wojkowiak, B. *Ann. Chim. (Paris)* **1964**, *9*, 5.
(13) Jackson, E. L.; Pasiut, L. *Ann. Chim. (Paris)* **1928**, *50*, 2249.
(14) This experiment was done by Jane J. Janas of these laboratories.

and the mixture was stirred overnight at room temperature. Acidification preceded a workup of washing by water and thiosulfate and of solvent drying and evaporation. A yellowish red liquid (6.80 g) was obtained: bp 43 °C (17 torr) [lit.[12] bp 54 °C (26 torr)]; IR (neat) 2990, 2980, 2940, 2270, 1560, 1385, 1340 cm^{-1}; ^1H NMR (CCl_4) δ 0.85–1.8 (m, 5 H), 2.2–2.5 (t, 2 H).

(b) Oxidation of 7. The 1-iodo-1-pentyne (1.94 g, 10 mmol) was oxidized as before in dry methanol (100 mL) with I_2 (5.08 g, 20 mmol) and I_2O_5 (1.67 g, 5 mmol). A red oil (1.81 g) was obtained: IR (neat) 2980, 2970, 2880, 1750, 1735, 1465, 1265, 1215, 1120, 1050 cm^{-1}; ^1H NMR (CCl_4) δ 0.8–1.9 (m, OH), 2.47–2.82 (m, 4 H), 3.15 (s, 8 H), 3.67 (s, 4 H), 3.8 (s, 1 H). A quantitative estimate by NMR for this mixture indicated 48% of **6**, 9% of the corresponding keto ester, and 43% of **7**.

Registry No. 1, 637-44-5; 2, 85810-81-7; 3, 932-88-7; 4, 88131-14-0; 6, 63608-61-7; 7, 14752-61-5; I_2O_5, 12029-98-0; I_2, 7553-56-2; α,β,β-triiodostyrene, 16141-17-6; α-iodo-β-methoxyphenylpropionic acid, 88131-15-1; phenylacetylene, 536-74-3; *trans*-cinnamic acid, 140-10-3; 2-hexynoic acid, 764-33-0; methyl 2-hexynoate, 18937-79-6; 1-pentyne, 627-19-0; methyl phenylglycoxylate, 15206-55-0; benzoylformic acid, 611-73-4.

Routes to *C*-Glycopyranosides via Sigmatropic Rearrangements[1a]

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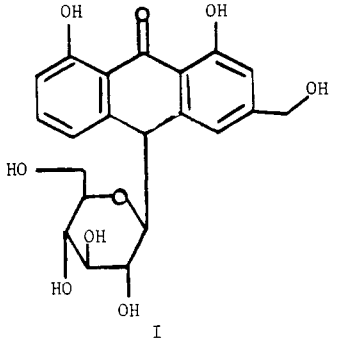
Claisen rearrangements have been applied to 1,5-anhydro-4,6-*O*-benzylidene-1,2-dideoxy-D-*ribo*-hex-1-enitol (1). The classical procedure succeeds, but the overall process is unsatisfactory because of the low conversion to the vinyl ether intermediate. Best results were had with the Eschenmoser procedure, and the *N,N*-dimethyl(hex-2′-enopyranosyl)acetamide produced, **7**, can be converted into the corresponding ethyl ester. However reduction of **7** with lithium triethoxyaluminum hydride gave the β-aldehyde **8** as the major product, indicating the ease with which these systems will anomerize. Attempts to apply the Still [2,3] sigmatropic rearrangement to **1** gave only modest yields of the desired hydroxymethyl product **12**. A more successful route to this substance was provided by reduction of the nitrile obtained from reacting tri-*O*-acetyl-D-glucal (**13**) with diethylaluminum cyanide.

2,6-Dialkylated pyran residues have been identified as components of natural products formally classified as carbohydrates for several years. One of the earliest known is barbaloin (I).[4] The comparable 2,5-dialkylfurans, al-



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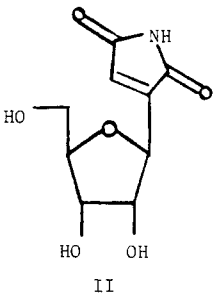

II

though later arrivals, have attracted more attention because of their presence in some biologically important *C*-nucleosides such as shodowmycin II.[5] Some of the most structurally intricate natural products isolated recently have been found to incorporatel 2,6-dialkylated pyran rings, and hence syntheses of this entity have been deemed worthy of attention.[6] Results with the furan counterparts have indicated that sugar-based syntheses of *C*-glycofuranosides could be highly stereocontrolled,[7] and hence we were interested in developing routes to *C*-glycopyranosides from hexopyrano sugar derivatives. In this and the accompanying paper[8] we discuss some of our recent results.

In choosing systems for study we noted that unsaturated sugars have proven to be versatile synthetic intermediates for carbohydrate[9] and noncarbohydrate[10] objectives, and hence we decided to make provisions for inclusion of olefinic residues in our *C*-glycopyranosides. The Claisen rearrangment had been first applied to unsaturated sugars

(1) (a) For a preliminary account, see: Fraser-Reid, B.; Dawe, R. D.; Tulshian, D. B. *Can. J. Chem.* **1979**, *57*, 1746. (b) Taken in Part from the Ph.D. Thesis of D.B.T., University of Maryland, 1981.

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(4) Mühlemann, H. *Pharm. Acta Helv.* **1952**, *27*, 17.

(5) Nishimura, N.; Mayama, M.; Komatsu, Y.; Kato, F.; Shimaoka, N.; Tanaka, Y. *J. Antibiot., Ser. A* **1966**, *17*, 148.

(6) For some very recent exammples see: Yougai, S.; Miwa, T. *J. Chem. Soc., Chem. Commun.* **1983**, *68*. Lewis, M. D.; Cha, J. K.; Kishi, Y. *J. Am. Chem. Soc.* **1982** *104* 4976. Reed, L. A., III; Yukishige, I.; Masamune, S.; Sharpless, K. B. *Ibid* **1982**, *104*, 6468. Danishefsky, S.; Kerwin, J. F., Jr.; Kobayashi, S. **1982**, *104*, 358. Ley, S. V.; Lygo, B.; Molines, H.; Morton, J. A. *Chem. Commun.* **1982**, 1251. Kozikowski, A. P.; Sorgi, K. L. *Tetrahedron Lett.* **1982**, *23*, 2281. Pougny, J.-R.; Nassr, M. A. M.; Sinaÿ, *Chem. Commun.* **1981**, 375. Grynkiewicz, G.; Zamojski, A. *Z. Naturforsch., Sect. B* **1980**, *35*, 1024.

(7) (a) For a thorough review see: Hanessian, S.; Pernet, A. G. *Adv. Carbohydr. Chem. Biochem.* **1976**, *33*, 111. (b) Cupps, T. L.; Wise, D. S.; Townsend, L. B. *J. Org. Chem.* **1982**, *47*, 5115. (c) Ohrui, H.; Jones, G. H.; Moffatt, J. G.; Madox, M. L.; Christensen, A. T.; Byram, S. K. *J. Am. Chem. Soc.* **1975**, *97*, 4602. (d) Kalvoda, L.; Farkas, J.; Sorm, F. *Tetrahedron Lett.* **1970**, 2297.

(8) Dawe, R. D.; Fraser-Reid, B. *J. Org. Chem.*, following paper in this issue.

(9) For a recent review see: Holder N. *Chem. Rev.* **1982**, *82*, 287.

(10) Corey, E. J.; Shibasaki, M.; Knolle, M. *Tetrahedron Lett.* **1977**, *1625*. Hernandez, O. *Ibid.* **1978**, 219. Ireland, R. E.; McGarvey, G. J.; Anderson, R. C.; Badond, R.; Fitzsimmons, B.; Thaisrivongs, S. *J. Am. Chem. Soc.* **1980**, *102* 6178.

0022-3263/84/1949-0518$01.50/0