Synthesis and Structural Analysis of 5-Deoxy-5-[(*RS*)-ethylphosphinyl]-α,β-L-idopyranoses

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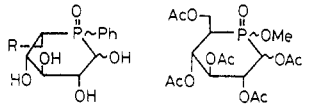
Received April 1, 1988

Treatment of (5*RS*)-3-*O*-acetyl-5-deoxy-5-(ethylmethoxyphosphinyl)-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranose (**5**) with dihydropyran in dichloromethane containing pyridinium *p*-toluenesulfonate gave the 6-*O*-(tetrahydropyran-2-yl) derivative **7** in 90% yield. Reduction of **7** with sodium dihydrobis(2-methoxyethoxy)aluminate followed by acid hydrolysis preponderantly provided the title compounds, the first unsubstituted L-idopyranoses having a phosphinyl group in the hemiacetal ring. These compounds were converted into four separable 1,2,3,4,6-penta-*O*-acetates **11a–d**, whose structures and $^4C_1$ (L) conformations were established by spectroscopy.

Because of a considerable interest in the physicochemical properties and potential biological activity, various sugar analogues having a phosphorus atom in place of oxygen in the hemiacetal ring have been prepared in recent years.[1-8] For example, the first synthesis of unsubstituted 5-deoxy-5-(ethylphosphinyl)-D-glucopyranoses (**8**) was performed[9] by starting with 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1**) by the sequence of **1** → **2** → **3** → **8** in 14 steps; later, the preparation of **8** from **1** was improved[10] to 10 steps in better overall yield by employing a partially different route involving the key intermediates **4–6** (Scheme I).

As for the preparation of the idose analogues, only 6-deoxy compounds have been reported so far; namely, 5,6-dideoxy-5-(phenylphosphinyl)-L-idopyranoses (**12**)[11-13] and the 6-deoxy-6-nitro derivatives **13**.[14] We now describe a selective synthesis of the first P-in-ring sugar analogue with the complete L-idose structure, 5-deoxy-5-(ethylphosphinyl)-L-idopyranoses (**10**).

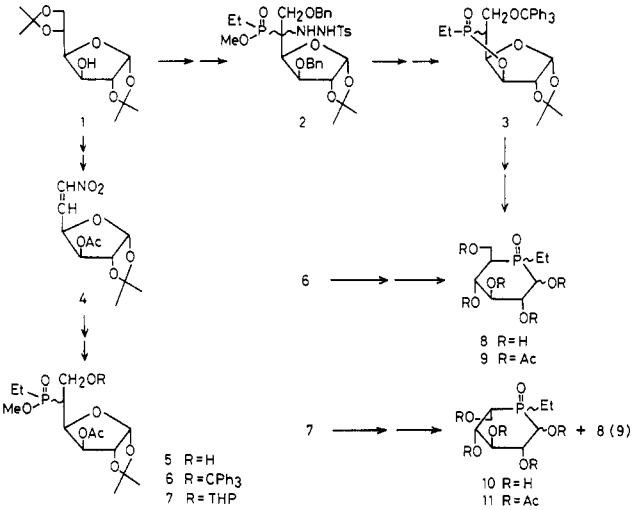


12 R=H
13 R=NO_2

14

Meanwhile, the 6-*O*-(tetrahydropyran-2-yl) compound **7** (prepared from **5**, see Scheme I) had been reported[10] to afford only **8** in an extremely low yield compared with the conversion of **6** to **8**. However, as use of the 6-*O*-(tetrahydropyran-2-yl) derivative **7** has an advantage over the 6-*O*-(triphenylmethyl) compound **6** because of its simple and high-yield preparation, we decided to investigate in more detail the ring transposition of **7**.

Scheme I. Preparation of 5-Deoxy-5-(ethylphosphinyl)-α,β-D-gluco-[9,10] and -L-idopyranoses: Bn = CH_2Ph, THP = (tetrahydropyran-2-yl)

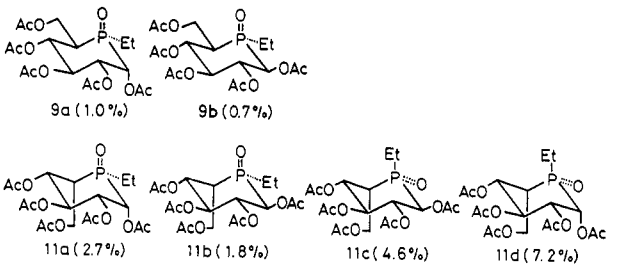


5 R=H
6 R=CPh_3
7 R=THP

8 R=H
9 R=Ac

10 R=H
11 R=Ac

Scheme II. Structures of the Products from 7[a]



9a (1.0%) 9b (0.7%)

11a (2.7%) 11b (1.8%) 11c (4.6%) 11d (7.2%)

[a] The figure in parentheses represents the overall yield from **7** after purification.

Compound **7** has now become available in 90% yield by treatment of **5** with dihydropyran in dichloromethane in the presence of pyridinium *p*-toluenesulfonate (PPTS); cf., 71% yield[10] when *p*-toluenesulfonic acid was used as the catalyst. Then, **7** was reduced with sodium dihydrobis(2-methoxyethoxy)aluminate (SDMA), followed by hydrolysis in ethanolic 0.5 M hydrogen chloride at 80 °C, thus affording a crude mixture of 5-deoxy-5-(ethyl-

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Table I. ^{1}H NMR (500 MHz) Parameters for 9a,b and 11a–d in $CDCl_3$[a]

	chemical shifts, δ										
compd	H-1	H-2	H-3	H-4	H-5	H-6	H-6′	AcO-1,2,3,4,6[b]	P-CH-C	P-CH′-C	P-C-CH_3
9a	5.85	5.54	5.45	5.57	2.49	4.45	4.40	2.20, 2.08, 2.07, 2.02, 1.98	2.19[c]	1.72	1.21
9b	5.37	5.71	5.22	5.58	2.36	4.47	4.42	2.16, 2.07, 2.06, 2.01, 1.99	2.07	2.00[c]	1.19
11a	5.78	5.59	5.42	5.53	3.06	4.56	4.49	2.17, 2.09, 2.08, 2.07, 2.01	2.05[c]	2.01[c]	1.29
11b	5.57	5.70	5.48	5.65	3.01	4.37	4.27	2.23, 2.15, 2.07, 2.03, 2.00	1.93	1.77	1.26
11c	5.97	5.15	5.64	5.06	2.88	4.53	4.51	2.27, 2.12, 2.10, 2.01, 2.01	2.32	1.85	1.37
11d	5.72	5.03	5.59	5.03	2.95	4.76	4.52	2.24, 2.09, 2.08, 2.05, 2.02	2.10[c]	2.00[c]	1.37

	coupling constants, Hz[e]																	
	$J_{1,2}$	$J_{1,P}$	$J_{1,5}$	$J_{2,3}$	$J_{2,P}$	$J_{3,4}$	$J_{4,5}$	$J_{4,P}$	$J_{5,6}$	$J_{5,6'}$	$J_{5,P}$	$J_{6,6'}$	$J_{6,P}$	$J_{6',P}$	$^2J_{H,P}$	$^2J_{H',P}$	$^2J_{H,H'}$	$^3J_{H,P}$	$^3J_{H,H}$
9a[f]	2.6	9.7	0	10.4	0.2	9.7	12.0	2.4	7.0	5.0	4.3	11.7	12.8	15.1	*d*	7.5	15.0	18.3	7.5
9b	11.0	3.6	0	9.9	3.0	9.8	11.7	2.9	7.4	5.2	3.1	11.8	11.8	15.2	7.7	*d*	15.0	19.2	7.7
11a	3.3	10.7	1.4	8.5	6.6	9.1	4.6	7.5	6.7	6.5	19.9	11.7	10.1	14.9	*d*	*d*	*d*	18.1	7.8
11b	10.7	3.0	0	9.2	3.5	10.1	5.4	3.5	3.4	4.0	21.2	12.3	23.8	8.0	6.1	7.8	15.6	17.9	7.8
11c	10.9	12.7	0	9.5	2.2	10.3	5.7	2.6	2.8	3.3	17.8	11.6	22.5	6.5	7.2	4.9	15.4	17.4	7.7
11d	3.0	7.6	1.1	9.7	2.8	8.7	4.7	6.5	4.3	6.8	15.9	11.9	11.4	8.2	*d*	*d*	*d*	17.6	7.7

[a] The assignments of all signals were made by employing a first-order analysis with the aid of a decoupling technique or, when necessary, by a simulation analysis. [b] Acetoxyl assignments may have to be interchanged. [c,d] These values are approximate[c] or uncertain,[d] becuase of overlapping with acetoxyl signals. [e] *J* values confirmed by double resonance. [f] Closer reexamination of some of the previously reported parameters (*J*) by simulation analysis has resulted in the slight correction of these values as in this table.

phosphinyl)-D-gluco- and -L-idopyranoses, which were characterized by conversion into the per-*O*-acetates by the usual method.[15] Purification on a silica gel column with 19:1 (v/v) ethyl acetate–ethanol as the eluant gave a colorless oil, which consisted (^{1}H NMR analysis) mostly of a mixture of the penta-*O*-acetates **11** (25% overall yield from **7**), contaminated with an extremely small proportion of peracetyl-5-deoxy-5-(ethylphosphinyl)-D-glucopyranoses (**9**). By rechromatography, the mixture was separated into five major fractions referred to as A–E according to their decreasing R_f values (0.60–0.50 with 9:1 AcOEt–EtOH).

Fraction A was found by ^{1}H NMR spectroscopy to be penta-*O*-acetyl-5-deoxy-5-[(*R*)-ethylphosphinyl]-α-D-glucopyranose (**9a**)[9,10] (see Scheme II).

Fraction B was a colorless gum from which, on dilution with ethyl acetate–hexane, the β-anomer **9b**[9,10] (identified spectroscopically) crystallized as colorless needles. The filtrate yielded a colorless syrup, which by high-resolution EI mass spectrometry had the same molecular composition ($C_{18}H_{27}O_{11}P$) as **9a** and **9b**. The precise structure for this product as penta-*O*-acetyl-5-deoxy-5-[(*R*)-ethylphosphinyl]-β-L-idopyranose (**11a**) was established by 500-MHz ^{1}H NMR spectroscopy (see below).

Structures of the α-anomer **11b**, its diastereomer **11c** (with regard to the ring-phosphorus atom), and its β-anomer **11d**, respectively, assigned to the remaining three products (all $C_{18}H_{27}O_{11}P$) obtained from fractions C (colorless needles), D (colorless syrup), and E (colorless syrup) on the basis of their spectral data; see Scheme II for the structures and yields of the products.

^{1}H NMR Spectral Analysis of Peracetyl 5-Deoxy-5-(ethylphosphinyl)-L-idopyranoses. For structural assignments of the four new products **11a–d** having the same molecular composition as those of the D-glucopyranose-type **9a,b**, the chemical shift of each proton signal and the dependence of the $^2J_{H,P}$, $^3J_{H,P}$, $^3J_{H,H}$, and $^4J_{H,H}$ values on their dihedral angles were carefully taken into consideration; the precise parameters obtained at 500 MHz for these compounds are summarized in Table I. Some characteristics features of **11a–d** are discussed here in detail for comparison with those of the D-glucopyranose analogues **9a,b**.

(1) The relatively large magnitudes of $J_{2,3}$ and $J_{3,4}$ (8.5–10.4 Hz) of all aldohexopyranoses **9a,b** and **11a–d** indicate that these compounds exist predominantly in the $^4C_1$ (D) or $^4C_1$ (L) conformation (in $CDCl_3$ at 27 °C). Therefore, the smaller magnitudes of $J_{4,5}$ (4.6–5.7 Hz) of **11a–d** compared with those (ca. 12 Hz) of the D-glucopyranose-type **9a,b** suggest the L-idopyranose configuration for these new products **11a–d**. In addition, a significant downfield shift (ca. 0.5–0.7 ppm) in the H-5 signals is observed for **11a–d** (compared with those of **9a,b**), and the magnitudes of $J_{5,P}$ (ca. 16–21 Hz) of **11a–d** are significantly larger than those (3–4 Hz) of **9a,b**. These differences are indicative of the gauche orientation of H—C(5)—P=O in **11a–d**, in contrast to the anti orientation[9,10] of this group in **9a,b** (see structural formulas in Scheme II).

(2) The orientation of the ring P=O group can normally be established[1,4] by the δ values of H-2 and H-4. In the present study an appreciable, upfield shift (0.4–0.6 ppm) of these signals is observed for **11c** and **11d**, thus showing the equatorial orientation (*S*) of the ring P=O for these compounds. The axial P=O orientation (*R*) is therefore assigned to the rest of the products (**9a,b** and **11a,b**).

(3) The anomeric orientation of C-1 is readily derived from the magnitudes of $J_{1,2}$ and $J_{1,5}$. The large magnitudes of $J_{1,2}$ (10.7–11.0 Hz) and the absence of $J_{1,5}$ indicate axial H-1 configuration for **9b**, **11b**, and **11c**, whereas the smaller $J_{1,2}$ values (2.6–3.3 Hz) point out the equatorial H-1 configuration for **9a**, **11a**, and **11d**. The presence of a small long-range coupling ($J_{1,5}$ = 1.1–1.4 Hz) in **11a** and **11d** further supports the equatorial H-5 configuration (i.e., the L-idopyranose structure). The anti orientation of H—C(1)—P=O for **9b** and **11b** is confirmed by the smaller magnitudes (3.0–3.6 Hz) of their $J_{1,P}$ and the slightly upfield shift in the H-1 signals compared with the corresponding parameters of other isomers **9a** and **11a,c,d** (having those groups in the gauche orientation).

The rest of the spectral data of **11a–d** is completely in conformity with the structures shown in Scheme II. The appreciable, additional shifts in some signals observed in the spectra[11] of the 5,6-dideoxy-L-idopyranose analogues **12** (due to the anisotropic effect of the *P*-phenyl ring) are excluded in the parameters for **11a–d**, and therefore the data shown in Table I are of high value to the structural analysis of related 5-deoxy-5-(phosphinyl)aldohexopyranoses.

It is also noteworthy that all of the 5-deoxy-5-(ethylphosphinyl)-L-idopyranoses **11a–d** predominantly exist in the $^4C_1$ (L) conformation. This presents a striking contrast to the case of per-*O*-acetyl-α- and -β-D-idopyranoses, for

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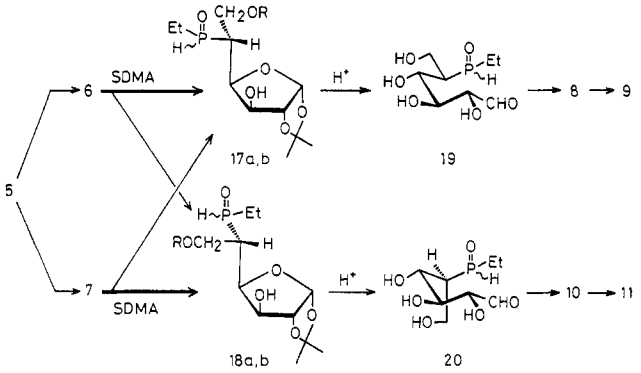
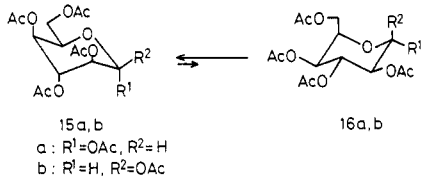
Scheme III. Possible Reaction Pathways for the Formation of the D-Gluco- (8, 9) and L-Idopyranoses (10, 11): a = CPh_3, b = THP



which the $^4C_1$ (D) conformation **15a,b** has been reported[16] to be more favorable than $^1C_4$ (D) (see **16,b**). As the latter



15a,b 16a,b

a: R^1=OAc, R^2=H

b: R^1=H, R^2=OAc

is the enantiomeric counterpart[17] of $^4C_1$ (L), the predominant conformation of **11a–d** in favor of $^4C_1$ (L) is most likely ascribed to the presence of stronger destabilizing interactions among the 1,3,5-syn-oriented two acetoxyl (AcO-2,4) and P=O (or P—Et) groups in the alternative conformation $^1C_4$ (L) of **11a–d** (which is analogous to **15a,b**), compared with the 1,3-diaxial repulsive influence exerted by the $AcOCH_2$-6 group in the $^4C_1$ (L) conformation of **11a–d**.

The preponderant formation of L-idopyranoses **10** (over D-glucopyranoses **8**) from **7**, which has become apparent from the present study, is rationalized most easily in terms of the thermodynamically controlled production of the sterically more favorable (5*S*) epimer **18b** (compared with the counterpart **17b**, see Scheme III) as the result of equilibration[4] at C-5 by the strongly basic SDMA during the reduction; this is based on inspection of the molecular models of the key intermediates **18b** and **17b** with regard to the steric congestion between HO-3 and the substituents at C-5 [i.e., $THPOCH_2$ vs EtPH(=O)]. On the other hand, in the case of the reduction of **6**,[9] the 6-*O*-(triphenylmethyl) group is considered to cause the reversal of the order of the relative size of the substituents at C-5 resulting in the predominant formation of **17a** as the more favorable intermediate (than **18a**, Scheme III), which eventually yields mainly **10**.

Although no naturally occurring D- or L-idoses have seemingly been found so far, extensive synthetic efforts have been made for analogues of D- and L-idoses for various purposes.[18] A preparative scheme for 5-deoxy-5-(ethylphosphinyl)-L-idopyranoses, which is regarded as complementary to the synthesis of the 5-deoxy-5-phosphinyl-D-glucopyranoses, has now been established. The extension of this work including improvement of the yields of the ring transposition products in relation to various kinds of substituents at P-5 and O-6 of the intermediates, as well as biological evaluation of the compounds, is in progress.

Experimental Section

Melting points were determined with a Yanagimoto MP-S3 instrument and are uncorrected. All reactions were monitored by TLC (Merck silica gel 60F, 0.25 mm) with (A) AcOEt, (B) 19:1 and (C) 9:1 AcOEt–EtOH, and (D) 5:3:1 2-propanol–AcOEt–water as the eluant; components were detected with 20% sulfuric acid–ethanol. Column chromatography was performed by using Wako C-200 silica gel or, when necessary, a Merck Lobar silica gel prepacked column (Size A). The ^1H NMR spectra were recorded in $CDCl_3$. Chemical shifts are reported as δ values relative to tetramethylsilane as the internal standard. The mass spectra are given in terms of m/z (relative intensity) compared with the base peak.

5(*RS*)-3-*O*-Acetyl-5-deoxy-5-(ethylmethoxyphosphinyl)-1,2-*O*-isopropylidene-6-*O*-(tetrahydropyran-2-yl)-α-D-*xylo*-hexofuranose 7.[10] A solution of **5**[10] (166 mg, 0.471 mmol) and dihydropyran (120 mg, 1.43 mmol) in dry dichloromethane (2 mL) containing PPTS[19] (36 mg, 0.14 mmol) was stirred for 6 h at room temperature. The solution was then diluted with ether, washed with half-saturated brine, dried (Na_2SO_4), and evaporated in vacuo. The residue was purified by short-path column chromatography, giving **7** (185 mg, 90% yield, ref 9, 71%) as a colorless syrup: R_f 0.40–0.55 (B); ^1H NMR (60 MHz) δ 1.40, 1.50 (6 H, 2 s, CMe_2), 0.4–2.3 [11 H, m, PCH_2CH_3, $(CH_2)_3CO$-6], 2.08 (3 H, s, AcO-3), 2.3–2.9 (1 H, m, H-5), 3.67, 3.74 (3 H, m, $^3J_{P,H}$ = 10.8 Hz, POMe), 3.5–3.9 (3 H, m, CH_2OCHO-6), 3.9–4.8 (4 H, m, H-2,4,6,6'), 5.23 (1 H, d, $J_{3,4}$ = 3.0 Hz, H-3), 5.88 (1 H, d, $J_{1,2}$ = 4.0 Hz, H-1); MS, m/z 436 (M^+).

1,2,3,4,6-Penta-*O*-acetyl-5-deoxy-5-[(*R*)-ethylphosphinyl]-α-D-glucopyranose (9a), Its β-Anomer 9b, the 5-[(*R*)-Ethylphosphinyl]-β-L-idopyranose (11a), Its α-Anomer 11b, the 5-[(*S*)-Ethylphosphinyl]-α-L-idopyranose (11c), and Its β-Anomer 11d. To a solution of **7** (352 mg, 0.807 mmol) in dry benzene (5 mL) was added, with stirring, a solution of SDMA (70% in toluene, 0.60 mL, 3.0 equiv) in dry benzene (2 mL) in small portions during 15 min at 5 °C under nitrogen. The stirring was continued at this temperature for ca. 1 h. Then water (0.5 mL) was added at 5 °C, and the mixture was stirred for 30 min and centrifuged to remove aluminum hydroxide; the precipitate was extracted with several portions of benzene. The organic layer was combined and evaporated in vacuo, giving crude (5*RS*)-5-deoxy-5-(ethylphosphinyl)-1,2-*O*-isopropylidene-6-*O*-(tetrahydropyran-2-yl)-α-D-*xylo*-hexofuranoses (**18b**, **17b**) as a colorless syrup: R_f 0.76 (A).

This was immediately treated with 1:1 ethanol–0.5 M hydrochloric acid (8 mL) at 90 °C for 3 h under nitrogen. After cooling, the products was neutralized with Amberlite IRA-45. The resin was filtered off and washed with aqueous ethanol. The filtrate was evaporated in vacuo to give a mixture of 5-deoxy-5-(ethylphosphinyl)-α,β-D-gluco- (**8**) and -L-idopyranoses (**10**) as a colorless syrup: R_f 0.40–0.50 (D).

This was dissolved in dry pyridine (3 mL) and acetic anhydride (1.5 mL) at 0 °C. The mixture was stirred at 20 °C overnight, diluted with a small amount of cold water, and concentrated in vacuo. The residue was dissolved in chloroform and washed with water. The organic layer was dried (Na_2SO_4) and evaporated in vacuo. The residue was chromatographed in a column of silica gel with 19:1 (v/v) AcOEt–EtOH to give a mixture of the per-*O*-acetates **9** and **11** [91 mg, 25% overall yield from **7**, R_f 0.5–0.3 (B)]. This was separated by column chromatography with the same eluant into five fractions, A–E.

Fraction A [R_f 0.60 (C)] gave **9a**[9,10] as a colorless syrup: 3.7 mg (1.0% overall yield from **7**); for 500-MHz ^1H NMR data, see Table I.

Fraction B [R_f 0.58 (C)] gave **9b**[9,10] as colorless needles: 2.7 mg (0.7%); mp 233 °C (from AcOEt–hexane, ref 8, mp 233 °C). The mother liquor gave **11a** as a colorless syrup: 10.0 mg (2.7%); for 500-MHz ^1H NMR data, see Table I; MS, m/z 450 (1.8, M^+),

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(17) See, e.g., Stoddart, J. F. *Sterochemistry of Carbohydrates*; Wiley: New York, 1971.

(18) See, e.g., Paulsen, H.; Trautwein, W. P.; Garrido-Espinosa, F.; Heyns, K. *Chem. Ber.* **1967**, *100*, 2822. Kovar, J. *Can. J. Chem.* **1970**, *48*, 2383. Ko, S. Y.; Lee, A. W. M.; Masamune, S.; Reed, L. A., III; Sharpless, K. B.; Walker, F. J. *Science (Washington, D.C.)* **1982**, *220*, 949.

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408 (5), 391 (59), 349 (56), 348 (54), 307 (34), 306 (30), 289 (57), 247 (39), 229 (31), 228 (33), 205 (17), 186 (37), 43 (100); exact mass calcd for $C_{18}H_{27}O_{11}P$ (M) 450.1291, found 450.1272.

Fraction C [R_f 0.56 (C)] gave **11b** as colorless needles: 6.7 mg (1.8%); mp 228–229 °C (from AcOEt–hexane); for 500-MHz ^{1}H NMR data, see Table I; MS, m/z 450 (0.55, M^+), 408 (13), 391 (13), 366 (21), 349 (100), 348 (39), 307 (44), 306 (41), 289 (44), 247 (43), 229 (42), 228 (69), 204 (24), 187 (28), 186 (57); exact mass calcd for $C_{18}H_{27}O_{11}P$ (M) 450.1291, found 450.1280.

Fraction D [R_f 0.53 (C)] gave **11c** as a colorless syrup: 16.7 mg (4.6%); for 500-MHz ^{1}H NMR data, see Table I; MS, m/z 450 (0.22, M^+), 408 (4.1), 366 (19), 349 (33), 307 (33), 306 (26), 289 (27), 288 (30), 247 (37), 228 (47), 205 (22), 186 (45), 43 (100); exact mass calcd for $C_{18}H_{27}O_{11}P$ (M) 450.1291, found 450.1261.

Fraction E [R_f 0.50 (C)] gave **11d** as a colorless syrup: 26.1 mg (7.2%); for 500-MHz ^{1}H NMR data, see Table I; MS, m/z 451 (3.3, M + 1), 450 (0.68, M^+), 435 (7), 408 (7), 391 (10), 366 (41), 349 (52), 337 (78), 307 (59), 306 (58), 289 (37), 261 (27), 247 (56), 228 (80), 186 (56), 163 (100), 141 (27), 122 (26); exact mass calcd for $C_{18}H_{27}O_{11}P$ (M) 450.1291, found 450.1266.

Besides these separated products, an unseparable mixture of **11a–d** (ca. 20 mg) was recovered as the intermediate fractions.

Total Synthesis of Cyclobutane Amino Acids from *Atelia herbert smithii*†

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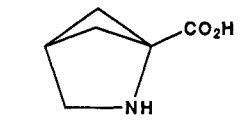
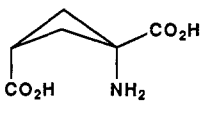
Received May 17, 1988

The syntheses of two amino acids from the seeds of the legume *Atelia herbert smithii*, 2,4-methanoproline and 2,4-methanoglutamic acid, are described. The synthesis of a third amino acid, *cis*-1-amino-3-(hydroxymethyl)cyclobutanecarboxylic acid and subsequent comparison with a natural sample show that it too is a component of the seeds. The synthesis of a fourth possible seed component, 2,4-methanopyroglutamic acid, is also described.

The seeds of the legume *Atelia herbert smithii*, found only in the Santa Rosa National Park in Costa Rica, are ignored by over 100 normal seed predators. This led Bell and co-workers to the isolation and structural solution by X-ray crystallography of two new amino acids: 2,4-methanoproline (**1**) and 2,4-methanoglutamic acid (**2**).[1] A minor ninhydrin-reacting component was also detected though its structure was not defined. The structure was postulated to be the hydroxy amino acid **3**.[2] A fourth compound, 2,4-methanopyroglutamic acid (**4**), although not isolated, was proposed as a possible seed component or an intermediate in the biosynthesis of the other three amino acids. The strain inherent in such an azabicyclo[2.1.1]-hexane lactam should make acid **4** a good acylating agent, and such activity may give rise to the observed seed avoidance.



1



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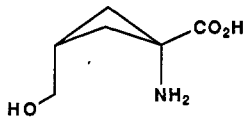
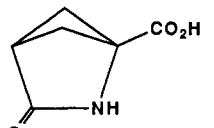


3



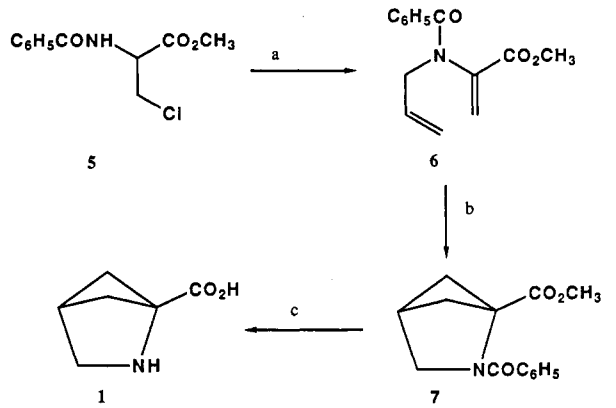
4

Besides their possible function as antifeedants, amino acids **1** and **2** are achiral proline and glutamic acid analogues, respectively. To facilitate investigation of their natural roles and to allow for other possible uses, we report here efficient syntheses of compounds **1–4**.[3]

Results

Our approach to the synthesis of the bicyclic amino acid **1** was suggested by the work of Liu and Hammond on the photochemistry of myrcene.[4] Acetophenone-sensitized photocyclization of myrcene leads cleanly to a bicyclo-[2.1.1]hexane. The analogous azahexadiene photoprecursor for the synthesis of the desired azabicyclo[2.1.1]hexane was synthesized in a straightforward manner (Scheme I).

Scheme I[a]



[a] (a) THF/KO-*t*-Bu, CH_2=$CHCH_2Br$; (b) $h\nu$, acetophenone, Pyrex; (c) 6 N HCl.

Serine was converted by known methods to the crystalline methyl 2-benzamido-3-chloropropionate (**5**) (83%).[5] The photoprecursor, azahexadiene **6**, was then prepared in one pot from chloride **5** by sequential dehydrohalogenation and amide allylation. Addition of chloride **5** to potassium *tert*-butoxide (2.2 equiv) in THF at −78 °C followed by allyl bromide (12 equiv) gave, after being warmed to room temperature and stirred for 4 h, the photoprecursor **6** (94%). Ether extraction followed by concentration gave product of sufficient purity for the next

† Taken from the thesis of P. Hughes, Cornell University, 1983.

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(2) Personal communication from R. Pryce.

(3) The synthesis of 2,4-methanoproline (**1**) was previously reported without experimental detail. (a) Hughes, P.; Martin, M.; Clardy, J. *Tetrahedron Lett.* **1980**, *21*, 4579. (b) Pirrung, M. *Tetrahedron Lett.* **1980**, *21*, 4577. A synthesis of 2,4-methanoglutamic acid was recently reported: Gaoni, Y. *Tetrahedron Lett.* **1988**, *29*, 1591.

(4) Liu, R. S. H.; Hammond, G. S. *J. Am. Chem. Soc.* **1964**, *86*, 1892.

(5) Painter, E. P. *J. Am. Chem. Soc.* **1947**, *69*, 229–232.

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