(q), 28.21 (q), 24.65 (q), 23.95 (q); MS (+EI, 15 eV), m/z (relative intensity) 319 (2), 201 (16), 174 (14), 162 (9), 146 (6), 145 (6), 118 (16), 106 (10), 105 (100), 104 (6), 77 (5), 42 (8). Anal. Calcd for $C_{22}H_{28}Cl_2N_2$: C, 67.5; H, 7.2; N, 7.2. Found: C, 67.6; H, 7.4; N, 7.4.

Minor Diastereomers. The solvent was evaporated from the combined supernatant liquor, and the residue was crystallized from petrol at −78 °C. Recrystallization from petrol gave one of the minor isomers [11 (X = Cl), "*dl*-I"] as white needles (248 mg, 10%): mp 52.4–53.9 °C; $[\alpha]^{25}_D$ +73.4° (*c* 1.5, benzene); IR ν_{max} ($CHCl_3$) 3010, 2964, 2930, 1602, 1494, 1452, 1377, 701 cm^{-1}; ^1H NMR (400 MHz) δ 7.27–7.12 (m, 10 H), 3.11–3.03 (m, 2 H), 2.59 (dd, 2 H, J = 14.6, 7.2 Hz), 2.24 (dd, 2 H, J = 14.6, 5.4 Hz), 1.53 (s, 6 H), 1.29 (d, 6 H, J = 7.1 Hz); ^{13}C NMR (22.5 MHz) δ 147.0 (s), 128.4 (d), 127.1 (d), 126.1 (d), 95.6 (s), 50.5 (t), 36.4 (d), 28.9 (q), 24.6 (q); MS (+EI, 12 eV) m/z (relative intensity) 355 (1), 279 (11), 201 (32), 184 (14), 182 (42), 174 (22), 163 (12), 162 (78), 147 (35), 146 (20), 106 (17), 105 (100), 104 (17). Anal. Calcd for $C_{22}H_{28}Cl_2N_2$: C, 67.5; H, 7.2; N, 7.2. Found: C, 67.6; H, 7.6; N, 7.4.

Crystallization from petrol at −78 °C of the mother liquor from the separation of the first minor diastereomer ("*dl*-I") followed by recrystallization at −15 °C afforded a second minor isomer 11 [(X = Cl), "*dl*-II"] as cubic crystals (206 mg, 8%): mp 49.5–50.8 °C; $[\alpha]^{25}_D$ +27.8° (*c* 1.1, benzene); IR ν_{max} (KBr) 3026, 2965, 2927, 1602, 1493, 1454, 1377, 764, 703, 639 cm^{-1}; ^1H NMR (400 MHz) δ 7.32–7.18 (m, 10 H), 3.22–3.14 (m, 2 H), 2.54 (dd, 2 H, J = 14.6, 6.7 Hz), 2.36 (dd, 2 H, J = 14.6, 5.6 Hz), 1.51 (s, 6 H), 1.27 (d, 6 H, J = 7.1 Hz); ^{13}C NMR (22.5 MHz) δ 147.4 (s), 128.6 (d), 127.0 (d), 126.2 (d), 96.1 (s), 49.9 (t), 36.5 (d), 28.6 (q), 24.2 (q); MS (+EI, 15 eV), m/z (relative intensity) 355 (1), 201 (6), 175 (4), 174 (4), 145 (8), 118 (8), 106 (21), 105 (100). Anal. Calcd for $C_{22}H_{28}Cl_2N_2$: C, 67.5; H, 7.2; N, 7.2. Found: C, 67.8; H, 7.6; N, 7.3.

(2*S*,2′*R*,4*S*,4′*S*)-(+)-2,2′-Dimethyl-4,4′-diphenyl-2,2′-azopentanenitrile (11, X = CN). Treatment of 11 (X = Cl) (391 mg, 1.0 mmol) under the conditions of method B gave a pale yellow oil (371 mg, 99%). Crystallization from methanol–pentane (−15°) followed by a further two recrystallizations afforded 11 (X = CN) as white needles (202 mg, 54%): mp 86.4–87.2 °C dec; $[\alpha]^{25}_D$ +43.6° (*c* 1.0, benzene); IR ν_{max} (KBr) 3026, 2964, 2925, 2897, 2239, 1602, 1495, 1447, 1256, 766, 702, 530 cm^{-1}; ^1H NMR (400 MHz), 7.33–7.14 (m, 10 H), 3.08–3.00 (m, 1 H), 3.00–2.92 (m, 1 H), 2.83 (dd, 1 H, J = 14.5, 9.3 Hz), 2.24 (dd, 1 H, J = 14.5, 5.0 Hz), 2.21 (dd, 1 H, J = 14.3, 7.8 Hz), 2.07 (dd, 1 H, J = 14.3, 6.1 Hz), 1.62 (s, 3 H), 1.32 (d, 3 H, J = 7.1 Hz), 1.23 (d, 3 H, J = 7.1 Hz), 0.99 (s, 3 H); ^{13}C NMR (100 MHz) δ 145.76 (s), 144.75 (s), 128.79 (d), 128.76 (d), 127.38 (d), 127.01 (d), 126.78 (d), 126.67 (d), 118.24 (s), 117.91 (s), 72.34 (s), 72.16 (s), 45.63 (t), 45.28 (t), 36.98 (d), 36.61 (d), 25.61 (q), 24.41 (q), 23.66 (q), 23.59 (q); MS (+EI, 15 eV), m/z (relative intensity) 344 (4), 302 (5), 239 (6), 226 (16), 211 (6), 173 (15), 172 (5), 171 (8), 119 (8), 106 (21), 105 (100), 104 (9). Anal. Calcd for $C_{24}H_{28}N_4$: C, 77.4; H, 7.6. Found: C, 77.4; H, 7.5.

Acknowledgment. This work was supported by the Australian Research Grants Committee. S.K.D. gratefully acknowledges a Commonwealth Postgraduate Award.

Supplementary Material Available: Tables of bond lengths, bond angles, hydrogen atom coordinates, and anisotropic thermal parameters for **2a** **3a**, and **4a** (3 pages). Ordering information is given on any current masthead page.

Notes

A Simple Preparation of Chiral Acetylenic Ethers

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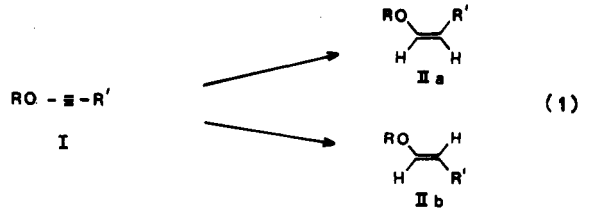
Received November 20, 1986

In the course of our work on the asymmetric enol ether–ketene cycloaddition reaction,[1] a number of optically active cis and trans *O*-alkyl enol ethers were required. While acetylenic ethers I appeared to be potentially excellent precursors of enol ethers IIa,b (eq 1), a search of



(1)

the literature revealed no *facile, general* approaches to this well-studied class of compounds[2] and virtually no reports on the preparation of chiral (nonracemic) derivatives.[3] In this paper a general, highly efficient, typically one-pot procedure for the preparation of a variety of optically active acetylenic ethers is reported.

Most alcohols on successive treatment in tetrahydrofuran with potassium hydride, trichloroethylene, *n*-butyllithium, and a primary iodide or water are converted in high yield to the acetylenic ether (eq 2),[4] which can be purified by simple filtration over silica gel and/or distillation. Examples of this method are given in Table I.

$$ROH \xrightarrow[\underline{n}\text{-}C_4H_9Li;\ R'I \text{ or } H_2O]{KH;\ Cl_2C=CHCl;} RO-\equiv-R'\ (H) \qquad (2)$$

The potassium alkoxide generates and attacks the dichloroacetylene;[2,5] the resulting adduct on treatment with

(1) Greene, A. E.; Charbonnier, F. *Tetrahedron Lett.* **1985**, *26*, 5525–5528.

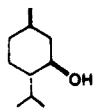
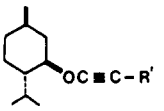
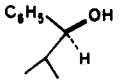
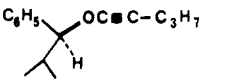
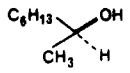
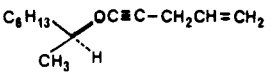
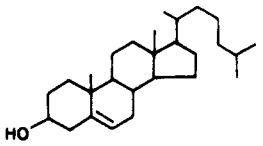
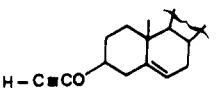
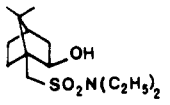
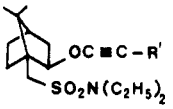
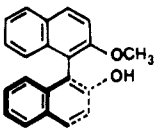
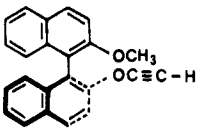
(2) For review, see: Arens, J. F. In *Advances in Organic Chemistry*; Raphael, R. A., Taylor, E. C., Wynberg, H., Eds.; Interscience: New York, 1960; Vol. II, pp 117–212. Brandsma, L.; Bos, H. J. T.; Arens, J. F. In *Chemistry of Acetylenes*; Viehe, H. G., Ed.; Marcel Dekker: New York, 1969; Chapter 11. Meerwein, H. In *Methoden der Organischen Chemie (Houben-Weyl)*, 4th ed.; Georg Thieme Verlag: Stuttgart, 1965; Vol. 6/3, Chapter 1, pp 116–118. Ben-Efraim, D. A. In *The Chemistry of the Carbon–Carbon Triple Bond*; Patai, S., Ed.; Wiley-Interscience: New York, 1978; Vol. 2, Chapter 18 and references cited therein.

(3) See, however: Olsman, H. *Proc. K. Ned. Akad. Wet. Ser. B: Palaeontol., Geol., Phys., Chem., Anthropol.* **1966**, *B69*, 629–644, 645–659, 660–674, 675–690; *Chem. Abstr.* **1967**, *66*, 64994x.

(4) While no extensive optimization studies have been carried out, 2 equiv of potassium hydride, 1 equiv of trichloroethylene, 2–3 equiv of butyllithium, and 2.5–5 equiv of the iodide have been found to produce satisfactory results.

0022-3263/87/1952-2919$01.50/0

Table I. Transformation of Alcohols to Acetylenic Ethers[a]

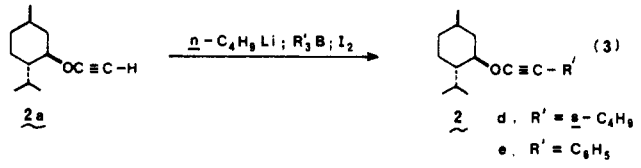
ROH	R′X	ROC≡CR′	yield,[b] %
			
1	(H_2O)	**2a**, R′ = H	88
	CH_3I	**2b**, R′ = CH_3	85, 87[c]
	C_2H_5I	**2c**, R′ = C_2H_5	87
			
3	n-C_3H_7I	4	66
			
5	CH_2=$CHCH_2I$	6	74
			
7	(H_2O)	8	73
			
9	(H_2O)	**10a**, R′ = H	70[d,e]
	CH_3I	**10b**, R′ = CH_3	79[d,e]
			
11	(H_2O)	12	72[d]

[a] For procedures, see Experimental Section. [b] Yields refer to isolated, chromatographically and spectroscopically homogeneous, material. [c] Yields for reactions run on 12.5 and 100 mmol, respectively. [d] Intermediate dichloro enol ether was isolated. [e] Li powder–*N*,*N*-dimethyl-1-naphthylamine was used in place of n-C_4H_9Li.

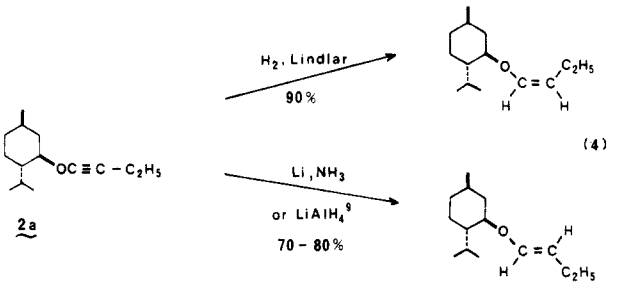
butyllithium suffers conversion to the corresponding acetylide,[6] which on alkylation or protonation yields the final product. Although several steps are typically effected in situ in this transformation, the sequence reproducibly affords excellent results.

Most reactions were run with 1–10 mmol of the alcohol, but as demonstrated by the conversion of 1 to **2b**, the transformation is equally efficient on the 100-mmol scale. It proved advantageous with alcohols **9** and **11**, however, to isolate the intermediate dichloro enol ethers prior to conversion to the acetylenic ethers.

The poor reactivity of the acetylides toward secondary halides can be nicely circumvented through the use of organoboranes.[7] For example, menthoxyacetylene (**2a**) is converted via the lithium borate to the *sec*-butyl derivative **2d** (60% yield, eq 3). Analogously, the phenyl derivative **2e** can also be prepared (85% yield).



That the chiral acetylenic ethers are, in fact, excellent precursors of stereochemically pure enol ethers[8] is illustrated in eq 4. It is expected that these readily available acetylenes will find several other useful applications in asymmetric synthesis.



Experimental Section

The solvents were normally distilled prior to use. Tetrahydrofuran and ether were distilled from sodium hydride–lithium aluminum hydride and hexamethylphosphoric triamide was distilled under vacuum from calcium hydride. Reaction mixtures were generally stirred under a nitrogen or argon atmosphere. Analytical thin-layer chromatography was performed on Merck $60F_{254}$ (0.25 mm) sheets, which were visualized with molybdo-

(5) See: Delavarenne, S. Y.; Viehe, H. G. In *Chemistry of Acetylenes*; Viehe, H. G., Ed.; Marcel Dekker: New York, 1969; Chapter 10 and references cited within. See also: Kende, A. S.; Fludzinski, P.; Hill, J. H.; Swenson, W.; Clardy, J. *J. Am. Chem. Soc.* **1984**, *106*, 3551–3562.
(6) Normant, J. *Bull. Soc. Chim. Fr.* **1963**, 1876–1897.
(7) Suzuki, A.; Miyaura, N.; Abiko, S.; Itoh, M.; Brown, H. C.; Sinclair, J. A.; Midland, M. M. *J. Am. Chem. Soc.* **1973**, *95*, 3080–3081. Midland, M. M.; Sinclair, J. A.; Brown, H. C. *J. Org. Chem.* **1974**, *39*, 731–732.
(8) For an alternative approach to chiral enol ethers, see: Charbonnier, F.; Moyano; A.; Greene, A. E. *J. Org. Chem.*, in press.
(9) The addition of 1 equiv of iodine prior to workup cleanly produced the *Z* iodo enol ether in 75% yield. See: Corey, E. J.; Kirst, H. A.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1970**, *92*, 6314–6319. Keul, H.; Choi, H.-S.; Kuczkowski, R. L. *J. Org. Chem.* **1985**, *50*, 3365–3371.

phosphoric acid in ethanol. Merck 70-230 silica gel 60 was employed for column chromatography. Melting points were obtained on a Büchi-Tottoli apparatus and were not corrected. Alcohols (-)-1, (S)-(-)-3, (S)-(+)-5, 7, and (R)-(+)-binaphthol were purchased from Aldrich. Alcohols 9[10] and 11[11] were obtained according to the literature procedures.

Typical Procedure. Propynyl Ether 2b. To 1.02 g (25.4 mmol) of oil-free potassium hydride suspended in 25 mL of tetrahydrofuran was added dropwise with stirring 1.96 g (12.5 mmol) of (-)-menthol in 25 mL of tetrahydrofuran. After the hydrogen evolution was complete, the mixture was cooled to -50 °C, treated with 1.64 g (12.5 mmol) of trichloroethylene in 15 mL of tetrahydrofuran, and then allowed to warm to room temperature. After being stirred for 1 h, the brown reaction mixture was treated dropwise at -70 °C with 12 mL (30.0 mmol) of a 2.5 M solution of *n*-butyllithium in hexane. After 0.5 h at -70 °C, the mixture was warmed to -40 °C over 0.5 h, and 8.90 g (62.7 mmol) of methyl iodide (filtered over alumina–phosphorus pentoxide) in 16 mL of hexamethylphosphoric triamide was added. The reaction mixture was stirred at room temperature for 2 h, treated with a small amount of methanol, and then poured into a cold saturated aqueous solution of ammonium chloride. The product was isolated with pentane in the usual manner and purified by dry column chromatography (silica gel pretreated with 2.5% v/v of triethylamine) with pentane and then by evaporative distillation [ca. 50 °C (0.05 torr)] to yield 2.08 g (85%) of propynyl ether **2b** as a clear, colorless oil: $[\alpha]^{20}_D$ -83° (*c* 1.4, cyclohexane); IR (film) 2955, 2920, 2270, 1450, 1250, 950, 910, 850 cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 0.8–1.6 (m, 16 H), 1.74 (s, 3 H), 2.0–2.5 (m, 2 H), 3.67 (m, 1 H); mass spectrum (chemical ionization), *m/e* 195 ($M^+ + 1$, 5%), 156 (100%), 139 (23%); calcd for $C_{10}H_{19}$ M_r 139.14867, found M_r (mass spectrum) 139.14881 ($M^+ - C_3H_3O$).

The acetylenic ethers **2a**,**c**, **4**, **6**, **8**, and **12** were prepared in essentially the same way.

Ethynyl ether 2a: $[\alpha]^{19}_D$ -88° (*c* 1.2, cyclohexane); IR (film) 3330, 2955, 2145, 1450, 1100, 945, 895, 840 cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 0.8–1.7 (m, 16 H), 1.50 (s, 1 H), 2.0–2.4 (m, 2 H), 3.85 (m, 1 H); mass spectrum (chemical ionization), *m/e* 181 ($M^+ + 1$, 5%), 156 (100%), 139 (58%).

Butynyl ether 2c: $[\alpha]^{21}_D$ -76° (*c* 1.3, cyclohexane); IR (film) 2950, 2920, 2260, 1450, 1240, 1230, 1205, 980, 945, 905, 845 cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 0.8–1.7 (m, 19 H), 2.0–2.4 (m + q, *J* = 6 Hz, 4 H), 3.70 (m, 1 H); mass spectrum (chemical ionization), *m/e* 209 ($M^+ + 1$, 4%), 156 (100%), 139 (26%).

Pentynyl ether 4: $[\alpha]^{21}_D$ -158° (*c* 1.2, cyclohexane); IR (film) 3060, 3040, 2960, 2270, 1460, 1240, 960, 940, 930, 915, 760, 705 cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 0.77 (d, *J* = 6 Hz, 3 H), 0.82 (t, *J* = 6 Hz, 3 H), 1.05 (d, *J* = 6 Hz, 3 H), 1.3–1.6 (m, 2 H), 1.97 (t, *J* = 6 Hz, 2 H), 2.14 (m, 1 H), 4.50 (d, *J* = 7 Hz, 1 H), 7.32 (br s, 5 H); mass spectrum (chemical ionization), *m/e* 217 ($M^+ + 1$, 13%), 150 (100%), 133 (57%).

Pentenynyl ether 6: $[\alpha]^{22}_D$ +7.6° (*c* 1.4, cyclohexane); IR (film) 3070, 2925, 2270, 1640, 1460, 1380, 1235, 990, 915, 840 cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 0.8–1.6 (m, 16 H), 2.90 (m, 2 H), 4.04 (m, 1 H), 4.9–5.4 (m, 3 H), 5.6–6.0 (m, 1 H); mass spectrum (chemical ionization), *m/e* 212 ($M^+ + 18$, 54%), 195 ($M^+ + 1$, 5%), 130 (100%).

Ethynyl Ether 8. In this case, the formation of the dichloro enol ether intermediate was carried out at reflux for 8 h. Ether **8**: mp 76–77 °C (pentane); $[\alpha]^{21}_D$ -28° (*c* 1.5, cyclohexane); IR (film) 3330, 2950, 2140, 1460, 1380, 1090, 955, 910, 840, 800 cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 0.8–2.6 (m, 44 H), 3.9 (m, 1 H), 5.4 (m, 1 H); mass spectrum (electron impact), *m/e* 410 (M^+, 17%), 369 (75%), 368 (100%). Anal. Calcd for $C_{29}H_{46}O$: C, 84.81; H, 11.29; M_r, 410.35486. Found: C, 84.46; H, 11.53; M_r (mass spectrum), 410.35573.

Ethynyl Ether 12. In this case, better results were obtained when the intermediate dichloro enol ether (secured after 6-h reflux) was isolated and subsequently treated in ether (7 mL, mmol) with 3 equiv of butyllithium (-70 → -10 °C, 35 min). Ether **12**: mp 143–144 °C; $[\alpha]^{21}_D$ +11.8° (*c* 1.7, chloroform); IR (film) 3310, 3060, 2160, 1625, 1595, 1280, 1265, 1255, 1220, 1080, 815, 750 cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 1.93 (s, 1 H), 3.77 (s, 3 H), 7.0–7.5 (m, 8 H), 7.7–8.1 (m, 4 H); mass spectrum (electron impact), *m/e* 324 (M^+, 45%), 282 (12%), 281 (40%), 268 (100%); calcd for $C_{23}H_{16}O_2$ M_r 324.11502, found M_r (mass spectrum) 324.11518.

Propynyl Ether 10b. To a stirred suspension of 96 mg (2.4 mmol) of oil-free potassium hydride in 2 mL of tetrahydrofuran at -10 °C was added 292 mg (1.01 mmol) of alcohol **9** in 2 mL of tetrahydrofuran. After the hydrogen evolution was complete, the suspension was treated at -50 °C with a solution of 162 mg (1.23 mmol) of trichloroethylene in 1 mL of dry tetrahydrofuran. The mixture was allowed to warm to room temperature over 1 h and was then poured into a saturated aqueous solution of ammonium chloride. Isolation of the product in the usual manner and purification by dry column chromatography (silica gel pretreated with 2.5% v/v of triethylamine) with 10% ether in pentane gave 318 mg (82%) of the dichloro enol ether: mp 119–120 °C (methylene chloride–hexane); $[\alpha]^{21}_D$ -49° (*c* 1.0, acetone); IR (NaCl) 3100, 2960, 1640, 1335, 1205, 1145, 1085, 955, 945, 820, 765, 705 cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 0.88 (br s, 6 H), 1.18 (t, *J* = 7 Hz, 6 H), 1.0–2.5 (m, 7 H), 2.76 (A of AB q, *J* = 13 Hz, 1 H), 3.2–3.6 (q, *J* = 7 Hz, 4 H; B of ABq, *J* = 13 Hz, 1 H), 4.76 (dd, *J* = 4, 6 Hz, 1 H), 5.36 (s, 1 H); mass spectrum (electron impact), *m/e* 384 (M^+, 1%), 272 (100%). Anal. Calcd for $C_{16}H_{27}O_3Cl_2NS$: C, 49.99; H, 7.08; Cl, 18.45. Found: C, 50.16; H, 7.11; Cl, 18.26. A mixture of 135 mg (0.35 mmol) of the dichloro enol ether, 7.8 mg (1.1 mmol) of lithium powder (2% sodium), and 60 μL (0.4 mmol) of *N,N*-dimethyl-1-naphthylamine in 2 mL of tetrahydrofuran was stirred at -35 °C for 1 h, whereupon 500 mg (3.52 mmol) of methyl iodide (filtered over alumina–phosphorus pentoxide) in 0.5 mL of hexamethylphosphoric triamide was added. The mixture was allowed to warm to room temperature over 1 h and then poured into 20 mL of a 0.5 M aqueous hydrochloric acid solution saturated with ammonium chloride. The product was isolated with ether in the usual way and purified by dry column chromatography (silica gel pretreated with 2.5% v/v of triethylamine) with ether in pentane to afford 110 mg (96%) of propynyl ether **10b**: $[\alpha]^{21}_D$ -26° (*c* 1.2, chloroform); IR (film) 2960, 2940, 2270, 1455, 1335, 1250, 1200, 1150, 1020, 935, 870, 775, 705 cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 0.88 (s, 3 H), 0.94 (s, 3 H), 1.18 (t, *J* = 7 Hz, 6 H), 1.0–2.2 (m, 7 H), 1.72 (s, 3 H), 2.70 (A of AB q, *J* = 13 Hz, 1 H), 3.1–3.5 (q, *J* = 7 Hz, 4 H; B of AB q, *J* = 13 Hz, 1 H), 4.50 (dd, *J* = 4, 8 Hz, 1 H); calcd for $C_{14}H_{26}O_2NS$ M_r 272.16847, found M_r (mass spectrum) 272.16797 ($M^+ - C_3H_3O$).

Ethynyl Ether 10a. This compound was obtained as described above for **10b** (water instead of methyl iodide–hexamethylphosphoric triamide). Ether **10a**: $[\alpha]^{21}_D$ -35° (*c* 1.0, chloroform); IR 3320, 2960, 2155, 1460, 1335, 1205, 1150, 1025, 940, 860, 775, 710 cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 0.88 (s, 3 H), 0.95 (s, 3 H), 1.21 (t, *J* = 7 Hz, 6 H), 1.50 (s, 1 H), 1.1–2.3 (m, 7 H), 2.22 (A of AB, *J* = 13 Hz, 1 H), 3.2–3.5 (q, *J* = 7 Hz, 4 H; B of AB, *J* = 13 Hz, 1 H), 4.64 (dd, *J* = 4, 8 Hz, 1 H); mass spectrum (chemical ionization), *m/e* 313 (M^+, 10%), 272 (100%).

Phenylethynyl Ether 2e. To a stirred solution of 180 mg (1.0 mmol) of ethynyl ether **2a** in 4 mL of tetrahydrofuran at -25 °C was added 0.44 mL (1.1 mmol) of a 2.5 M solution of *n*-butyllithium in hexane. The reaction mixture was allowed to warm to 0 °C and maintained at this temperature for 30 min, whereupon a solution of 245 mg (1.0 mmol) of triphenylborane in 4 mL of tetrahydrofuran was added dropwise. After being stirred at 0 °C for an additional 30 min, the reaction mixture was cooled to -80 °C and treated dropwise over 30 min with a solution of 254 mg (1.0 mmol) of iodine in 4 mL of tetrahydrofuran. After an additional 20 min at -80 °C, the mixture was poured into 30 mL of 40% aqueous potassium hydroxide. The product was extracted into pentane, which was washed with an aqueous solution of sodium thiosulfate. After being dried over sodium sulfate, the solvents were removed under reduced pressure to afford the crude product, which was purified by dry column chromatography (silica gel pretreated with 2.5% v/v of triethylamine) with pentane to give 217 mg (85%) of phenylethynyl ether **2e**: $[\alpha]^{21}_D$ -60° (*c* 1.5, cyclohexane); IR (film) 3080, 3060, 2960, 2250, 1595, 1450, 1315, 1065, 1020, 940, 900, 840, 755, 695 cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 0.7–1.0 (m, 9 H), 1.0–1.8 (m, 7 H), 2.3 (m, 2 H), 3.9 (m, 1 H), 7.0–7.5 (m, 5 H); mass spectrum (electron impact), *m/e* 256 (M^+, 1%), 139 (30%), 118 (53%), 83 (100%); calcd for $C_{10}H_{19}$ M_r

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139.14867, found M_r (mass spectrum) 139.14796 ($M^+ - C_8H_5O$).

3-Methylpentynyl Ether 2d. This compound was obtained as described above for **2e** (tri-*sec*-butylborane in place of triphenylborane). Ether **2d**: $[\alpha]^{19}_D$ −61° (*c* 1.1, cyclohexane); IR (film) 2950, 2260, 1475, 1370, 1250, 1235, 1215, 1150, 1100, 1090, 965, 950, 915, 820 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 0.8–1.0 (m, 12 H), 1.10 (d, *J* = 7 Hz, 3 H), 1.1–1.8 (m, 9 H), 2.3 (m, 3 H), 3.71 (m, 1 H); mass spectrum (chemical ionization), *m/e* 237 (M + 1, 5%), 156 (100%), 139 (25%).

Acknowledgment. We thank Dr. Luche for his interest in our work and the CNRS (UA 332) for financial support. A.M. is grateful to NATO for a post-doctoral fellowship.

Registry No. **1**, 2216-51-5; **2a**, 108167-50-6; **2b**, 108167-51-7; **2c**, 108266-28-0; **2d**, 108167-59-5; **2e**, 108167-60-8; **3**, 34857-28-8; **4**, 108167-52-8; **5**, 6169-06-8; **6**, 108167-53-9; **7**, 57-88-5; **8**, 108167-54-0; **9**, 108167-55-1; **9** (dichloro enol ether), 108167-61-9; **10a**, 108167-56-2; **10b**, 108167-57-3; **11**, 79547-82-3; **12**, 108167-58-4; CH_3I, 74-88-4; C_2H_5I, 75-03-6; n-C_3H_7I, 107-08-4; CH_2=$CHCH_2I$, 556-56-9; triphenylborane, 960-71-4; tri-*sec*-butylborane, 1113-78-6; trichloroethylene, 79-01-6.

An Efficient Synthesis of Partially Protected α-D-Ribofuranosides from D-Ribose by Way of a Unique Selective Debenzylation Reaction

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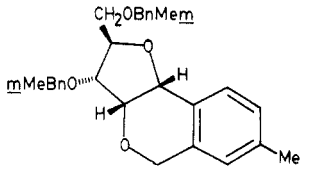
Received November 13, 1986

Selectively protected D-ribofuranose derivatives constitute highly useful synthetic precursors of modified nucleosides such as, for example, (2-deoxy-2-halo-D-arabinofuranosyl)cytosine and -uracil.[1-3] Differentiation of the two secondary positions is, however, a difficult problem, which has precluded a more extensive use of such derivatives: thus, benzylation[4] of methyl 2,3-*O*-dibutylstannylene-α- and -β-D-ribofuranoside, partial de-*O*-acylation[5] of the corresponding peracetates, and mild hydrolysis[6] of 2,3-*O*-(dimethylamino)alkylidene acetals proceed indeed with a modest degree of regioselectivity. There are only two processes of preparative value that allow the formation of partially protected ribofuranoses from the parent sugar: the simultaneous protection of positions 3 and 5 of the furanosides using a tetraisopropyldisiloxane-1,3-diyl group[7,8] and the hydrolysis of tri-*O*-benzoyl-β-D-ribofuranosyl bromide, a reaction that affords 1,3,5-tri-*O*-benzoyl-α-D-ribofuranose in good yield.[9] In spite of its limited stability and its susceptibility to acyl group migration, the latter compound has been used successfully as an intermediate in the synthesis of a few arabino nucleosides.[3,10] However, most of the partially protected ribofuranose derivatives used in nucleoside synthesis (2-*O*-methyl,[11] 2-*O*-benzyl,[12] 3-*O*-benzyl,[4] 3,5-di-*O*-benzyl[1a,2]) have been prepared from other sugars (D-arabinose, D-xylose, or D-glucose) by way of lengthy procedures involving, at some stage, an inversion of configuration or a chain-shortening step. We report, in this paper, a novel reaction that makes selectively protected α-D-ribofuranosides readily available from D-ribose; the resulting derivatives are ideally suited for conversion into 2-substituted arabinofuranosides and the corresponding nucleosides.

During previous investigations on the behavior of benzylated sugars in the presence of a Lewis acid,[13] we had observed that two different reactions occurred when methyl 2,3,5-tri-*O*-(3-methylbenzyl)-β-D-ribofuranoside was treated with tin(IV) chloride: intramolecular alkylation[14] of the 2-*O*-benzyl group, to form an internal *C*-glycoside (30%) (compound **1**), and cleavage of this group with anomerization, to give methyl 3,5-di-*O*-(3-methylbenzyl)-α-D-ribofuranoside (**2**) as the major product (50%).



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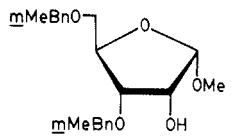

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As it is likely that the two processes involve a common intermediate,[15] we considered that it might be possible to increase the effectiveness of the unusual selective debenzylation pathway by using benzyl groups less prone to electrophilic substitution. Replacement of the 3-methylbenzyl groups by 4-chlorobenzyl groups indeed effectively suppressed the C-glycosidation component of the reaction: compound **3**, prepared from methyl D-ribofuranoside under standard conditions, afforded almost exclusively[16] methyl 3,5-di-*O*-(4-chlorobenzyl)-α-D-ribofuranoside **4**[17] on reaction with tin(IV) chloride (Scheme I). This remarkable reaction thus brings about *the cleavage of the 4-chlorobenzyl group at O-2 specifically and the simultaneous inversion of the anomeric configuration.* As α-ribofuranosides constitute much better substrates for nucleophilic displacements at C-2 than the corresponding β-isomers,[2] anomerization is a particularly fortunate feature of this reaction: for example, we have obtained D-arabino azido sugar **8** from compound **4** by way of triflate **7** in 77% overall yield. The remaining 4-chlorobenzyl groups were then cleaved[18] and the azido group reduced by hydrogenolysis, thus providing methyl 2-amino-2-deoxy-α-D-arabinofuranoside **9**[19] in four steps only from **3**.

As previously suggested,[15] formation of **4** might involve initially a tin(IV)-mediated anomerization of the β-glyco-

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0022-3263/87/1952-2922$01.50/0