δ 10.94, 21.49, 22.84, 31.06, 51.32, 52.12, 173.11, 204.07. Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 61.01; H, 9.01.

***N*-Benzyl-5-ethyl-3,4-dihydro-2-pyridone (3).** Methyl 4-formylhexanoate (**2**, 3.00 g, 19.0 mmol), benzylamine (2.07 mL, 2.03 g, 19.0 mmol, 1.0 equiv), and dry toluene (20.0 mL) were placed in a 50-mL round-bottomed flask equipped with a magnetic stirring bar and a Dean–Stark trap. The reaction mixture was heated at reflux for 6 h, and 10 mL of the toluene–water azeotrope was drained off. An additional 30 mL of fresh toluene was added, and the solution was heated at 95 °C for 12 h. The reaction mixture was heated to reflux, and 20 mL of the toluene–methanol azeotrope was drained off. The remaining solvent was removed with a rotary evaporator to give a crude product, which was purified by bulb-to-bulb distillation under reduced pressure to afford 3.93 g (96%) of **3** as a colorless liquid: bp 120–130 °C (0.15–0.50 Torr); IR (film) 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (t, 3, J = 7.4), 2.02 (q, 2, J = 7.4), 2.27 (t, 2, J = 8.0), 2.58 (t, 2, J = 8.0), 4.67 (s, 2), 5.75 (quintet, 1, J = 1.3), 7.28 (m, 5); ^{13}C NMR ($CDCl_3$) δ 12.09, 23.93, 26.50, 31.03, 48.55, 121.64, 122.70, 127.04, 127.26, 128.30, 137.16, 168.56. Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51. Found: C, 77.96; H, 7.98; N, 6.45.

***N*-Benzyl-5-ethyl-1,2,3,4-tetrahydropyridine (4). (a) From *N*-Benzyl-5-ethyl-3,4-dihydro-2-pyridone (3).** To a flame-dried 50-mL round-bottomed flask equipped with a magnetic stirring bar was added $LiAlH_4$ (1.30 g, 34.2 mmol, 7.0 equiv) and dry THF (10.0 mL). The gray suspension was cooled to 0 °C in an ice bath and placed under a nitrogen atmosphere. A solution of lactam **3** (1.05 g, 4.89 mmol) in 5.0 mL of dry THF was added over a 10-min period. After 30 min at 0 °C and 24 h at room temperature, the solution was cooled in an ice bath and the reaction was quenched by the slow addition of water (1.30 mL), 15% NaOH (1.30 mL), and water (3.90 mL). The resulting salts were filtered and washed with ether. The ether filtrate was dried over $MgSO_4$, filtered, and reduced in volume to afford 0.98 g of crude material. The product was purified by bulb-to-bulb distillation under reduced pressure to give 0.873 g (89%) of **4** as a colorless liquid: bp 95–100 °C (0.30 Torr) [lit.[1b] bp 91–94 °C (0.25 Torr)]; IR (film) 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (t, 3, J = 7.4), 1.89 (m, 6), 2.73 (t, 2, J = 5.4), 3.87 (s, 2), 5.76 (s, 1), 7.28 (m, 5); ^{13}C NMR ($CDCl_3$) δ 13.07, 22.54, 24.55, 28.21, 47.34, 59.89, 112.34, 126.82, 128.10, 128.20, 130.43, 138.70. Anal. Calcd for $C_{14}H_{19}N$: C, 83.53; H, 9.51; N, 6.96. Found: C, 83.56; H, 9.56; N, 6.82.

(b) From Butanal. The foregoing procedure was employed without purification of intermediates. Piperidine (25.00 g, 29.00 mL, 0.294 mol) and anhydrous K_2CO_3 (6.00 g, 0.0434 mol) gave rise to 19.81 g of crude 1-(*N*-piperidinyl)-1-butene (**1**) as a colorless oil. A solution of this material and methyl acrylate (13.66 g, 14.28 mL, 0.159 mol, 1.25 equiv) in 100 mL of acetonitrile was heated at reflux for 21.5 h to obtain 17.72 g of aldehyde ester **2** as a light, yellow oil. This material was refluxed with benzylamine (12.24 g, 0.114 mol, 1.02 equiv) in 120 mL of dry toluene with removal of water to obtain 25.56 g of *N*-benzyl-5-ethyl-3,4-dihydro-2-pyridone (**3**) as a light yellow oil. Lactam **3** was reduced as indicated in the foregoing procedure with $LiAlH_4$ (8.88 g, 0.254 mol, 2.0 equiv) to obtain 22.22 g of crude **4**. Purification by bulb-to-bulb distillation under reduced pressure gave 20.43 g (80% from butanal) of **4** as a light yellow oil, identical spectrally with that obtained by method a.

Acknowledgment. This work was supported by a research grant from the National Science Foundation (CHE 8418437).

Communications

Retention of Configuration in the Coupling of Aluminated Heterocycles with Glycopyranosyl Fluorides

Summary: Coupling reactions between glycopyranosyl fluorides and 2-(diethylaluminio)furan and 2-(diethylaluminio)-1-methylpyrrole giving the corresponding sugar heterocycles are observed to proceed with retention of configuration at the anomeric center. Couplings of the same aluminated heterocycles with ribofuranosyl fluorides gave predominantly the β-ribofuranosyl heterocycle.

Sir: In connection with our ongoing studies toward the total synthesis of *C*-glycosyl antibiotics,[1] we became interested in the preparation of glycopyranosylfurans. Although there is ample precedent in the literature for the construction of glucosyl heterocyclic ring systems from various precursors,[2] recent reports concerning the coupling of sugar fluorides with organoaluminum reagents[3] suggested an alternative, more convergent route to glycopyranosylfurans. This communication reports that coupling for glycopyranosyl fluorides with certain aluminated heterocycles occurs readily, and moreover, *the coupling proceeds with retention of configuration at the anomeric center.* Ribofuranosyl fluorides in similar coupling reactions give predominantly the β-ribofuranosyl heterocycle.

With the recently developed reagents for the preparation of particular anomeric glycosyl fluorides[4,5] and the constant need for new *C*-glycosyl forming reactions for total synthesis of natural products and biologically active compounds, this methodology may prove to be particularly useful.

The sugar fluorides were prepared according to literature procedures. Thus 2,3,4,6-tetra-*O*-benzyl-β-D-glyco-

(1) Ravidomycin: Findlay, J. A.; Liu, J.-S.; Radics, L.; Rakhit, S. *Can. J. Chem.* **1981**, *59*, 3018. Findlay, J. A.; Liu, J.-S.; Radics L. *Can. J. Chem.* **1983**, *61*, 323. Synthetic studies include: Findlay, J. A.; Daljeet, A.; Murray, P. J.; Rej, R. N. *Can. J. Chem.* **1987**, *65*, 427. McKenzie, T. C.; Hassen, W. *Tetrahedron Lett.* **1987**, *28*, 2563. McKenzie, T. C.; Hassen, W.; Macdonald, S. J. F. *Tetrahedron Lett.* **1987**, *28*, 5435. Macdonald, S. J. F.; McKenzie, T. C.; Hassen, W. D. *J. Chem. Soc., Chem. Commun.* **1987**, *1528*. Outten, R. A.; Daves, G. D. *J. Org. Chem.* **1987**, *52*, 5064. Toromycin: Hori, S.; Fukase, H.; Mizuta, E.; Hatano, K.; Mizano, K. *Chem. Pharm. Bull.* **1980**, *28*, 3601. Albacarcin: Matson, J. A.; Myllymaki, R. W.; Doyle, T. W.; Bush, J. A. U.S. Pat 4 461 831, 1984; *Chem. Abstr.* **1985**, *102*, P4456a. Gilvocarcin: Takahashi, K.; Yoshida, M.; Tomita, F.; Shirahata, K. *J. Antibiot.* **1981**, *34*, 271. Virenomycin: Brazhnikova, M.; Kudinova, M. K.; Kulyaeva, V. V.; Potapova, N. P.; Rubasheva, L. M.; Rozynova, B. V.; Horvath, G. *Antibiotika (Moscow)* **1984**, *29*, 884; *Chem. Abstr.* **1985**, *102*, 185366q. Chrysomycin: Weiss, V.; Yoshihira, K.; Highet, R. J.; White, R. J.; Wei, T. T. *J. Antibiot.* **1982**, *35*, 1194.

(2) For examples, see: Buchanan, J. G. In *Progress in the Chemistry of Organic Natural Products*; Herz, W.; Grisebach, H., Kirby, G. W.; Ed.; Springer-Verlag: New York, 1983; Vol. 44, pp 243–299. Schmidt, R. R.; Effenberger, G. *Liebigs Ann. Chem.* **1987**, 825.

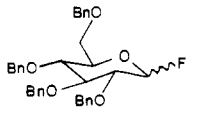
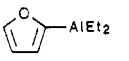
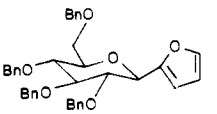
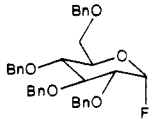
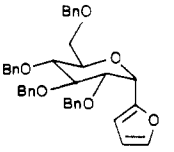
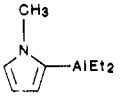
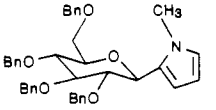
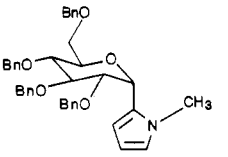
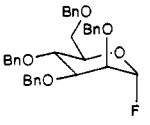
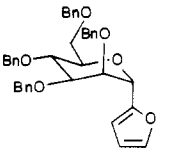
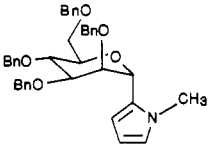
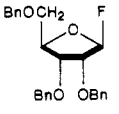
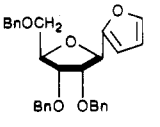
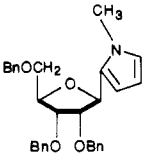
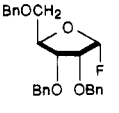
(3) (a) Nicolaou, K. C.; Dolle, R. E.; Chucholowski, A.; Randall, J. L. *J. Chem. Soc., Chem. Commun.* **1984**, 1153, 1155. (b) Nicolaou, K. C.; Dolle, R. E.; Papahatjis, D. P.; Randall, J. L. *J. Am. Chem. Soc.* **1984**, *106*, 4189. (c) Posner, G. H.; Haines, S. R. *Tetrahedron Lett.* **1985**, *26*, 1823.

(4) Rosenbrook, W.; Riley, D. A.; Lartey, P. A. *Tetrahedron Lett.* **1985**, *26*, 3. Posner, G. H.; Haines, S. R. *Tetrahedron Lett.* **1985**, *26*, 5.

(5) Hayashi, M.; Hashimoto, S.; Noyori, R. *Chem. Lett.* **1984**, 1747. Szarek, W. A.; Grynkiewicz, G.; Doboszewski, B.; Hay, G. W. *Chem. Lett.* **1984**, 1751.

0022-3263/88/1953-3371$01.50/0

Table I. Products from the Coupling Reactions

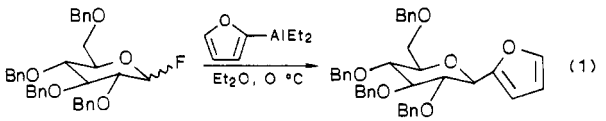
sugar (Bn is $PhCH_2$)	aluminated heterocycle	product	yield,[a] %
 1[b] $\beta:\alpha = 2.5:1$	 3		45[c]
 2	3		62[d]
1	 4		70[e]
2	4		79[f]
 5	3		70[g]
5	4		77[g]
 6	3	 7	39[h]
6	4	 8	82
 9	3	7	51[i,j]
9	4	8	44

[a] Yields refer to pure isolated products. [b] Pure β-fluoride is unobtainable as the R_f's of both and anomers are identical in numerous solvent systems. [c] The crude yield of reasonably pure material (by ^1H NMR) was 78%; considerable loss of product occurred on chromatography. [d] A 3:1 $\alpha:\beta$ mixture of products was obtained for this coupling reaction. [e] 14% of the β-anomer was observed in the ^1H NMR spectrum of the crude material. Only the α-anomer could actually be isolated. [f] 7% yield of the β-anomer was also isolated. [g] The β-mannopyranosyl fluoride was unobtainable; treatment of the mannopyranoside with DAST gave the α-fluoride only. [h] The crude yield of reasonably pure material (by ^1H NMR) was 70%; considerable loss of product occurred on chromatography. [i] When reaction times are longer than 30 min another unidentified product (not the α-anomer) begins to be formed. [j] Attempted epimerization of a mixture of the anomers to the β-anomer only with $CDCl_3$/trifluoroacetic acid (ref 11) failed.

pyranosyl fluoride (1) was prepared as the major product ($\beta:\alpha$, 2.5:1) by treatment of the corresponding pyranoside with diethylaminosulfur trifluoride (DAST),[4] and the α-fluoride (2) by treatment of the pyranoside with pyridine–HF.[5] The aluminated heterocycles were prepared by lithiation of the heterocycles (furan[6] and 1-methylpyrrole[7]) and subsequent reaction with diethylaluminum chloride.

(6) Ramanathan, V.; Levine, R. *J. Org. Chem.* **1962**, *27*, 1216.

The first coupling was carried out by addition of the mainly β-fluoride (1) to 5 equiv of (diethylaluminio)furan (3) at 0 °C (eq 1). The reaction was monitored by TLC



β:α = 2.5:1

crude yield 78%
purified yield 45%

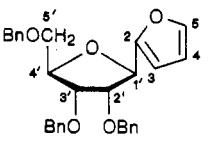
and was over within 5 min. After quenching with a mixture of water, brine and a saturated solution of sodium hydrogen carbonate (1:1:1 v:v:v), and workup,[8] the crude product (78% yield of reasonably pure material) was purified by chromatography and recrystallization to give 2-(2,3,4,6-tetra-*O*-benzyl-β-D-glycopyranosyl)furan as white crystals in 45% yield.

The retention of configuration of this coupling reaction is demonstrated by the results given in Table I.[9] The stereochemistry of the products was determined by decoupling and 2-D COSY NMR experiments, in which the diastereotopic nature of the methylenes of the benzyl protecting groups caused considerable difficulties in the assignment of the anomeric protons.

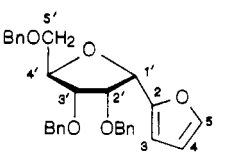
The mechanistic reasons for high retention of configuration in the coupling reaction is not yet known. For these examples though it appears that oxonium ions are not likely to be intermediates. Posner had demonstrated stereospecificity in the case of a bridged 1,6-anhydro sugar where one fluorine isomer reacted with retention of configuration at C-6 (cf. ref 3c).

In contrast to the retention of configuration observed with couplings of pyranosyl fluorides, coupling with ribofuranosyl fluorides gave predominantly the β-coupled products (Table I).[9] In one experiment however, starting with an anomeric mixture of ribofuranosyl fluorides **6** and **9** and using an acidic workup, a separable 1:1 mixture of anomeric (ribofuranosyl)furans **7** and **10** (56% total yield) was obtained. Having both anomers facilitated the assignment of the stereochemistry of the coupled products, principally through NOE experiments.

Thus for **7** ($J_{1'2'}$ = 6.1 Hz) irradiation of H-1′ gave NOE enhancements at H-3 (4.4%), H-4′ (3.9%), and H-2′ (3.8%). Irradiation of the two H-5′ signals gave enhancements at H-3′ (4.5%) and H-4′ (11.6%) but none at H-1′, H-3, H-4, or H-5.



7



10

For **10** ($J_{1'2'}$ = 9.8 Hz) irradiation of H-1′ gave NOE enhancements at H-3 (4.7%), 2H-5′ (4.9%), and H-2′ (2.3%). Irradiation of the two H-5′ signals gave enhancement at H-1′ (12.5%) (no enhancements at H-3′ or H-4′ were observed due to the proximity in chemical shifts of H-3′, H-4′, and H-5′).

The coupling reaction has been attempted with other aluminated heterocycles (1-methylimidazole, thiophene, and thiazole) and benzene derivatives without much success.[10] It is not yet clearly understood why these couplings fail, while those with aluminated 1-methylpyrrole and furan succeed. The use of benzyl protecting groups on the sugar is also important, as the use of ester protecting groups (acetate or benzoate) results in either a substantial drop in yield or no reaction at all.

The synthetic and mechanistic aspects of these reactions are being actively pursued in these laboratories. The complete spectroscopic analysis and experimental details of these and other examples will be described elsewhere in due course.

Acknowledgment is made to the National Institutes of Health (CA 36868-03) for financial support and to Dr. K. Belmore (University of Alabama) and Dr. R. Jones (Emory University) for NMR experiments.

(7) Chadwick, D. J.; Willbe, C. *J. Chem. Soc., Perkin Trans. I* **1977**, 887.

(8) Although this workup produces insoluble aluminum salts, it avoids the possibility of epimerization that is associated with an acidic workup.

(9) All new compounds gave satisfactory spectral and analytical data. A representative experimental procedure is as follows. To a stirred solution of 1-methylpyrrole (0.82 mL, 9.2 mmol) in dry diethyl ether (30 mL) under a nitrogen atmosphere was added freshly distilled tetramethylethylenediamine (1.39 mL, 9.2 mmol) and *n*-butyllithium (2.5 M solution in hexanes) (3.7 mL, 9.2 mmol). The mixture was stirred at room temperature for $^1/_2$ h and then cooled to −78 °C. After purging the solution with dry nitrogen, diethylaluminum chloride (1.8 M solution in toluene) (5.1 mL, 9.2 mmol) was added and the mixture allowed to warm to room temperature and then stirred overnight. A white precipitate was formed. To this mixture cooled to 0 °C was added a nitrogen-purged solution of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl fluoride (a 2.5:1 mixture of β:α anomers) in toluene (dried over 4A molecular sieves) (10 mL of solution, 1.00 g, 1.84 mmol), and the coupling was followed by TLC (80:20 hexanes/ethyl acetate). After 1 h the reaction was quenched with a mixture of water, brine, and a saturated sodium hydrogen carbonate solution (1:1:1, v:v:v, 60 mL) and stirred for $^1/_2$ h. The product was extracted with diethyl ether (3 × 50 mL) and the combined extracts were washed with 1 M hydrochloric acid (4 × 25 mL) and water (1 × 25 mL) and then dried ($MgSO_4$). Solvent removal and chromatography on Davisil eluting with hexanes/ethyl acetate (90:10), followed by recrystallization (hexanes/ethyl acetate) gave 2-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)-1-methylpyrrole (0.77 g, 70%) as a white solid, mp 107–108 °C.

(10) The exception to this statement is the coupling between aluminated thiophene and the β-ribofuranosyl fluoride which proceeds in moderate yield.

(11) Maeba, I.; Iwata, K.; Usami, F.; Furukawa, H. *J. Org. Chem.* **1983**, *48*, 2998.

Simon J. F. Macdonald, Wouter B. Huizinga
Thomas C. McKenzie*
Department of Chemistry
University of Alabama
Tuscaloosa, Alabama 35487
Received March 8, 1988

Accelerated Inverse Electron Demand Diels–Alder Reactions of 1-Oxa-1,3-butadienes: [4 + 2] Cycloaddition Reactions of β,γ-Unsaturated α-Keto Esters

Summary: The demonstration and full investigation of the scope of the accelerated 4π participation of methyl *trans*-4-methoxy-2-oxo-3-butenoate (**1**) and methyl *trans*-4-phenyl-2-oxo-3-butenoate (**2**), electron-deficient 1-oxa-1,3-butadienes bearing a C-2 electron-withdrawing substituent, in productive endo selective inverse electron demand Diels–Alder reactions suitable for the preparation of 2-alkoxy-3,4-dihydro-2*H*-pyran-6-carboxylates are detailed.

Sir: The 4π participation of simple α,β-unsaturated aldehydes and ketones, electron-deficient heterodienes bearing a terminal oxygen atom, in $LUMO_{diene}$-controlled Diels–Alder reactions typically suffers from low conversions, competitive polymerization, and harsh reaction conditions.[1,2] Consequently, a limited number of 1-oxa-

0022-3263/88/1953-3373$01.50/0