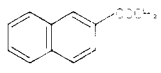
Table II. Asymmetric Reduction of Various Aromatic Ketones with Modified Reagent Prepared from Sodium Borohydride and $(CH_3)_2CHCOOH$ in the Presence of 1 in Tetrahydrofuran at 25 °C[a]

run[i]	ketones	yield,[b] %	$[\alpha]^{20}_D$	optical yield, %[c]
11	$C_6H_5COCH_3$	77	+33.6[d]	64
12	$C_6H_5COC_2H_5$	56	+29.5	63
13	$C_6H_5COC_3H_7$-*n*	66	+23.9[e]	55
14	$C_6H_5COC_3H_7$-*i*	80	+8.44[f]	18
15		100	+22.3[g]	53
16	*i*-$C_4H_9COCH_3$	70	−2.53[h]	12

[a] Conditions: reactions for 72 h; $NaBH_4$, 30 mmol; $(CH_3)_2CHCOOH$, 30 mmol; 1, 120 mmol; ketone, 30 mmol; total volume of the solvent, 50 mL. [b] Determined on the basis of relative peak areas of carbinol and unreacted ketone by GLC. [c] Optical yield was calculated by optical rotation. [d] Maximum value for $[\alpha]^{23}_D$ −52.5° (*c* 2.27, CH_2Cl_2).[15] [e] Maximum value for $[\alpha]^{20}_D$ − 43.6° (*c* 4.18, C_6H_6).[16] [f] Maximum value for $[\alpha]^{20}_D$ +47.7° (*c* 6.8, diethyl ether).[17] [g] Maximum value for $[\alpha]^{20}_D$ −41.9° (*c* 5.0, C_2H_5OH).[18] [h] Maximum value for $[\alpha]^{23-25}_D$ +21.1 (neat).[19] The optical rotations of carbinols were measured in the same solvents reported above. [i] The absolute configuration was *R* in all cases.

in tetrahydrofuran by the solubility limitation of 1 under the same conditions.

By use of the most effective reagent prepared from sodium borohydride and $(CH_3)_2CHCOOH$, a series of ketones were examined in the presence of 1 when the molar ratio of sodium borohydride/$(CH_3)_2CHCOOH$/1 was 1:1:4, and the reactions were found to proceed with varing degrees of success (Table II). Acetophenone, propiophenone, phenyl *n*-propyl ketone, and β-naphthyl methyl ketone appear to lead to the corresponding phenylcarbinols and a naphthylcarbinol in reasonably high optical yield (≥50%), whereas phenyl isopropyl ketone and isobutyl methyl ketone gave rather low percentages of asymmetric induction. For reasons still not understood at present, under all conditions used this system gave chiral phenylcarbinols possessing the *R* configuration.

The convenience of the experimental procedure and the ready availability of 1 by one-step condensation from D-glucose and acetone as well as great potential for more pronounced stereoselectivity for examining the modification of reagents (the combination of sodium borohydride/carboxylic acid/hydroxymonosaccharide derivative) make the present method attractive, despite the lack of consistently good asymmetric reduction on various ketones.

Experimental Section

Reagents. The ketones used were purified by being dried over CaH_2 and subsequently distilled under an atmosphere of nitrogen. Tetrahydrofuran was heated under reflux over sodium wire and distilled over $LiAlH_4$ under a nitrogen atmosphere. Carboxylic acids were distilled twice in a nitrogen atmosphere. Sodium borohydride was purified twice by recrystallization from 2,5,8-trioxanonane (diglyme). 1,2:5,6-Di-*O*-isopropylidene-α-glucofuranose was prepared according to a previous method.[10]

All the materials described were stored under a nitrogen atmosphere prior to use.

Instruments. Rotations were taken on a Zeiss Visual polarimeter with readings to ±0.02°. Gas chromatographic determinations were made on a Simazu GC-6A using a silicon SE-30 prepared column.

Procedures. All the experiments were carried out under a nitrogen atmosphere. The following is a detailed description of a typical experiment. A solution containing 2.64 g (30 mmol) of $(CH_3)_2CHCOOH$ in 10 mL of THF at 0 °C was added to 20 mL of a THF suspension containing sodium borohydride (30 mmol). A thick white precipitate appeared along with evolution of about 30 mmol of hydrogen. Three hours after the initial mixing, 31.2 g (120 mmol) of 1 in 20 mL of THF was added to the reagent formed. After the mixture was stirred for 1 h at 30 °C, to the resulting reagent was added propiophenone (4.02 g, 30 mmol) at 25 °C within 5 min of mixing, and the reduction mixture was stirred at 25 °C for 72 h. The reaction mixture was then hydrolyzed with excess 1 N HCl solution. The mixture was stirred an additional 1 h to hydrolyze compound 1 completely. Sodium hydroxide solution (50%) was added and the pH adjusted to 11. The ether extracts were washed with H_2O (three times), dried ($MgSO_4$), and concentrated to give a colorless oil. The crude product was purified by fractional distillation under reduced pressure. The purity was determined by GLC. Neither 1 nor any other compounds except unreacted ketone was detected by TLC, GLC, and GPC. Pure carbinol was isolated by preparative TLC. The optical yield was obtained from the known maximum rotation of the carbinol and the optical rotation of the sample isolated in the same solvent.

Registry No. 1, 28528-94-1; propiophenone, 93-55-0; sodium borohydride, 16940-66-2; acetic acid, 64-19-7; propanoic acid, 79-09-4; decanoic acid, 334-48-5; 2-methylpropanoic acid, 79-31-2; 2,2-dimethylpropanoic acid, 75-98-9; diphenylacetic acid, 117-34-0; α-ethylbenzeneacetic acid, 90-27-7; (*R*)-α-ethylbenzenemethanol, 1565-74-8; acetophenone, 98-86-2; butyrophenone, 495-40-9; isobutyrophenone, 611-70-1; 2-acetylnaphthalene, 93-08-3; 4-methyl-2-pentanone, 108-10-1; (*R*)-α-methylbenzenemethanol, 1517-69-7; (*R*)-α-propylbenzenemethanol, 22144-60-1; (*R*)-α-(1-methylethyl)-benzenemethanol, 14898-86-3; (*R*)-α-methyl-2-naphthalenemethanol, 52193-85-8; (*R*)-4-methyl-2-pentanol, 16404-54-9.

Stereoselective Synthesis of (±)-1-*O*-Methylloganin, 10-Hydroxyloganin, Secologanin, and Sweroside Aglucons from a Common 1-Hydroxy-4a,5,8,8a-tetrahydroisochromene Synthon[1]

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We have been investigating routes for the total synthesis of cyclopentanoid monterpenes ("iridoids"[3]) in which we are currently interested from a biogenetic and pharmacological viewpoint. One synthetic strategy has led, through a fruitful collaboration with researchers at Hoffmann-La Roche, to an efficient synthesis of (±)-1-*O*-methylsweroside (**2**) and (±)-1-*O*-methylsecologanin (**3**) aglucons from the (±)-1-hydroxy-4a,5,8,8a-tetrahydroisochromene synthon (**1**).[4] We now describe a modification of our original chemistry for the synthetic utilization of **1**,[4] which enables the synthesis of the following four racemic aglucon *O*-methyl ethers from **1**: 10-hydroxyloganin (**4**) and loganin (**5**), as well as **2** and **3**, formally. These new results nicely complement the synthesis of **2**–**5** carried out

(1) Supported in part by a research grant from the National Institutes of Health (CA 17127).

(2) Research Career Development Awardee of the National Cancer Institute (CA 00253), 1976–1981.

(3) Briggs, L. H.; Cain, B. F.; LeQuesne, P. W.; Shoolery, J. N. *Tetrahedron Lett.* **1963**, 69.

(4) Hutchinson, C. R.; Mattes, K. C.; Nakane, M.; Partidge, J. J.; Uskokovic, M. R. *Helv. Chim. Acta* **1979**, *61*, 1221.

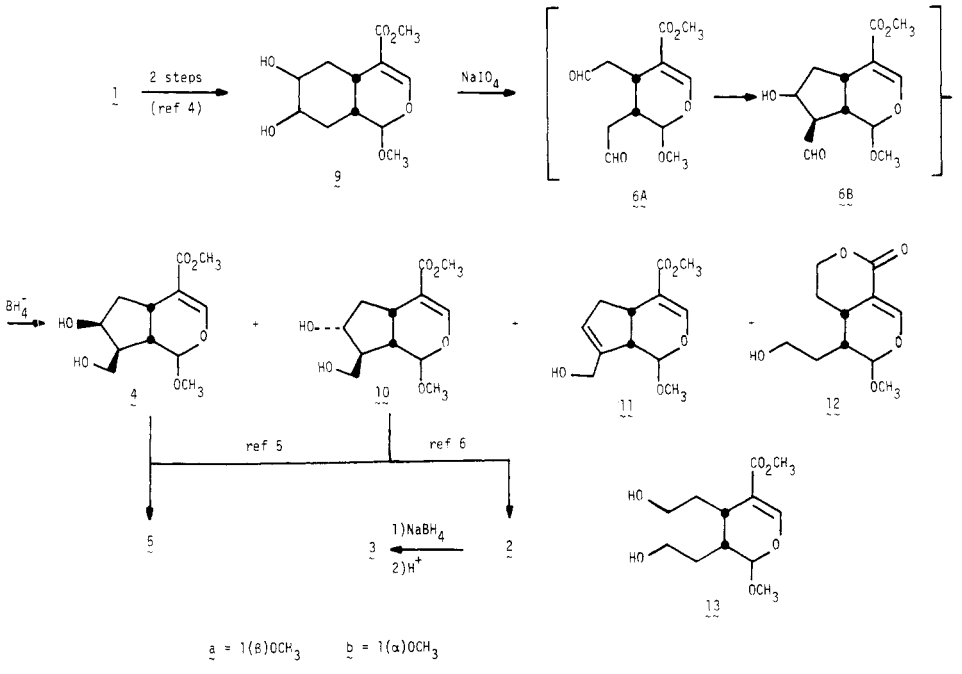
0022-3263/80/1945-4233$01.00/0

Table I. Products of Aldol Cyclization-Reduction of 6A[a]

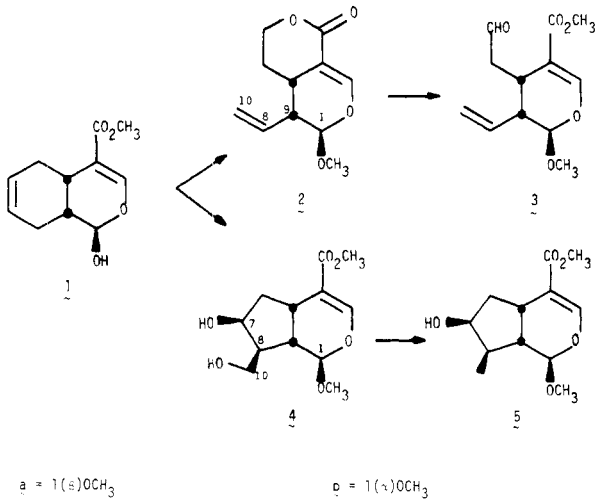
expt	base (equiv), solvent	temp, °C, time	% yield[b,f] 4	10	11	12	13
1	Et_3N (1.0), *i*-PrOH	25, 3 h		29		34	
2	$Mg(OMe)_2$ (1.1), MeOH	0, 5 min	26	21		7	13
3	Mg(O-*t*-Bu)Cl (14), THF	25, 4 h	t[c]	t	42	19	
4	Zn(O-*t*-Bu)Cl (6), THF	25, 18 h	t	t	t	33	
5	$LiN(i\text{-}Pr)_2$ (1.1), THF	−78, 15 s[d]	t	t	t	50	
6	Et_3N (2.2), Me_3SiCl, THF	−15–0, 75 min	9	48	t		
7	Pyr (1.5 mL), Ac_2O	25, 3.4 h		31	5		
8	Pyr (1.5 mL), $(i\text{-}Pr)_2NEt$ (1.5), Ac_2O	25, 2.5 h		33	11		
9	$(i\text{-}Pr)_2NEt$ (1.5), Ac_2O, 4-DMAP (cat.)	0, 24 h[e]		48	5		

[a] The reactions were run until **6A** had almost disappeared (TLC) and were then reductively worked up as described in the experimental section. [b] No entry indicates that the product's yield was <2%. [c] t indicates that the product's yield was 2–5%. [d] Saturated aqueous NH_4Cl was added before reductive workup. A longer reaction time (20 min) gave 10% **12** plus only very polar side products. [e] The reaction was incomplete after ca. 3 h. [f] Minor products other than those shown also were formed, which in part accounted for the mass balance.

Scheme I

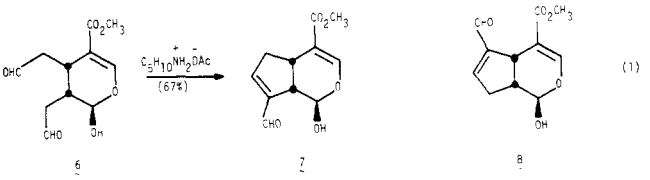


earlier by Tietze[5] and Kinast and Tietze[6] and represent the most efficient synthetic routes to **2–5** to be described in the literature.[7]



(5) Tietze, L.-F. *Chem. Ber.* **1974**, *107*, 2499.
(6) Kinast, G.; Tietze, L.-F. *Chem. Ber.* **1976**, *109*, 3626.

The strategy for our total synthesis of the title compounds is based on the observation of Büchi et al.[8] that the intramolecular aldol condensation of **6** is regiospecific, yielding only aldehyde **7**; none of the isomer **8** is formed under their cyclization conditions (eq 1). We felt that if



(1)

the intramolecular aldol condensation product of **6** formed with the desired stereoselectivity [7α or 7β OH, 8β CHO], this product could be diverted to **4** or its C-7 epimer by reduction with $NaBH_4$ in situ. This goal has been achieved as described below.

We were stimulated to consider the practicality of a synthesis of **2–5** from **1** by the results of expt 1, Table I.

(7) (a) Büchi, G.; Carlson, J. A.; Powell, J. E., Jr.; Tietze, L.-F. *J. Am. Chem. Soc.* **1973**, *95*, 540. (b) Partidge, J. J.; Chadha, N. K.; Uskokovic, M. R. *Ibid.* **1973**, *95*, 532. (c) Au-Yeung, B.-W.; Fleming, I. *J. Chem. Soc., Chem. Commun.* **1977**, 81.
(8) Büchi, G.; Schneider, R. S.; Wild, J. *J. Am. Chem. Soc.* **1967**, *89*, 2776.

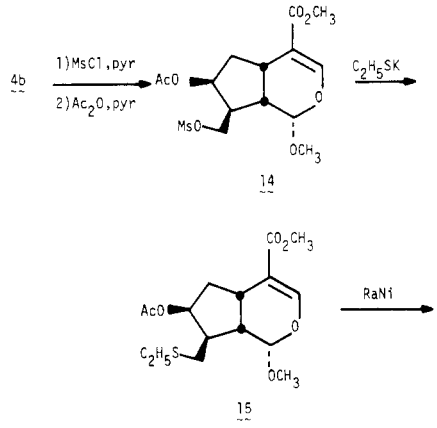
These particular experimental conditions had been chosen in an attempt to trap the C-7 aldehyde of **6A** (Scheme I) as its 7-*O*-methyl acylal with the carboxyl group for possible simplification of our earlier synthesis of **2** and **3**.[4] The formation of 1-*O*-methyl-7-epi-10-hydroxyloganin aglucon (**10**) in this experiment led us to examine other reaction conditions that would be expected to enhance the yield of aldol products (**4**, **10**) relative to the yield of the dehydrated aldol product **11** and **12** or **13**, both of which result from the reduction of uncyclized **6**.

It is stated[9] that for the intermolecular aldol condensation of two aldehydes the reaction at equilibrium favors the aldol product (despite the fact that enolate formation is the rate-determining step) yet is reversible in protic solvents. We thus decided to examine reagents that might influence the stereoselectivity of the aldol reaction of **6A**—formation of **4** vs. **10**—via intramolecular chelation and/or aldol trapping effects exerted on intermediate **6B**.

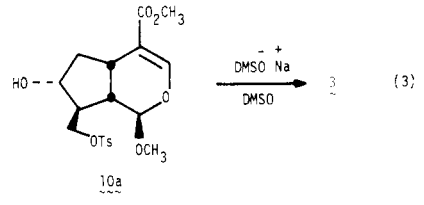
Table I lists the results of nine experiments which were designed to test the above propositions. Since **6A** was too unstable for purification before being used as the starting material, it was formed from **9**[4] and then was used directly for the aldol condensations. Thus, the yields of **4** and **10**–**13** given in Table I are the three-step, overall reaction yields from diol **9**. Clearly, the experimental conditions that could trap aldol product **6B** irreversibly (expt 6–9) had a more specific influence on the reaction stereoselectivity than those conditions that could form intramolecular chelates[10] of **6B** (expt 2–5) prior to reduction of the C-10 aldehyde. The fact that only the 7α alcohol diastereomer (**10**) formed under the former reaction conditions probably reflects trapping of the kinetic aldol condensation product, since the 7β alcohol diastereomer (**4**) should be the thermodynamic product.[11] In distinct contrast, the result of expt 2 shows that a weakly basic reagent which is capable of forming an intramolecular chelate with **6A**, as its enolate, or with **6B**, can influence the aldol reaction's stereoselectivity to yield more of the thermodynamic product **4** than that formed in the presence of either a weak base (expt 1) or strong base (expt 5) alone. It seems very likely to us that the chelating base favored the formation of **4** because intramolecular chelates of this diastereomer are easier to form than the chelates of **10**, at least as deduced from inspection of Dreiding molecular models.

The base strength is also known to be an important factor in aldol condensations,[9] which the results of expt 3–5 demonstrate. The formation of **11** only in expt 3 reflects the tendency of the aldol products **4** and **10** to dehydrate on prolonged exposure to base. The low mass balances of expt 4 and 5 plus the predominant recovery of starting material (**6A** → **12**) reflect that the base was too weak to effect the aldol reaction (expt 4) or that the base caused extensive side reactions (expt 5) leading to very polar compounds of unknown nature.

The synthesis of **4** and **10** by the aldol condensation of **6A** is a formal synthesis of **5a**, since the latter compound has been prepared from its 7α epimer through S_N2 displacement of a 7α-mesylate with $Et_4N^+AcO^-$[7a] followed by the C-7β acetate's hydrolysis and since 7-epi-7-*O*-acetyl-**5a** has been prepared from 7-*O*-acetyl-**10a** in 53% overall yield by a three-step reaction sequence.[5] We confirmed the latter report by transforming **4b** to the previously unknown **5b** in 39% overall yield with Tietze's methods[5] (eq 2).



Similarly, the synthesis of **10** from **6A** is a formal synthesis of **3** since Kinast and Tietze have converted the monotosylate of **10a** to **3** in 67% yield by a biomimetic Grob fragmentation (eq 3). It is also known that **2** results



in high yield from **3** upon treatment of the latter compound with $NaBH_4$ for a prolonged time.[4,13] However, we did not corroborate these observations in the present study.

The formal synthesis of racemic **2** and **3** we describe herein is one step shorter than our synthetic route published earlier,[4] but its overall yield (ca. 18%) is not as good as the latter's (24–27%). On the other hand, the synthesis of **4** and **10** is the most efficient preparation of these iridoid aglucons so far reported.

Experimental Section

General. All reagents and solvents were commercial grade. Solvents were glass distilled and dried by standard procedures before use, if necessary. IR spectra were run on a Perkin-Elmer 257 grating spectrometer. UV spectra were run on a Cary 15 recording spectrometer. NMR spectra were determined at 90 MHz on a Varian EM-390 or on a Bruker HX-90E spectrometer in $CDCl_3$. Chemical shifts were referenced to Me_4Si or to $CHCl_3$ (δ_H 7.26) as internal standard. Mass spectra were run at 70 eV on a Finnegan 1015 mass spectrometer with a M6000 data system (low resolution) or on an AEI MS 9 mass spectrometer with a Nova 2 data system (high resolution). Melting points are uncorrected. Evaporation in vacuo refers to rotary evaporation at <35 °C under H_2O aspirator vacuum. PLC refers to thick-layer chromatography using silica gel PF_{254} (Machery and Nagel).

Aldol Cyclization–Reduction of 6A. The experimental descriptions given below for expt 2 and 9, Table I, typify how we carried out all of these transformations. The most significant variations in experimental conditions that we used for the other aldol cyclization–reduction reactions with **6A** are listed in Table I (expt 1 and 3–8). Additional experimental details for expt 1 and 3–8 are summarized in Table II.

Experiment 9. Diol **9**[4] (340 mg, 1.31 mmol, ca. 3:2 (β:α) C-1 epimers mixture) dissolved in H_2O–MeOH (1:10, 6 mL) was

(9) March, J. "Advanced Organic Chemistry", 2nd ed.; McGraw-Hill: New York, 1977; p 850. Nielsen, A. T.; Houlihan, W. J. *Org. React.* **1968**, *16*, 1.

(10) Cf.: House, H. O.; Crumrine, D. S.; Teranishi, A. Y.; Olmstead, H. D. *J. Am. Chem. Soc.* **1973**, *95*, 3310; Stork, G.; d'Angelo, J. *Ibid.* **1974**, *96*, 7114; ref 9.

(11) We presume that **4** is the thermodynamic product because (a) it would be the expected diastereomer to be formed via the *Z* enolate of **6A**'s C-10 aldehyde[12] and (b) its 7β alcohol is exo and thus less sterically encumbered than a 7α endo alcohol.

(12) Kleschick, W. A.; Buse, T.; Heathcock, C. H. *J. Am. Chem. Soc.* **1977**, *99*, 247.

(13) Battersby, A. R.; Burnett, A. R.; Parsons, P. G. *J. Chem. Soc. C* **1969**, 1187, 1193.

Table II. Summary Experimental Details for Experiments 1 and 3-8

expt	6A, mmol	solvent, mL	$NaBH_4$, mmoles; reduction temperature, °C[a]
1	0.28	3	0.27; 22
3	0.21	3	0.27; 22
4	0.20	3.5	0.27; 22
5	0.30	3	0.27; 22
6	0.29[b]	3	0.54; 22
7	0.40	3	0.54; -78
8	0.32	3	0.54; -78

[a] In all cases, MeOH (3 mL) was added along with the $NaBH_4$ to the crude reaction products. [b] The amount of Me_3SiCl was 0.3 mmol.

treated with $NaIO_4$ (310 mg, 1.6 mmol) with magnetic stirring at 25 °C for 1 h. The crude dialdehyde **6A** was extracted into EtOAc (2 × 25 mL), and the combined EtOAc extracts were washed with 5% aqueous $Na_2S_2O_3$ and then brine and dried with Na_2SO_4. Evaporation in vacuo gave crude **6A** (320 mg, 1.25 mmol, 95%).

A portion of this dialdehyde **6A** (92 mg, 0.36 mmol) dissolved in Ac_2O (4 mL) at ice-bath temperatures was treated with (*i*-Pr)$_2$NEt (100 μL) and 4-(dimethylamino)pyridine (3 mg). The reaction mixture was stirred magnetically at ice-bath temperatures for 24 h, and then it was poured onto ice (10 g) containing excess solid $NaHCO_3$. After 1 h the crude reaction products were extracted into EtOAc (3 × 20 mL); the combined EtOAc extracts were washed with brine, 1 N HCl, saturated aqueous $NaHCO_3$, and brine and then dried with Na_2SO_4. After solvent removal in vacuo, the resulting oil was dissolved in MeOH (5 mL), cooled to -78 °C, and treated with excess $NaBH_4$ (20 mg) at this temperature for 2 h. The crude reaction products were extracted into EtOAc (3 × 15 mL) after acidification of the cold reaction mixture with 1 N HCl and the combined EtOAc extracts were washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), and evaporated in vacuo to give a yellow oil. Generally, PLC purification of this oil as described below for expt 2 gave the individual C-1 epimers of compounds **4** and **10**-**13**. However, for expt 9, the crude mixture of **10** and **11** was acetylated (Ac_2O-pyridine (2:1), 3 mL; 25 °C; 18 h; workup by quenching with ice (20 g), Et_2O extraction, and 1 N HCl, saturated aqueous $NaHCO_3$, brine treatment) and the crude acetates (75 mg) obtained by solvent removal were purified by PLC in EtOAc-Skelly B (1:1) to give 7,10-diacetyl-**10a,b** (58 mg, 48%) and 10-acetyl-**11a,b**[5] (5 mg, 5%). The structures of these two acetates were confirmed by correlation to **10a,b** and **11a,b**.

Experiment 2. Crude **6A** (300 mg, 1.16 mmol) in absolute MeOH (3 mL) was added to $Mg(OMe)_2$ (from Mg metal turnings, 30 mg, 1.25 mmol) in absolute MeOH (10 mL) at 0 °C udner N_2. After the mixture was stirred for 5 min, $NaBH_4$ (43 mg, excess) was added to the reaction mixture and stirring was continued for 30 min at 0 °C. Then solid NH_4Cl (100 mg) was added to the mixture and the solvent was removed in vacuo. The resulting oily solid was extracted with EtOAc (2 × 75 mL), and the combined EtOAc extracts were washed with brine and dried over Na_2SO_4. Solvent removal in vacuo gave an oily residue that was purified by PLC in $CHCl_3$-MeOH (15:1, twice developed) to give, in order of increasing polarity, **4b** (26 mg, 10%), **4a**[6] (39 mg, 16%), **12**[4] (16 mg, 7%), **13**[4] (33 mg, 13%), **10a**[5] (33 mg, 13%), and **10b** (22 mg, 7%).

The IR, ^1H NMR, and mass spectral data of the already known compounds were consistent with the literature values.[4-6] **4b**: IR ($CHCl_3$) ν 3500, 1705, 1635, 1440 cm^{-1}; UV (MeOH) 236 nm (ϵ 1.06 × 10^4); ^1H NMR δ 7.39 (d, J = 1.3 Hz, 1 H), 4.88 (d, J = 3.0 Hz, 1 H), 4.41 (m, 1 H), 3.85 (m, 2 H), 3.70 (s, 3 H), 3.42 (s, 3 H), 3.05 (m, 1 H), 2.57-1.60 (m, 4 H); mass spectrum, m/e (relative intensity) 258.1110 (2) (calcd for $C_{12}H_{18}O_6$ 258.1101), 240 (3), 227 (5), 226 (11), 210 (6), 209 (6), 208 (15), 195 (3), 190 (9), 180 (3), 179 (3), 178 (7), 177 (5), 176 (6), 84 (97). **10b**: IR ($CHCl_3$) ν 3480, 1705, 1635, 1440, 1290 cm^{-1}; UV (MeOH) 237 nm (ϵ 1.02 × 10^4); ^1H NMR δ 7.42 (d, J = 1.2 Hz, 1 H), 4.93 (d, J = 2.1 Hz, 1 H), 3.98 (m, 1 H), 3.70 (s, 3 H), 3.70 (m, 2 H), 3.50 (s, 3 H), 3.00-1.20 (m, 4 H); mass spectrum, m/e (relative intensity) 258.1106 (10) (calcd for $C_{12}H_{18}O_6$ 258.1101), 227 (3), 226 (6), 222 (5), 209 (3), 208 (5), 195 (6), 191 (4), 190 (22), 178 (6), 177 (5), 163 (3), 157 (4), 146 (3), 139 (10), 84 (100). Compound **10a**'s structure was confirmed by its conversion to the known 7,10-diacetyl-**4a** according to Tietze.[5]

Synthesis of 7-*O*-Acetyl-5b. This compound was obtained from **4b** by Tietze's methods[5] via intermediates **14** [IR ($CHCl_3$) ν 1740, 1710, 1640, 1635, 1440 cm^{-1}; UV (MeOH) 235 nm (ϵ 1.04 × 10^4); ^1H NMR δ 7.41 (d, J = 1.2 Hz, 1 H), 5.36 (dt, J = 2.1, 5.4 Hz, 1 H), 4.88 (d, J = 3.3 Hz, 1 H), 4.30 (d, J = 7.5 Hz, 2 H plus ABXm, 2 H), 3.69 (s, 3 H), 3.42 (s, 3 H), 2.77 (s, 3 H), 2.01 (s, 3 H), 3.14-1.65 (m, 3 H); mass spectrum, m/e (relative intensity) 378.0986 (6) (calcd for $C_{13}H_{20}O_8S$ 378.0985), 347 (13), 318 (44), 286 (34), 251 (16), 222 (28), 191 (40), 84 (100)] and **15** [IR ($CHCl_3$) ν 1730, 1709, 1640, 1635, 1440 cm^{-1}; UV (MeOH) 236 nm (ϵ 1.03 × 10^4); ^1H NMR δ 7.42 (d, J = 1.6 Hz, 1 H), 5.30 (m, 1 H), 5.02 (d, J = 3.6 Hz, 1 H), 3.70 (s, 3 H), 3.40 (s, 3 H), 3.10-2.70 (m, 1 H), 2.53 (q, J = 7.5 Hz, 2 H), 2.70-1.60 (m + s, 9 H), 1.25 (t, J = 7.5 Hz, 3 H); mass spectrum, m/e (relative intensity) 344.1297 (7) (calcd for $C_{16}H_{24}O_6S$ 344.1293), 312 (33), 283 (17), 252 (12), 223 (33), 209 (24), 191 (29), 177 (56), 75 (100)]. 7-*O*-Acetyl-**5b**: ^1H NMR δ 7.41 (d, J = 1.3 Hz, 1 H), 5.23 (dt, J = 3.0, 6.5 Hz, 1 H), 4.91 (d, J = 3.2 Hz, 1 H), 3.71 (s, 3 H), 3.43 (s, 3 H), 3.04 (q, J = 8.9 Hz, 1 H), 2.56-1.66 (m, 4 H), 2.04 (s, 3 H), 1.02 (d, J = 7.0 Hz, 3 H). The rest of this compound's spectral parameters were equivalent to those of 7-*O*-acetyl-**5a**.[5]

Registry No. 4a, 61557-82-2; **4a** 7,10-diacetyl derivative, 61557-84-4; **4b**, 74742-20-4; **5a** 7-*O*-acetyl derivative, 29971-34-4; **5b**, 39947-66-5; **5b** 7-*O*-acetyl derivative, 74742-21-5; **6Aa**, 67488-17-9; **6Ab**, 67487-44-9; **6B**, 74684-71-2; **9**, 74684-72-3; **10a**, 61557-83-3; **10a** 7,10-diacetyl derivative, 74742-22-6; **10b**, 74742-23-7; **10b** 7,10-diacetyl derivative, 74742-24-8; **11a**, 73610-58-9; **11a** 10-acetyl derivative, 73582-38-4; **11b**, 74742-25-9; **11b** 10-acetyl derivative, 74742-26-0; **12a**, 67441-38-7; **12b**, 67463-67-6; **13a**, 67487-45-0; **13b**, 67488-18-0; **14**, 74742-27-1; **15**, 74742-28-2.

Preparative Methods for Ergoline Synthons: Uhle's Ketone and the C-Homo Analogue

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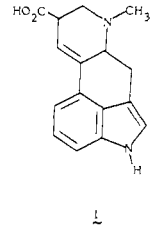
The ergoline nucleus has long been viewed as a challenging target for total synthesis with attempts dating back to the classic work by Uhle[1] and culminating in the synthesis of lysergic acid (**1**) by Kornfeld, Woodward, and



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co-workers.[2] Continuing research in this area has concentrated on sequence simplification, novel approaches, and the development of new synthons.[3-5] Most of these efforts have proceeded through the tricyclic ketone **8** first

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