Experimental Section

^{1}H NMR spectra were obtained on a Varian T-60 spectrometer. Mass spectra were obtained on a Perkin-Elmer Hitachi Model RMU-6E spectrometer. *N*-Benzoyl-3-piperidinone was prepared by oxidation of *N*-benzoyl-3-hydroxypiperidine.[8]

Reaction of Oxygen and Sodium Methoxide with *N*-Benzoyl-3-piperidinone. *N*-Benzoyl-1-3-piperidinone (1.0 g, 4.9 mmol) and sodium methoxide (0.27 g, 4.9 mmol) in methanol (100 mL) were stirred for 6.5 h at room temperature while oxygen was bubbled through the mixture. Acidification (5% HCl), extraction with methylene chloride (5 × 25 mL), drying ($MgSO_4$), and removal of the methylene chloride gave methyl 4-benzamidobutanoate[3] (1.03 g, 4.7 mmol, 95%), which was identical with an authentic sample prepared by treatment of the anion of 4-benzamidobutanoic acid with methyl iodide as described below. The ester was purified by chromatography on an alumina column with elution by chloroform: IR (thin film) 3322 (NH), 1739 (CO_2Me), 1639 (NHCOPh), 1538 (NHCOPh) cm^{-1}; NMR ($CDCl_3$) δ 7.85 (m, 2 H), 7.45 (m, 3 H), 7.1 (m, NH), 3.64 (s, 3 H), 3.48 (d, t, 2 H), 2.41 (t, 2 H), 1.97 (m, 2 H); EI-MS (70 eV), *m/e* (relative intensity) 221 (7), 134 (7), 116 (15), 105 (100), 77 (30); UV (95% EtOH) 227 nm.

In reactions where oxygen was not added deliberately but where air was present, yields of 7–25% of methyl 4-benzamidobutanoate were obtained with reaction times of up to 68 h.

Deuterium Exchange of *N*-Benzoyl-3-piperidinone. A solution of the piperidinone (0.05 g) in chloroform-*d* (0.5 mL) was shaken with solutions of sodium deuteroxide (0.1–13%) in deuterium oxide (0.5 mL) at ambient temperature. ^{1}H NMR spectra were taken at various time intervals. No deuteration was observed with 0.1% NaOD after 1 h. With 0.3% NaOD the C-2 protons exchanged more rapidly than the C-4 protons; after 20 min 80% deuteration at C-2 and 37% at C-4 was observed. Complete deuteration at both C-2 and C-4 was observed with concentrations of 5% or higher of NaOD. The infrared spectrum of the deuterated material showed a weak C–D stretching vibration at 2488 cm^{-1} and the ^{1}H NMR spectrum for the alkane protons was simplified: δ 3.72 (t, 2 H), 1.99 (t, 2 H). Both 2- and 4-methylene groups were deuterated by refluxing *N*-benzoyl-3-piperidinone in benzene with 1 equiv of sodium hydride for 2–20 h followed by addition of deuterium oxide. Apparently the deuteroxide that is formed catalyzes the exchange of all the protons adjacent to the 3-carbonyl group.

Methyl 4-Benzamidobutanoate. The methods used in this preparation differ from those reported previously.[3] 2-Pyrrolidinone (17 g, 0.20 mol) was refluxed with concentrated sulfuric acid (40 mL) in water (500 mL) for 2 h. The solution was made strongly alkaline with 40% aqueous sodium hydroxide. Benzoyl chloride (26 mL, 0.20 mol) was added to the cooled solution during 30 min. The solution was filtered and acidified to pH 3–5 by addition of concentrated hydrochloric acid. The white precipitate of 4-benzamidobutanoic acid (19 g, 0.09 mol, 46%) was filtered, washed twice with water, and dried. The acid (4.0 g, 0.019 mol), methyl iodide (4.0 g, 0.028 mol), and potassium carbonate (3.0 g, 0.026 mol) were stirred in methanol (20 mL) for 42 h at room temperature. The sample was filtered and the methanol removed. Water (10 mL) was added to the residue, and the mixture was extracted with methylene chloride (5 × 15 mL). The methylene chloride solution was dried ($MgSO_4$). Removal of the solvent yielded the ester (2.9 g, 0.013 mol, 69%). The properties of this ester were identical with those reported for the product of the reaction of *N*-benzoyl-3-piperidinone with oxygen and sodium methoxide.

Registry No. *N*-Benzoyl-3-piperidinone, 67452-85-1; methyl 4-benzamidobutanoate, 87461-71-0.

(8) Hirsh, J. A.; Jarmas, A. A. *J. Org. Chem.* **1978**, *43*, 4106. Hecker, L. I.; Saavedra, J. E. *Carcinogenesis* **1980**, *1*, 1017.

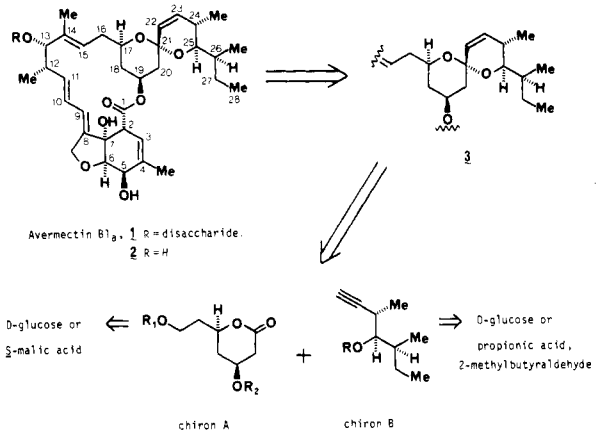
Communications

Stereocontrolled Synthesis of the Spiro Ketal Unit of Avermectin B_{1a} Aglycon

Summary: A stereocontrolled total synthesis of the 1,7-dioxaspiro[5.5]undecene subunit of the avermectin B_{1a} aglycon is presented based on the "chiron" approach which utilizes optically active starting materials.

Sir: The avermectins are a group of fermentation products of *Streptomyces avermitilis*, which possess potent anthelmintic and insecticidal activities.[1] Avermectin B_{1a} (1), the most active member of this family,[2] is a glycosidic derivative of a pentacyclic 16-membered lactone, which appears to act by interference with invertebrate neurotransmission.[3] In this paper, we report the total synthesis of the 1,7-dioxaspiro[5.5]undecane subunit **3** of avermectin B_{1a} aglycon **2** in optically pure form (Scheme I).

Scheme I



Two elegant syntheses of milbemycin B_3, an antibiotic which is structurally related but somewhat simpler in overall features compared to the avermectins, have been recently reported.[4,5] In one of these,[5] the antibiotic was

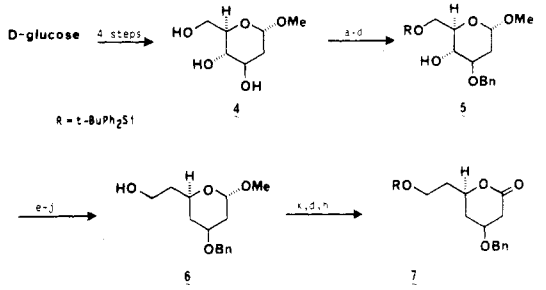
(1) Burg, R. W.; Miller, B. M.; Baker, E. E.; Birnbaum, J.; Currie, S. A.; Hartman, R.; Kong, Y. L.; Monaghan, R. L.; Olson, G.; Putter, I.; Tunac, J. B.; Wallick, H.; Stapley, E. O.; Oiwa, R.; Omura, S. *Antimicrob. Agents Chemother.* **1979**, *15*, 361. Miller, T. W.; Chaiet, L.; Cole, D. J.; Cole, L. J.; Flor, J. E.; Goegelman, R. T.; Gullo, V. P.; Joshua, H.; Kempf, A. J.; Krellwitz, W. R.; Monaghan, R. L.; Ormond, R. E.; Wilson, K. E.; Albers-Schonberg, G.; Putter, I. *Ibid.* **1979**, *15*, 368. Albers-Schonberg, G.; Arison, B. H.; Chabala, J. C.; Douglas, A. W.; Eskola, P.; Fisher, M. H.; Lusi, A.; Mrozik, H.; Smith, J. L.; Tolman, R. L. *J. Am. Chem. Soc.* **1981**, *103*, 4216. Springer, J. P.; Arison, B. H.; Hirshfield, J. M.; Hoogsteen, K. *Ibid.* **1981**, *103*, 4221.

(2) Mrozik, H.; Eskola, P.; Fisher, M. H. *Tetrahedron Lett.* **1982**, *23*, 2377.

(3) Chabala, J. C.; Rosegay, A.; Walsh, M. A. R. *J. Agric. Food Chem.* **1981**, *29*, 881.

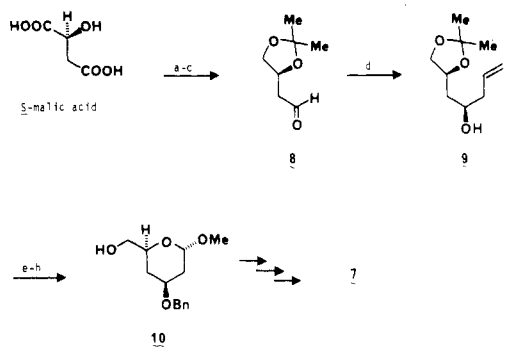
0022-3263/83/1948-4427$01.50/0

Scheme II[a]



[a] (a) PhCHO, H^+. (b) KH, BnBr. (c) *p*-TsOH, H_2O, MeOH. (d) *t*-$BuPh_2SiCl$, py. (e) NaH, CS_2, MeI. (f) Bu_3SnH. (g) Bu_4NF. (h) PCC. (i) $Ph_3P{=}CH_2$. (j) 9-BBN; NaOH, H_2O_2. (k) Aqueous HOAc, Δ.

Scheme III[a]

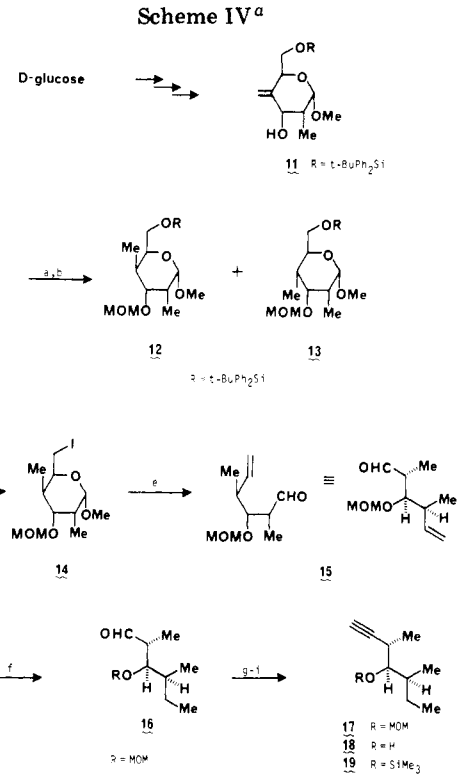


[a] (a) $BH_3{\cdot}Me_2S$. (b) acetone, H^+. (c) PCC. (d) allylmagnesium bromide. (e) KH, BnBr. (f) TFA. (g) ozone, Me_2S. (h) MeOH, $BF_3{\cdot}Et_2O$.

synthesized in optically active form. Our synthetic route to the spiro ketal unit **3** is based on the "chiron"[6] approach which utilizes readily available optically pure precursors as building blocks. Formation of the spiro ketal was envisioned to proceed through condensation of two chirons such as an acetylide and a lactone, reduction to the cis olefin, and eventual internal ketalization, relying on anomeric stereoselection[7,8] to generate the thermodynamically favored isomer as found in the natural product. The above mentioned chirons were envisaged to arise from D-glucose and (*S*)-malic acid by systematic chemical manipulation, so as to reach the desired level of convergence in the carbon framework, substitution pattern, and sense of chirality with the target.

The synthesis of the lactone unit from D-glucose calls for deoxygenations at C-2 and C-4, which could be easily achieved as shown in Scheme II. The triol **4**, readily available from D-glucose,[9] was systematically protected by using well-established methodology[10] to give **5**, which was

Scheme IV[a]



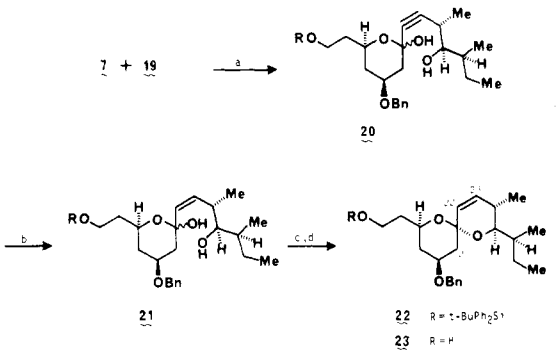
[a] (a) H_2, $Pd(OH)_2$. (b) CH_3OCH_2Cl, *i*-Pr_2NEt. (c) *n*-Bu_4NF. (d) Tf_2O, py; *n*-Bu_4NI. (e) Zn, EtOH, 45 °C. (f) H_2, Rh/Al_2O_3, benzene. (g) CBr_4-Ph_3P, CH_2Cl_2; *n*-BuLi. (h) Me_3SiBr, CH_2Cl_2, −30 °C. (i) Me_3SiCl, CH_2Cl_2, Et_3N, DMAP.

deoxygenated by the Barton procedure[11] to give the corresponding dideoxy derivative as a syrup, after removal of the silyl ether; $[\alpha]_D$ +115° (*c* 3.4, CH_2Cl_2).[12] Chain extension led to **6**, which after acid hydrolysis and selective silylation of the primary hydroxyl group[10] followed by PCC oxidation[13] gave the desired lactone **7** (syrup; $[\alpha]_D$ +21.6° (*c* 1.36, EtOAc) in good overall yield.

The same lactone was concurrently synthesized from natural (*S*)-(−)-malic acid, as shown in Scheme III. Reduction of the acid with borane–methyl sulfide complex[14] followed by ketalization with acetone/*p*-TsOH[15] afforded the known 9:1 mixture of alcohol acetals (92% overall from malic acid),[17] which after separation[16] and oxidation of the desired isomer with PCC gave aldehyde **8**. Treatment of **8** with allylmagnesium bromide gave an almost 1:1 mixture of homoallylic alcohols (75%), which could be separated by chromatography. The more polar component, **9**, was benzylated, the olefinic linkage oxidatively degraded, and the resulting product converted to a mixture of glycosides **10**. The latter was chain extended and further elaborated as shown in Scheme II to give lactone **7**, identical in all respects with a sample obtained from D-glucose.[18]

(4) Smith, A. B., III; Schow, S. R.; Bloom, J. D.; Thompson, A. S.; Winzenberg, K. N. *J. Am. Chem. Soc.* **1982**, *104*, 4015.
(5) Williams, D. R.; Barner, B. A.; Nishitani, K.; Phillips, J. G. *J. Am. Chem. Soc.* **1982**, *104*, 4708. Williams, D. R.; Barner, B. A. *Tetrahedron Lett.* **1983**, *24*, 427.
(6) We have recently introduced this term to describe a chiral, enantiomerically pure synthon. See for example: Hanessian, S. In "Total Synthesis of Natural Products—The 'Chiron' Approach"; Baldwin, J. E., Ed.; Pergamon Press: Oxford, U. K., in press.
(7) For a discussion see: Lemieux, R. U.; Koto, S. *Tetrahedron* **1974**, *30*, 1933 and references cited therein.
(8) For the uses and implications of this term see: Hanessian, S.; Roy, R. *J. Am. Chem. Soc.* **1979**, *101*, 5839.
(9) Inglis, G. R.; Schwarz, J. C. P.; McLaren, L. *J. Chem. Soc.* **1962**, 1014. Manolopoulos, P. T.; Mednick, M.; Lichtin, N. N. *J. Am. Chem. Soc.* **1962**, *84*, 2203. Corey, E. J.; Weigel, L. O.; Chamberlin, A. R.; Lipshutz, B. *Ibid.* **1980**, *102*, 1439.
(10) Hanessian, S.; Lavallée, P. *Can. J. Chem.* **1975**, *53*, 2975.
(11) Barton, D. H. R.; Subramanian, R. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1718.
(12) New compounds were characterized by spectroscopic and microanalytical methods.
(13) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.
(14) Lane, C. F.; Myatt, H. L.; Daniels, J.; Hopps, H. B. *J. Org. Chem.* **1974**, *39*, 3052.
(15) Mori, K.; Takigawa, T.; Matsuo, T. *Tetrahedron* **1979**, *35*, 933. Hayashi, H.; Nakanishi, K.; Brandon, C.; Marmur, J. *J. Am. Chem. Soc.* **1973**, *95*, 8749.
(16) Meyers, A. I.; Lawson, J. P. *Tetrahedron Lett.* **1982**, *23*, 4883 and references cited therein.
(17) Hanessian, S.; Ugolini, A.; Glamyan, A., unpublished results.

Scheme V[a]



[a] (a) *n*-BuLi, THF, −78 °C; $BF_3 \cdot Et_2O$, then add lactone; H_3O^+. (b) H_2, $Pd/BaSO_4$, EtOAc, py. (c) $BF_3 \cdot Et_2O$, THF. (d) *n*-Bu_4NF, THF.

With lactone **7** secured by two routes, we turned our attention to the acetylenic component, representing the right half of the spiro ketal and required for the key carbon bond-forming reaction. The synthesis was accomplished from an intermediate, **11**, employed in the construction of the C(19)–C(29) aliphatic segment of (+)-rifamycin S,[19] which is readily available from D-glucose (Scheme IV).

Thus, exocyclic olefin **11** was hydrogenated by using $Pd(OH)_2$[20] to give a 4:1 mixture of axial to equatorial C-4 methyl derivatives (92%), which could be separated by flash chromatography,[21] after conversion to a methoxymethyl (MOM) ether (89%), into the required axial C-4 methyl isomer **12** ($[\alpha]_D$ +32.4° (*c* 0.66, $CHCl_3$)) and its epimer **13**. Desilylation of **12** and halogenation of the resulting alcohol according to the procedure of Binkley[22] gave the primary iodide **14**: 77% two steps; $[\alpha]_D$ +60° (*c* 0.86, $CHCl_3$). Now that the template effect of the cyclic carbohydrate derivatives had been fully exploited, the synthesis was continued by unravelling an acyclic structure. Thus, warming **14** in aqueous ethanol containing Zn dust afforded aldehyde **15** (88%, syrup), as described for other methyl 6-halo-6-deoxyhexopyranosides.[23] Hydrogenation of **15** with Rh/Al_2O_3 as a catalyst yielded aldehyde **16** (quantitative), which was transformed into acetylene **17** by reaction with triphenylphosphine–carbon tetrabromide, followed by treatment with *n*-butyllithium[24] (84%, two steps). Cleavage of the acetal protecting group in **17** with trimethylsilyl bromide[25] gave **18**, which, after silylation with trimethylsilyl chloride, afforded **19** (80%, two steps), representing a protected acyclic equivalent of the right-hand segment present in the intended target. In a parallel study, racemic **16** was prepared by condensation of (*E*)-methylketene ethyl trimethylsilyl acetal[26] with 2-methylbutanal followed by protection of the alcohol function as a MOM ether and reduction of the ester moiety with DIBAL.

With the desired chiral, enantiomerically pure components in hand, we next addressed the question of assembling the carbon backbone of our target (Scheme V). It is known that, unlike esters, lactones react with acetylides to give hemiacetals instead of carbinols.[27] Thus, pretreatment of the lithium acetylide, derived from **19** (1 equiv), in THF at −78 °C with $BF_3 \cdot Et_2O$ (1.9 equiv, 10 min) followed by addition of lactone **7** (1 equiv) gave hemiacetal **20** in 38% yield (90% based on recovered lactone).[28] Hydrolysis of the Me_3Si ether followed by careful partial reduction of the acetylenic linkage by using $Pd/BaSO_4$ in EtOAc/py[29] yielded the cis olefin **21**, which after brief exposure to 0.05% $BF_3 \cdot Et_2O$ (10 min, 25 °C) in THF led to the desired spiro ketal **22** as the only detectable isomer (80%, two steps), which was isolated as a syrup, $[\alpha]_D$ +58.7° (*c* 0.62, CH_2Cl_2). Finally, desilylation with fluoride ion afforded alcohol **23** ($[\alpha]_D$ +105° (*c* 0.315, CH_2Cl_2)) as a syrup. The complete assignment of the spiro ketal stereochemistry was aided by NOE and proton homonuclear correlation (COSY) experiments.[30]

Spiro ketal **23** is thus readily accessible in enantiomerically pure form for further elaboration into the target structure. Studies along these lines are in progress.[31]

Acknowledgment. We thank the Natural Sciences and Engineering Council of Canada, le Ministère de l'éducation du Québec, and Merck-Frosst Laboratories for generous financial assistance. We also thank Phan Viet Minh Tan for recording the 400-MHz ^1H NMR spectra and Michael Evans for mass spectra.

Registry No. **2**, 71828-14-3; **4**, 13145-22-7; **5**, 87318-93-2; **6**, 87318-94-3; **7**, 87318-95-4; **8**, 32233-44-6; **9** (isomer 1), 87318-96-5; **9** (isomer 2), 87318-97-6; **10** (isomer 1), 87391-88-6; **10** (isomer 2), 82300-42-3; **11**, 82707-03-7; **12**, 87318-98-7; **12** de(MOM), 87318-99-8; **13**, 87319-00-4; **13** de(MOM), 87319-01-5; **14**, 87319-02-6; **15**, 87319-03-7; **16**, 87319-04-8; (±)-**16**, 87391-89-7; **17**, 87319-05-9; **18**, 87319-06-0; **19**, 87319-07-1; **20**, 87319-08-2; **21**, 87319-09-3; **22**, 87319-10-6; **23**, 87319-11-7; $Ph_3P{=}CH_2$, 3487-44-3; (*S*)-(−)-malic acid, 97-67-6; (*S*)-2,2-dimethyl-1,3-dioxolane-4-acetic acid, 87319-12-8; (*R*)-2,2-dimethyl-1,3-dioxolane-4-acetic acid, 87319-13-9; (*E*)-methylketene ethyl trimethylsilyl acetal, 73967-97-2; (±)-2-methylbutanal, 57456-98-1.

(18) Some attempts were made to favor the formation of the desired isomer in the Grignard reaction. Unfortunately, due to the acyclic nature of the aldehyde, it was not possible to enhance the ratio of the required isomer, and a separation was necessary. However, the unwanted isomer could be recycled via an oxidation reduction sequence. See, for example: Meyers, A. I.; Lawson, J.; Amos, R. A.; Walker, D. G.; Spohn, R. F. *Pure Appl. Chem.* **1982**, *54*, 2537.

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(20) Perlman, W. M. *Tetrahedron Lett.* **1967**, 1663.

(21) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(22) Binkley, R. W.; Ambrose, M. G.; Hehemann, D. G. *J. Org. Chem.* **1980**, *45*, 4387. See also: Leroux, J.; Perlin, A. S. *Carbohydr. Res.* **1976**, *47*, C8; **1978**, *67*, 163.

(23) Bernet, B.; Vasella, A. *Helv. Chim. Acta* **1979**, *62*, 1990.

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(25) Hanessian, S.; Delorme, D.; Dufresne, Y., unpublished results.

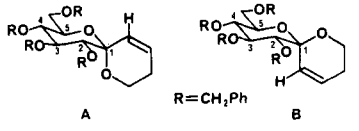
(26) Chan, T. H.; Aida, T.; Lau, P. W. K.; Gorys, V.; Harpp, D. N. *Tetrahedron Lett.* **1979**, 4029.

(27) (a) Chabala, J. C.; Vincent, J. E. *Tetrahedron Lett.* **1978**, 937. (b) Jacobson, R.; Taylor, R. J.; Williams, H. J.; Smith, L. R. *J. Org. Chem.* **1982**, *47*, 3140. (c) Lin, C. H.; Alexander, D. L. *Ibid.* **1982**, *47*, 615. (d) Ogura, H.; Takahashi, H. *Synth. Commun.* **1973**, *3*, 135. (e) Lin, C. H.; Stein, S. J. *Ibid.* **1976**, *6*, 503.

(28) Whereas significant amounts of elimination products were obtained upon condensation of the Li salt of **19** and lactone **7**, only traces were found by using a modification of Yamaguchi's procedure. For a recent application to the opening of epoxides see: Yamaguchi, M.; Hirao, I. *Tetrahedron Lett.* **1983**, *24*, 391.

(29) Kocienski, P. J.; Cernigliaro, G. J. *J. Org. Chem.* **1976**, *41*, 2927. See also ref 27c.

(30) Irradiation of the C-22 proton resulted in a roughly 6% signal enhancement (12% NOE) of the C-20 axial proton, thereby confirming the structure of **23**. Protons at C-17 and C-19 would have been affected had the other spiro ketal been present. This observation was further substantiated from NOE studies on the two isomeric spiro ketal structures A and B, independently synthesized in our laboratory as model studies. In the case of A, irradiation of the vinylic proton resulted in an enhancement of the signal of the C-2 proton only (17% NOE), whereas with B, signals of protons at C-3 and C-5 were enhanced (~27% NOE for each).



(31) Portions of this work were presented at the Annual Chemical Congress, Lancaster, U.K., April 11–13, 1983; Symposium on Asymmetric Synthesis, p 2.6.

Supplementary Material Available: Synthetic procedures and data for **20**, **22**, and **23** and ^{1}H NMR spectra for **22** and **23** (4 pages). Ordering information is given on any current masthead page.

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‡ NSERCC predoctoral fellow, 1982-1983.

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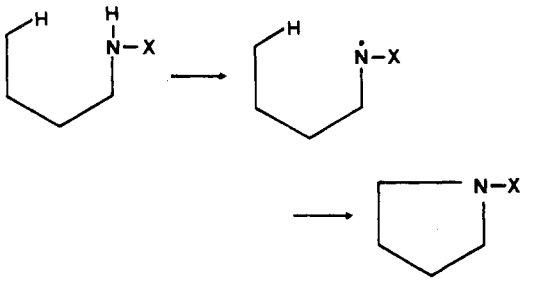
Intramolecular Functionalization of Phosphoramidate Radicals. Synthesis of 1,4-Epimine Compounds

Summary: Photolysis of the diethyl, diphenyl, and dibenzyl phosphoramidates **1a-c**, **3**, and **5a** in the presence of lead tetraacetate and iodine results in the formation of the corresponding *N*-dioxyphosphinyl 1,4-epimine compounds **2a-c**, **4**, and **6**, respectively, in excellent yields, thus providing an effective synthetic method for pyrrolidines.

Sir: Intramolecular hydrogen abstraction from hetero radicals which leads to the remote functionalization of nonactivated carbon centers is an important target for organic chemists.[1-3] Although the reactions initiated by oxy radicals have been the subject of numerous studies,[2] those associated with nitrogen radicals have received comparatively little attention.[3] The sole reaction[4] of this type which has proved of significant value for the preparation of cyclic amines is the thermal or photochemical fragmentation of *N*-halo amines (Hofmann-Löffler-Freytag reaction). In spite of the fact that this reaction represents the earliest example of intramolecular functionalization of a nonactivated carbon, only limited use has been made of it in complex or sensitive molecules owing to the highly acidic conditions required.[8] Furthermore, secondary cyclic amines are only obtained in poor yields when the Hofmann-Löffler-Freytag reaction was applied to primary amines.

Recently we reported[9] the intramolecular functionalization of the C-18 and C-19 steroidal methyl groups by neutral aminyl radicals of the R-N̈-NO_2 (R = steroidal nucleous) type, generated in situ by photolysis of *N*-iodo nitroamines. This procedure provides a convenient synthesis of *N*-nitro 1,4-epimine compounds under mild conditions, and it is an advantageous alternative method to the Hofmann-Löffler-Freytag reaction which overcomes the problem associated with the strong acidic media required in the latter.

Continuing our investigations in this field, we now report the synthesis of epimine compounds by remote functionalization initiated by phosphoramidate radicals which were generated by photolysis of the corresponding *N*-iodo derivatives (eq 1). In all the reported cases, the epimine



(1)

X = $P(O)(OEt)_2$, $P(O)(OPh)_2$, $P(O)(OCH_2Ph)_2$

compounds were obtained with excellent yields. When the free secondary cyclic amines are desired, the dioxyphosphinyl moiety could be easily removed, especially when compared with the nitro group, initially used as the nitrogen radical stabilizing group.

Diethyl *N*-(3β-acetoxy-5α-cholestan-6β-yl)phosphoramidate (**1a**) was prepared by reaction of 6β-amino-5α-cholestan-3β-ol[10] (1 mmol) with diethyl phosphorochloridate (1.1 mmol) in dry chloroform (1 mL) in the presence of triethylamine (2 mmol) and subsequent acetylation. Intramolecular cyclization of the diethyl phosphoramidate **1a** (1 mmol) was accomplished by reaction with lead tetraacetate (10 mmol) and iodine[11] (5 mmol) in cyclohexane (75 mL) under reflux and irradiation with two 100-W tungsten-filament lamps for 2 h, yielding quantitatively diethyl *N*-(3β-acetoxy-5α-cholestan-6β,19-epimino)phosphonate (**2a**). All spectroscopic data[12] (IR, ^{1}H NMR, and MS) are consistent with the structure proposed for the product; thus, high-resolution mass spectroscopy indicates a molecular formula of $C_{33}H_{58}NO_5P$, and in its ^{1}H NMR spectrum the two protons at C-19 appear as a broad singlet at δ 3.08.

The triterpene 3β-phosphoramidate derivative **3**[13] also reacted smoothly, under similar conditions, to give the 3β,24-epimine compound **4** in 90% yield.[14]

We next turned our attention to the functionalization of the C-18 methyl group in the steroidal 20(*S*)-

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(4) Hydrogen abstraction by nitrogen radicals has also been postulated by Barton et al[5] during the photolysis of *N*-iodo amides, although only lactones have been isolated from this reaction. The formation of epimine compounds by photolysis of steroidal azides has been the object of controversy,[6] but at least in one case[7] 6β,19-epimino-5α-pregnane has been obtained in low yield (6%) from 6β-azido-5α-pregnane.

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(11) Lead tetraacetate and iodine were added in portions every 15 min along the reaction.

(12) Compound **2a**: amorphous; IR ($CHCl_3$) ν_{max} 1720, 1230 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.71 (3 H, s, C-18 H), 3.08 (2 H, br s, C-19 H), 3.57 (1 H, m, $W_{1/2}$ = 10 Hz, C-6α H); MS, *m/e* (assignment, relative intensity) 579.4016 (M^+, $C_{33}H_{58}NO_5P$, 10), 316.1309 ($C_{14}H_{23}NO_5P$, 100).

(13) Betancor, C.; Freire, R.; González, A. G.; Salazar, J. A.; Pascard, C.; Prange, C. *Phytochemistry* **1980**, *19*, 1989.

(14) Compound **4**: mp 154-156 °C (*n*-pentane); $[\alpha]_D$ +18° ($CHCl_3$); IR ($CHCl_3$) ν_{max} 1730, 1230 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.45 (1 H, m, $W_{1/2}$ = 11 Hz, C-3α H), 2.76, 3.56 (2 H, AB, *J* = 11 Hz, C-24 H); MS, *m/e* (relative intensity) 619 (M^+, 100).

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