can be determined easily. In 2-chloropyrazine 64 data sets were sufficient to find the values $^1J_{C_3H_3}$ = 192.57 Hz, $^1J_{C_5H_5}$ = 185.67 Hz, and $^1J_{C_6H_6}$ = 186.41 Hz, which agree with one-dimensional results within ±0.05 Hz. Since increments of t_1 were 10 ms, the lines folded in only once.

If small changes of $^1J_{CH}$ (such as solvent effects) must be measured very accurately, the spectral band width can be reduced by increasing the evolution time in large steps. The lines will fold in several times, but their relative positions will be measured with superior resolution.

Spin manipulations can be extended to CH_2 and CH_3 groups as well as some other pairs of nuclei. Details will be published in a subsequent paper together with practical applications.

Acknowledgment. Stimulating discussions with Professor T. C. Wong are greatly appreciated. The NT-300 spectrometer was purchased partially through a grant from the National Science Foundation (PCM-8115599).

Stereoselective Total Synthesis of Pyrrolizidine Alkaloid Bases: (−)-Rosmarinecine and (−)-Isoretronecanol

Kuniaki Tatsuta,* Hideaki Takahashi, Yoshiya Amemiya, and Mitsuhiro Kinoshita

Department of Applied Chemistry, Keio University Hiyoshi, Kohoku, Yokohama 223, Japan

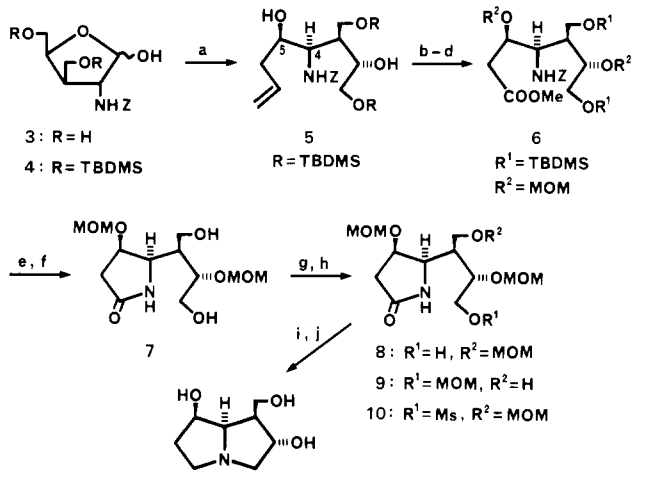
Received January 17, 1983

The pyrrolizidine alkaloids, which occur naturally in various plant species, in general consist of a pyrrolizidine ("necine") base and a carboxylic ("necic") acid. Their structures, syntheses, and physiological properties have been continuously and amply reviewed;[1] however, completely stereoselective syntheses of optically active necine bases have not been reported to date.[2]

Thus, we focused on the stereoselective total synthesis of "natural" necine bases, (−)-rosmarinecine (**1**)[3] and (−)-isoretronecanol (**2**)[2,4] from D-glucosamine.

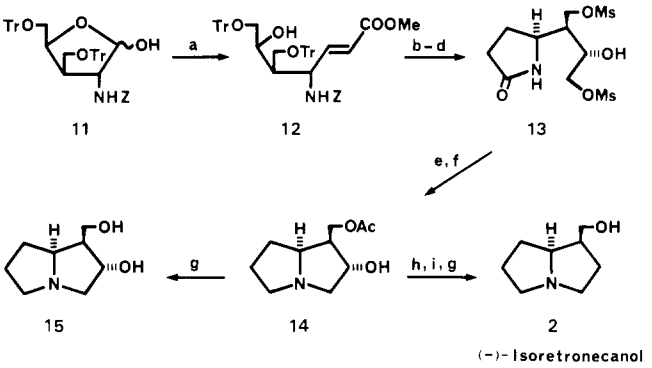
The first target was (−)-rosmarinecine (**1**, Scheme I). Methyl 2-amino-2,3-dideoxy-3-*C*-formyl-α-D-xylofuranoside-(3′*R*)-5-hemiacetal,[5] which has been already derived for the synthesis in three steps from methyl α-D-glucosaminide through the skeletal rearrangement of the *N*,*O*-*o*-benzenedisulfonyl derivative in our laboratories, was converted to the corresponding furanose **3**[6] successively by N-benzyloxycarbonylation [benzyl *S*-(4,6-dimethylpyrimidin-2-yl)thiocarbonate,[7] aqueous methanol, 1.5 h],

Scheme I[a]



[a] Key: (a) from 4, CH_2=$CHCH_2MgBr$, ether, 5 °C, 30 min; 20 °C, 30 min; reflux, 3 h; (b) $NaIO_4$, $KMnO_4$, aqueous *t*-BuOH and then 5% K_2CO_3, 15 h; (c) CH_2N_2, ether, 30 min; (d) MOMCl, *i*-Pr_2EtN, $CHCl_3$, 60 °C, 5 h; (e) 3 atm of H_2, 5% Pd–C, THF, AcOH, 3 h; (f) Bu_4NF, THF, 5 °C, 30 min; (g) 7 → 8 + 9, MOMCl, *i*-Pr_2EtN, THF, 6 h; (h) 8 → 10, MsCl, Py, 1 h; (i) from 10, BH_3·Me_2S, THF, 60 °C, 5 h; (j) 0.5 N HCl, dioxane, 80 °C, 6 h.

Scheme II[a]



[a] Key: (a) Ph_3P=CHCOOMe, toluene, 60 °C, 62 h; (b) 3 atm of H_2, 5% Pd-C, THF, AcOH, 5 h; (c) Amberlyst 15, MeOH, 60 °C, 5 h; (d) MsCl, py, 0 °C, 2 h; (e) BH_3·Me_2S, THF, 60 °C, 12 h; (f) KOAc, DMSO, 80 °C, 4 h; (g) NH_3, MeOH, 40 h; (h) $SOCl_2$, reflux, 3 h; (i) 3 atm H_2, Raney Ni, EtOH, 15 h.

hydride reduction (sodium borohydride, methanol), and acid hydrolysis (6 N hydrochloric acid, 1 h). Compound **3** contains already felicitously placed functional groups and an anomeric carbon of potential value for the stereoselective introduction of a hydroxyl group and carbon chain.

Silylation of **3** [*tert*-butyldimethylsilyl (TBDMS) chloride, pyridine, 15 h] gave the disilyl furanose **4** (87%), which was submitted to Grignard reaction with 7 equiv of allylmagnesium bromide in ether to afford the single *threo*[8] amido alcohol **5** [92%, oil, $[\alpha]^{19}_D$ −10° ($CHCl_3$)]. The *R* configuration of the newly formed alcohol at C-5 is assigned on the presumption of a stereoselectively chelation-controlled approach[8c,d] of the reactant to the anomeric carbon of **4** and is confirmed by the successful transformation to natural rosmarinecine (**1**). Oxidation[9] of **5** (5 equiv of sodium metaperiodate and 1.5 equiv of potassium per-

(1) For examples, see: Bull, L. B.; Culvenor, C. C. J.; Dick, A. T. "The Pyrrolizidine Alkaloids"; North-Holland: Amsterdam, 1968. Wood, H. C. S.; Wrigglesworth, R. "Rodd's Chemistry of Carbon Compounds"; Coffey, S., Ed.; Elsevier: Amsterdam, 1977; Vol. IVB, pp 7–62. Robins, D. J. *Adv. Heterocycl. Chem.* **1979**, *24*, 247–291.

(2) Three syntheses affording optically active (−)-isoretronecanol have been reported [(a) Rüeger, H.; Benn, M. *Heterocycles* **1982**, *19*, 1677–1680. (b) Robins, D. J.; Sakdarat, S. *J. Chem. Soc., Perkin Trans. 1*, **1981**, 909–913. Robins, D. J.; Sakdarat, S. *J. Chem. Soc., Chem. Commun.* **1979**, 1181–1182. (c) Takano, S.; Ogawa, N.; Ogasawara, K. *Heterocycles* **1981**, *16*, 915–916] with >90%, 90%, and 33% optical purity, respectively. A synthon for some necines has been synthesized with 99% optical purity: Rüeger, H.; Benn, M. *Heterocycles* **1982**, *19*, 23–25.

(3) (a) Richardson, M. F.; Warren, F. L. *J. Chem. Soc.* **1943**, 452–454. (b) Porter, L. A.; Geissman, T. A. *J. Org. Chem.* **1962**, *27*, 4132–4134. (c) The natural alkaloid rosmarinine, from which (−)-rosmarinecine (**1**) could be obtained by alkaline hydrolysis, was provided by Prof. S. E. Drewes, University of Natal, S. Africa; see ref 3a.

(4) Adams, R.; Hamlin, K. E., Jr. *J. Am. Chem. Soc.* **1942**, *64*, 2597–2599. Recent synthesis of the racemate: Iwashita, T.; Kusumi, T.; Kakisawa, H. *J. Org. Chem.* **1982**, *47*, 230–233 and references therein.

(5) Tatsuta, K.; Miyashita, S.; Akimoto, K.; Kinoshita, M. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 3254–3256.

(6) All new compounds reported have been fully characterized by IR, ^1H NMR, and high-resolution mass spectroscopy and/or combustion analysis.

(7) Purchased from Aldrich Chemical Co. See also: (a) Nagasawa, T.; Kuroiwa, K.; Narita, K.; Isowa, Y. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 1269–1272. (b) Ikeda, D.; Miyasaka, T.; Yoshida, M.; Horiuchi, Y.; Kondo, S.; Umezawa, H. *J. Antibiot.* **1979**, *32*, 1365–1366.

(8) (a) Still, W. C.; McDonald, J. H., III *Tetrahedron Lett.* **1980**, *21*, 1031–1034. (b) Evans, D. A.; Nelson, J. V.; Taber, T. R. *Top. Stereochem.* **1982**, *13*, 1–115. (c) Tsuda, Y.; Nunozawa, T.; Yoshimoto, K. *Chem. Pharm. Bull.* **1980**, *28*, 3223–3231. (d) Kinoshita, M.; Ohsawa, N.; Gomi, S. *Carbohydr. Res.* **1982**, *109*, 5–23.

(9) ApSimon, J. W.; Chau, A. S. Y.; Craig, W. G.; Krehm, H. *Can. J. Chem.* **1967**, *45*, 1439–1445.

0002-7863/83/1505-4096$01.50/0

manganate) afforded the carboxylic acid, and subsequent esterification (diazomethane) and then methoxymethylation [methoxymethyl chloride (MOMCl) and diisopropylethylamine] produced the protected ester **6** [92%, oil, $[\alpha]^{20}_D$ +11° ($CHCl_3$)]. The N-blocking group was first removed by reduction to give the γ-lactam with cyclization and the silyl group removed (tetrabutylammonium fluoride) to yield the diol **7** [93%, oil, $[\alpha]^{20}_D$ −11° ($CHCl_3$)]. Selective methoxymethylation of **7** (1.5 equiv of MOMCl) gave a mixture of trimethoxymethyl derivatives **8** [51%, oil, $[\alpha]^{20}_D$ +1.0° ($CHCl_3$)] and **9** [34%, oil, $[\alpha]^{20}_D$ −52° ($CHCl_3$)]. The major product **8** was found to be converted to the desired mesylate **10** [93%, oil, $[\alpha]^{20}_D$ −12° ($CHCl_3$)], the structure of which was supported by the ^1H NMR spectrum. The minor product **9** could be effectively recycled to **7** by selective hydrolysis (80%, a catalytic amount of camphorsulfonic acid in methanol). Treatment of **10** with 4.5 equiv of borane–methyl sulfide[10] to give the pyrrolizidine skeleton with intramolecular S_N2 displacement of the intermediary pyrrolidine derivative, followed by cleavage of MOM protecting group (0.5 N HCl) afforded (−)-rosmarinecine [**1**: 54%, $[\alpha]^{21}_D$ −121° (EtOH); picrate (needles from EtOH): mp 175 °C, $[\alpha]^{21}_D$ −60° (MeOH)] identical in all respects with that obtained from natural sources.[3c,11]

With the use of similar strategy, the stereoselective synthesis of (−)-isoretronecanol (**2**) was accomplished as outlined in Scheme II, starting again from the key intermediate **3**. The ditrityl derivative **11**, obtained from **3** [trityl (Tr) chloride, pyridine, 70 °C, 26 h], was subjected to Wittig reaction [3 equiv of (methoxycarbonyl)methylenetriphenylphosphorane] to give the unsaturated ester **12** [85%, mp 210 °C, $[\alpha]^{29}_D$ −14° ($CHCl_3$)]. Reduction of **12** gave the γ-lactam, which was in turn treated with Amberlyst 15 resin (H-type) in methanol to remove the trityl group and then mesylated to afford the dimesylate **13** [80%, oil, $[\alpha]^{30}_D$ +1.5° (MeOH)]. Borane reduction of **13** to give the monomesyl pyrrolizidine derivative, followed by treatment with 3.5 equiv of potassium acetate gave the monoacetate **14** (90%), which was deacetylated by methanolic ammonia to afford (−)-7-deoxyrosmarinecine [**15**: 84%, $[\alpha]^{25}_D$ −115° (EtOH); picrolonate (needles from EtOH): mp 206 °C].[12] On the other hand, by the standard procedures,[12] **14** was converted to (−)-isoretronecanol [**2**: 74%, $[\alpha]^{20}_D$ −91° (EtOH); picrate (needles from EtOH): mp 199 °C, $[\alpha]^{20}_D$ −29° (MeOH)].[13] The synthetic products **15** and **2** were identical in all respects with (−)-7-deoxyrosmarinecine and (−)-isoretronecanol obtained from natural sources, completing the stereoselective synthesis of natural pyrrolizidine mono- (**2**), di- (**15**), and triol (**1**).

Acknowledgment. We are grateful to the Institute of Microbial Chemistry for the generous support of our program and thank Y. Kanemura for his technical assistance. We also are indebted to Professors S. E. Drewes,[3c] L. W. Smith,[11,13] H. Kakisawa,[13] and H. W. Pinnick[13] for kindly providing the authentic samples and/or the ^1H NMR spectra.

Registry No. 1, 520-61-6; **2**, 526-63-6; **3**, 85781-28-8; **4**, 85781-29-9; **5**, 85781-30-2; **6**, 85781-31-3; **7**, 85781-32-4; **8**, 85781-33-5; **9**, 85781-34-6; **10**, 85781-35-7; **11**, 85781-36-8; **12**, 85781-37-9; **13**, 85781-38-0; **14**, 85781-39-1; **15**, 85848-68-6; TBDMS, 18162-48-6; TrCl, 76-83-5; (methoxycarbonyl)methylenetriphenylphosphorane, 2605-67-6; allyl bromide, 106-95-6; benzyl *S*-(4,6-dimethylpyrimidin-2-yl)thiocarbonate, 42116-21-2; methyl 2-amino-2,3-dideoxy-3-*c*-formyl-α-D-xylofuranoside-3'*R*-5-hemiacetal, 84034-70-8.

Supplementary Material Available: Characterization data for compounds **1**, **2**, **5**, **7**–**10**, and **15** (9 pages). Ordering information is given on any current masthead page.

(10) Ohfune, Y.; Tomita, M. *J. Am. Chem. Soc.* **1982**, *104*, 3511–3513.
(11) The ^1H NMR of the natural product was provided by Prof. L. W. Smith, CSIRO, Australia.
(12) Aasen, A. J.; Culvenor, C. C. J. *J. Org. Chem.* **1969**, *34*, 4143–4147.
(13) Authentic samples of the natural and racemic products were provided by Prof. L. W. Smith, CSIRO, Australia and Prof. H. Kakisawa, The University of Tsukuba, respectively, and the ^1H NMR spectra were also provided by them and Prof. H. W. Pinnick, The University of Georgia.

Do Complexes of Composition $MnLX_2$ (L = Tertiary Phosphine) Really Exist? Do They Reversibly Bind Dioxygen?

H. D. Burkett, V. F. Newberry, W. E. Hill,* and S. D. Worley*

Department of Chemistry, Auburn University Auburn University, Alabama 36849

Received November 24, 1982

McAuliffe and co-workers have reported the preparation and partial characterization of a series of manganese(II) complexes of the general formula $MnLX_2$ (L = tertiary phosphine, X = anion) that they claim resemble hemoglobin and myoglobin in that the complexes reversibly interact with dioxygen and other small molecules.[1] Such compounds would be expected to have extensive industrial application in the purification of gas streams, for oxygen storage devices, and possibly even as catalysts for important oxidation reactions. However, Green and co-workers have cast doubt on the early work of McAuliffe by claiming that they were not able to prepare the complexes and observe reversible interaction with dioxygen.[2] In fact they suggest that the dramatic color changes that the MnX_2/L system undergoes upon exposure to dioxygen are due to a transient Mn(III) species that ultimately decomposes by oxidizing the tertiary phosphine present; they further postulate that color changes upon dioxygen uptake would continue as long as tertiary phosphines remain present. McAuliffe has recently rebutted the claims of Green and co-workers by emphasizing the need for preparing the $MnLX_2$ complexes under "absolutely anhydrous" conditions and by ensuring that excess phosphine is not present during the dioxygen uptake experiments.[3] In these laboratories work has been undertaken aimed toward answering the questions that have been raised concerning the existence of the $MnLX_2$ complexes and the nature of the interaction of the complexes, if they do exist, with dioxygen. The primary approach here has been to use infrared spectroscopy as a probe in investigating the possible binding of dioxygen to the alleged complexes.

A considerable amount of effort was expended here in attempting to isolate the $MnLX_2$ complexes by the procedures used by McAuliffe et al. under anhydrous conditions in the absence of oxygen. Complexes could be produced that did reversibly interact with dioxygen, did undergo the marked color changes reported earlier,[1,2] and did provide elemental analyses in accord with the formula $MnLX_2$; however, even the most meticulous sample deposition and pellet preparation procedures under inert, anhydrous conditions always provided solid-state samples that exhibited infrared bands near 3500–3450, 1600, and 550 cm^{-1} attributable to moisture contamination. Such samples did indeed uptake some dioxygen (not quantitative) and change color reversibly, but any cycling of intensity of infrared bands upon exposure/evacuation cycles bore a direct relationship to the intensities of the "water bands" such that no definitive conclusions could be made. It was apparent that the samples were undergoing decomposition to phosphine oxide and/or the $MnL'X_2$ (L' = phosphine oxide) complexes as was evidenced by intense infrared bands growing with time at ca. 1150 cm^{-1}. Ultimately these complexes were no longer active in dioxygen uptake or color change.

It was decided that a new approach for preparation of the infrared samples was necessary. After considerable work, we have developed a means of preparing $MnLX_2$ complexes in an infrared

(1) McAuliffe, C. A.; Al-Khateeb, H.; Jones, M. H.; Levason, W.; Minten, K.; McCullough, F. P. *J. Chem. Soc., Chem. Commun.* **1979**, 736. Hosseiny, A.; McAuliffe, C. A.; Minten, K.; Parrott, M. J.; Pritchard, R.; Tames, J. *Inorg. Chim. Acta* **1980**, *39*, 227. Hosseiny, A.; Mackie, A. G.; McAuliffe, C. A.; Minten, K. *Ibid.* **1981**, *49*, 99. Barber, M.; Bordoli, R. S.; Hosseiny, A.; Minten, K.; Perkin, C. R.; Sedgwick, R. D.; McAuliffe, C. A. *Ibid.* **1980**, *45*, L89. McAuliffe, C. A.; Al-Khateeb, H. *Ibid.* **1980**, *45*, L195.
(2) Brown, R. M.; Bull, R. E.; Green, M. L. H.; Grebenik, P. D.; Martin-Polo, J. J.; Mingos, D. M. P. *J. Organomet. Chem.* **1980**, *201*, 437.
(3) McAuliffe, C. A. *J. Organomet. Chem.* **1982**, *228*, 255.

0002-7863/83/1505-4097$01.50/0