

mixture was stirred for 30 min. Methyl triflate (20 equiv) was added dropwise, and the reaction mixture was warmed gradually to room temperature and stirred for 5 h. Triethylamine (60 equiv) was added and the reaction mixture stirred for 15 min. The polymer was filtered and suspended in acetone in order to remove the molecular sieves. The polymer was further washed with DMSO, acetone, CH_2Cl_2 , and THF.

Analytical samples of the intermediates and the final product were cleaved from the solid support following published procedures^[12] and were purified by flash column chromatography.

10b: ^1H NMR (CDCl_3): δ = 7.89 (d, J = 7.3 Hz, 2 H, SO_2Ph), 7.46 (m, 1 H, SO_2Ph), 7.38 (m, 2 H, SO_2Ph), 7.34–7.18 (m, 10 H, Bn), 4.77–4.67 (m, 3 H), 4.64 (d, J = 8.2 Hz, 1 H), 4.59 (d, J = 11 Hz, 1 H), 3.84–3.78 (m, 1 H), 3.72–3.65 (m, 1 H), 3.63–3.57 (m, 2 H), 3.56–3.48 (m, 1 H), 3.45–3.39 (m, 1 H), 2.53 (q, J = 7.6 Hz, 2 H, SCH_2CH_3), 1.91 (m, 1 H), 1.14 (t, J = 7.6 Hz, 3 H, SCH_2CH_3); Positive-ion electrospray (ES) MS: m/z : 566.2 ($[M]^+ + \text{Na}^+$); Negative-ion ES MS: 578.2 ($[M]^- + \text{Cl}^-$).

27b: ^1H NMR (CDCl_3): δ = 7.86 (m, 2 H), 7.68–7.56 (m, 3 H), 7.50–7.17 (m, 65 H), 6.24 (d, J = 6.0 Hz, 1 H), 5.29–5.25 (m, 1 H), 5.20–5.14 (m, 1 H), 5.11–4.99 (m, 7 H), 4.89–4.42 (m, 34 H), 4.37–4.28 (m, 3 H), 4.12–3.94 (m, 7 H), 4.00–3.82 (m, 8 H), 3.79–3.53 (m, 21 H), 1.11–1.04 (dd, J = 6.3, 6.2 Hz, 6 H); Positive-ion ES MS: 1490.5 ($[M]^+ + \text{Na}^+$); Negative-ion ES MS: 1466.7 ($[M]^- - \text{H}^+$).

Received: November 1, 1997 [Z 11109IE]
German version: *Angew. Chem.* **1998**, *110*, 831–834

Keywords: glycals • glycosylations • oligosaccharides • solid-phase synthesis

The Total Synthesis of Eleutherobin: A Surprise Ending**

Xiao-Tao Chen, Bishan Zhou, Samit K. Bhattacharya,
Clare E. Gutteridge, Thomas R. R. Pettus, and
Samuel J. Danishefsky*

In memory of John K. Stille

The “eleuthesides” comprise^[1] a family of marine-derived natural products that exhibit cytotoxic activity.^[1, 2] Most intriguing of these is eleutherobin (**1**),^[3] which has a modality of action and a potency to warrant its inclusion with paclitaxel, the epothilones, and discodermolide as actual or potential anticancer agents of mechanistic commonality. The first total synthesis of eleutherobin (as well as that of sarcodictyin A) was recently disclosed by Nicolaou et al.^[4]

Our own efforts pursuant to the synthesis of the eleuthesides were recently described.^[5] The most advanced compound in our synthesis was the ketone **2**. We viewed this compound as a platform structure through which naturally occurring eleuthesides could be reached, and a large number of analogues could be fashioned. We turned to the synthesis of eleutherobin (**1**) from **2** (Scheme 1). The conventional approach to this kind of problem would be to develop a method to convert **2** into a suitable glycosyl acceptor (**3**) by overall addition of a C_1 fragment to carbon 3. We would also synthesize a glycosyl donor (cf. suitably activated arabinosyl donor **4**). Classical glycosylation could eventually lead to **1**. In this simple formulation, we do not yet address the question of the order of introduction of the sugar and the urocanic acid appendages.

It seemed possible that one-carbon homologation of enol triflate **5**^[6] could serve as a possible route to reach acceptor **3**. In the event, ketone **2** was converted into **5** by deprotonation and enol triflation. We shall return to this compound shortly.

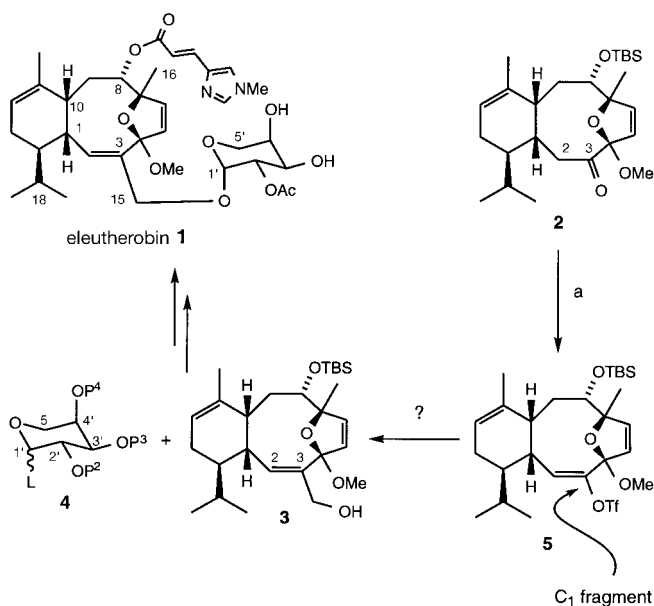
While the matter of the relative configurations of the aglycone and carbohydrate sectors of eleutherobin had not yet been proven to our satisfaction,^[7] we began with the assumption that the compound is derived from D-arabinose.^[4] Following peracetylation and introduction of an ethylthiol group at the anomeric carbon of D-arabinose, compound **6** became available (Scheme 2). Hydrolysis of the three acetate

- [1] A. Varki, *Glycobiology* **1993**, *3*, 97; A. Giannis, *Angew. Chem.* **1994**, *106*, 188; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 178; T. Feizi, *Curr. Opin. Struct. Biol.* **1993**, *3*, 701.
- [2] P. Falk, T. Boren, S. Normark, *Methods Enzymol.* **1994**, *236*, 353, and references therein.
- [3] T. Boren, P. Falk, K. A. Roth, G. Larson, S. Normark, *Science* **1993**, *262*, 1892.
- [4] J. Alper, *Science* **1993**, *260*, 159.
- [5] a) D. Y. Graham, G. M. Lew, P. D. Klein, D. G. Evans, D. J. Evans, Z. A. Saeed, H. M. Malaty, *Ann. Intern. Med.* **1992**, *116*, 705; b) E. Hentschel, G. Brandstatter, B. Dragosics, A. M. Hirschl, H. Nemeg, K. Schutze, M. Taufer, H. Wurzer, *N. Eng. J. Med.* **1993**, *328*, 308.
- [6] For syntheses of the Le^b oligosaccharide see: S. S. Rana, J. J. Barlow, K. L. Matta *Carbohydr. Res.* **1981**, *96*, 231; U. Spohr, R. U. Lemieux *ibid.* **1988**, *174*, 211.
- [7] S. J. Danishefsky, M. T. Bilodeau, *Angew. Chem.* **1996**, *108*, 1482; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1380; P. H. Seeberger, M. T. Bilodeau, S. J. Danishefsky, *Aldrichimica Acta* **1997**, *30*, 75.
- [8] D. A. Griffith, S. J. Danishefsky, *J. Am. Chem. Soc.* **1990**, *112*, 5811; T. Hamada, A. Nishida, O. Yonemitsu, *ibid.* **1986**, *108*, 140.
- [9] C. Zheng, P. H. Seeberger, S. J. Danishefsky, *J. Org. Chem.* **1998**, *63*, 1126.
- [10] J. T. Randolph, S. J. Danishefsky, *Angew. Chem.* **1994**, *106*, 1538; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1470.
- [11] For couplings of thiodonors with glycals see: P. H. Seeberger, M. Eckhardt, C. E. Gutteridge, S. J. Danishefsky *J. Am. Chem. Soc.* **1997**, *119*, 10064. For activation of thiodonors see: H. Lönn *Carbohydr. Res.* **1985**, *135*, 105; *ibid.* **1985**, *139*, 115; H. Lönn *J. Carbohydr. Chem.* **1987**, *6*, 301; P. Fügedi, P. J. Garegg *Carbohydr. Res.* **1986**, *149*, C9.
- [12] J. T. Randolph, K. F. McClure, S. J. Danishefsky, *J. Am. Chem. Soc.* **1995**, *117*, 5712.

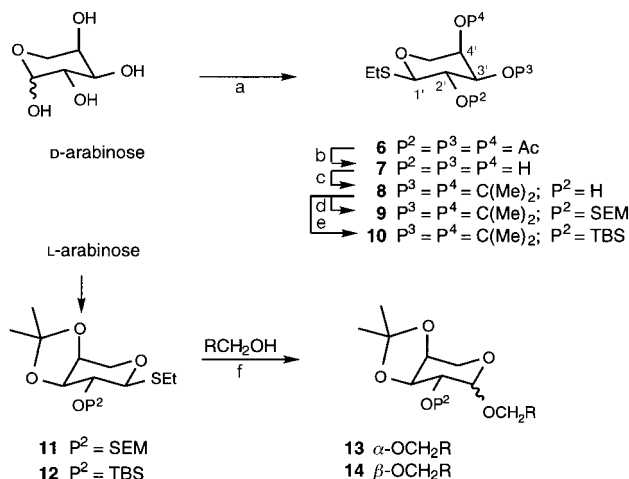
[*] Prof. S. J. Danishefsky,^[+] X.-T. Chen, B. Zhou, Dr. S. K. Bhattacharya, Dr. C. E. Gutteridge, Dr. T. R. R. Pettus
Department of Chemistry, Columbia University
Havemeyer Hall, New York, NY 10027 (USA)

[+] Other address:
Laboratory for Bioorganic Chemistry,
The Sloan-Kettering Institute for Cancer Research
1275 York Avenue, New York, NY 10021 (USA)
Fax: (+1) 212-772-8691
E-mail: c-kandell@ski.mskcc.org

[**] Graduate Fellowships are gratefully acknowledged by X.-T.C. (Kagawa Academy of Science and Technology) and B.Z. (Pharmacia - Upjohn). Postdoctoral Fellowships are gratefully acknowledged by C.E.G. (The Royal Commission for the Exhibition of 1851) and T.R.R.P. (The National Science Foundation). We are grateful to Vinka Parmakovich and Barbara Sporer of the Columbia University Mass Spectral Facility. We also thank Professor Fenical, University of California, San Diego, for kindly providing us spectral data and a copy of the NMR spectrum of natural eleutherobin.



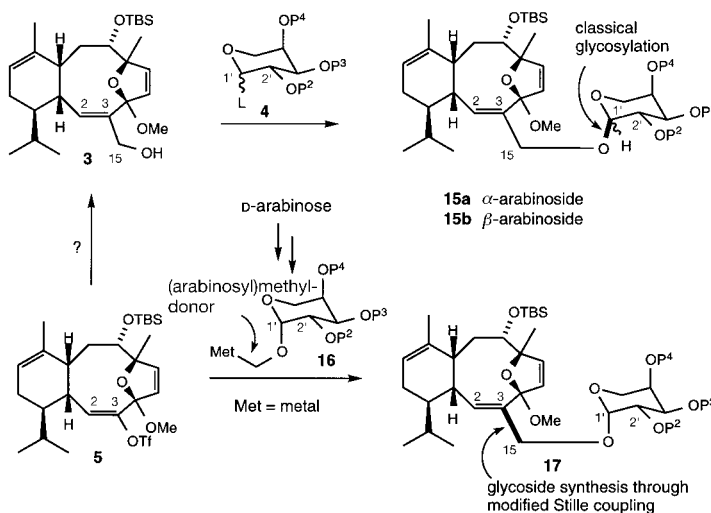
Scheme 1. Conventional glycosylation approach toward the synthesis of **1**. a) KDA/THF, $-78^{\circ}\text{C} \rightarrow 0^{\circ}\text{C} \rightarrow -78^{\circ}\text{C}$, *N*-(5-chloro-2-pyridyl)triflimide $\approx 80\%$. KDA = potassium diisopropylamide; L = glycosyl donor function; $\text{P}^2, \text{P}^3, \text{P}^4$ = suitable protecting groups.



Scheme 2. Synthesis of the potential arabinosyl donors. a) Ac_2O , pyridine, DMAP, $0^{\circ}\text{C} \rightarrow 20^{\circ}\text{C}$, 100%; EtSH, $\text{BF}_3 \cdot \text{Et}_2\text{O}$, CH_2Cl_2 , 20°C , 83% ($\alpha:\beta > 10:1$); b) NaOMe, MeOH, 20°C , 100%; c) 2,2-dimethoxypropane, *p*-TsOH, 20°C , 96%; d) SEM-Cl, $i\text{Pr}_2\text{NEt}$, CH_2Cl_2 , 20°C , 82%; e) TBS-Cl, imidazole, DMAP, CH_2Cl_2 , 20°C , 93%; f) MeOTf, DTBP, $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ (1:2), molecular sieves (4 Å), 0°C . DMAP = 4-dimethylaminopyridine; DTBP = 2,6-di-*tert*-butylpyridine; SEM = 2-(trimethylsilyl)ethoxymethyl; TBS = *tert*-butyldimethylsilyl.

groups gave rise to **7**. The *cis*-related vicinal hydroxy groups at carbons 3' and 4' were engaged in an isopropylidene linkage (see **8**). The lone hydroxy group at C2' was protected either as a SEM ether (see **9**) or as a TBS ether (see **10**). Following an identical series of steps, starting with L-arabinose, the *ent*-compounds **11** and **12** were also in hand. We explored the use of these potential arabinosyl donors with a variety of model primary alcohol glycosyl acceptors such as benzyl or cinnamyl alcohol. Unfortunately, under a variety of activation conditions, we consistently encountered approximate 1:1 mixtures of α - and β -arabinosides (see **13** and **14** in L-series, Scheme 2).^[8]

The thought of subjecting an acceptor of the type **3**, perhaps derivable from **5**, to a stereorandom glycosylation by a system of the type **4** (**3** + **4** $\rightarrow$ **15**) was dismaying (Scheme 3). This



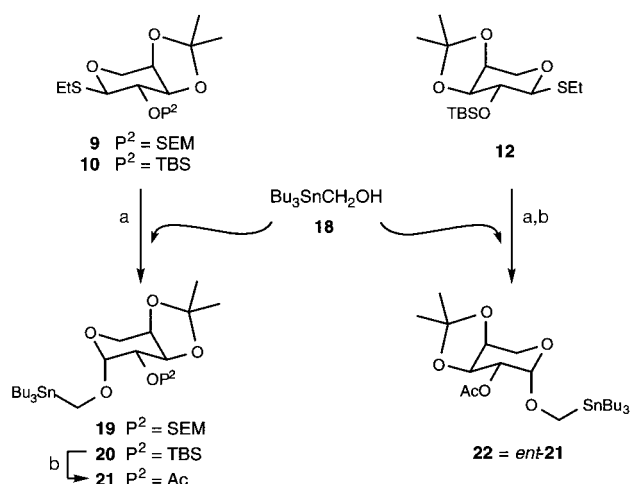
Scheme 3. Glycosylation strategies. Met = metal.

bleak prospect led us to wonder about the possibility of conducting the merger of the aglycone and carbohydrate domains in a nonconventional manner. The stereochemistry of the anomeric carbon of the carbohydrate domain would be defined in advance, (see (arabinosyl)methyl ("oxycarba") donor type **16**). Perhaps, a direct coupling of triflate **5** with **16** could be conducted to lead to the bidomainal compound **17**. Thus, formation of a carbon–carbon bond ($\text{C}_3\text{--C}_{15}$) rather than a conventional glycosylation ($\text{C}_{15}\text{--O--C}_1$) would be used to join the domains.

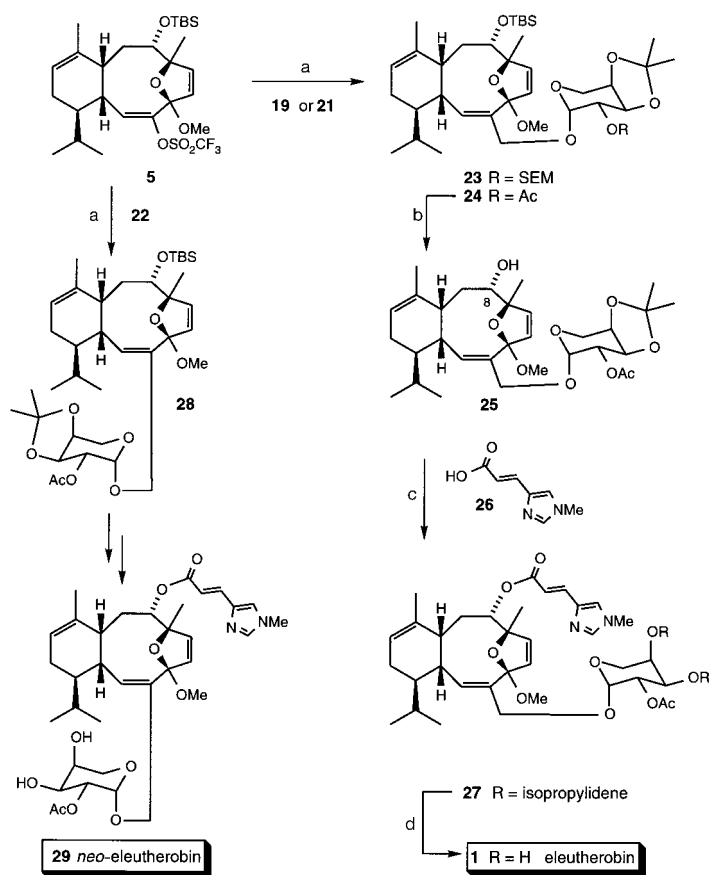
For our first exploration into the possibility of such a coupling, we focused on a permutation wherein the metal in **16**^[9] would be tin in the form of a tri-*n*-butylstannyl function. What we would be seeking would be an "sp³ version" of the Stille reaction.^[10] While there was precedent for transferring simple alkoxyalkyl ligands in a few select cases by an sp³ Stille-like coupling,^[11, 12] no one, to our knowledge, had reported on the possibility of delivering a fully developed carbohydrate by an "oxycarba" transfer through such a process.

To explore this possibility, we synthesized the novel potential (arabinosyl)methyl donors **19** and **20** (Scheme 4). The previously described **9** was used as a classical donor in a Lönn–Garegg glycosylation^[13] with tri-*n*-butylstannylmethanol (**18**).^[14] We obtained a 93% yield of a 1:1 mixture of glycosides which was readily separated into its components. For the moment only the β -form^[8] **19** was of interest. Similarly, the thioethyl donor, **10** served to glycosylate **18**, affording a 1:1 mixture of separable glycosides. Only the β form^[8] **20** was employed. Cleavage of the TBS group and installation of an acetate led to **21**. In an identical way, the *ent*-(arabinosyl)-methyl donor **22** was prepared from **12**.

In the event, modified Stille coupling of vinyl triflate **5** with **19** or **21** gave rise, in 40–50% yields, to **23** and **24**, respectively (Scheme 5). From compound **24**, the pathway to eleutherobin (**1**) was straightforward. The hydroxy group at C8 was



Scheme 4. Synthesis of the (arabinosyl)methyl donors for Stille coupling. a) MeOTf, DTBP, $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ (1:2), molecular sieves (4 Å), 0 °C, 93 % ($\alpha:\beta = 1:1$); b) TBAF, THF, 20 °C, $\approx 98\%$; Ac_2O , DMAP, CH_2Cl_2 , 20 °C, $\approx 99\%$. DMAP = 4-dimethylaminopyridine; DTBP = 2,6-di-*tert*-butylpyridine; TBAF = tetrabutylammonium fluoride.



Scheme 5. Synthesis of eleutherobin and *neoeleutherobin*. a) $\text{Pd}(\text{PPh}_3)_4$, LiCl, 2-amino-5-chloropyridine, THF, Δ , $\approx 40\text{--}50\%$; b) TBAF, THF, 20 °C, 67 %; c) DCC, DMAP, PhCH_3 , 50 °C, $\approx 80\%$; d) PPTS, MeOH, Δ , $\approx 70\%$. DCC = dicyclohexylcarbodiimide, DMAP = 4-dimethylaminopyridine; PPTS = pyridinium *p*-toluenesulfonate; TBAF = tetrabutylammonium fluoride.

liberated (see compound **25**) and acylated with (*E*)-*N*(1)-methylurocanic acid **26**^[15] to afford **27**, as shown. Removal of the acetonide protecting group, released eleutherobin itself.

The 500 MHz NMR spectrum (and optical rotation) of fully synthetic eleutherobin corresponded very closely to the spectrum of natural eleutherobin, recorded and forwarded to us by Fenical et al.^[16] A sample of naturally derived eleutherobin was not available for direct comparison in our laboratory.

At this stage, we could not be confident that the spectral consequences of having an enantiomeric L-arabinose-derived sugar domain attached to the same aglycone (i.e. *neoeleutherobin*, vide infra) would be significant. If the two domains were virtually noninteractive, the differences between the two permutations might be difficultly discernible. To check this point, we proceeded to synthesize the only viable alternative version of eleutherobin. For this purpose, **22** was coupled with vinyl triflate **5** to produce **28**. Following an identical series of steps used in the previous series, compound **29** was in hand.^[17]

Examination of the 500 MHz NMR spectrum of **29**, which we call *neoeleutherobin*, revealed small, but clear-cut, differences with the spectrum of eleutherobin itself, provided by Fenical et al. Hence, we can rigorously assert that the relative chiralities of the aglycone and arabinose domains of eleutherobin are as shown in **1**, and that the total synthesis of eleutherobin has been accomplished.

We are hopeful that our synthesis, though not currently without weaknesses, will yield amounts of eleutherobin adequate for in vivo evaluation. The generation of families of analogues and their evaluation can certainly be accomplished. These efforts are under way. Moreover, the synthesis serves to highlight a new strategy for generation of certain kinds of glycosides. Studies directed toward establishing the scope and limitation of the modified Stille approach, as well as attempts to include other metals in the general paradigm, **5** + **16** $\rightarrow$ **17**, are in progress.

Received: December 22, 1997 [Z11287IE]
 German version: *Angew. Chem.* **1998**, *110*, 835–838

Keywords: antitumor agents • eleutherobin • glycosylations • Stille coupling • total synthesis

- [1] For sarcodictyins see: a) M. D'Ambrosio, A. Guerriero, F. Pietra, *Helv. Chim. Acta* **1987**, *70*, 2019; b) *ibid.* **1988**, *71*, 964.
- [2] For eleuthosides see: S. Ketzinel, A. Rudi, M. Schleyer, Y. Benayahu, Y. Kashman, *J. Nat. Prod.* **1996**, *59*, 873. Pending development of an official name for this exciting family of natural products, we are referring to them as "eleuthosides" based on eleutherobin as the key member of the grouping.
- [3] a) W. H. Fenical, P. R. Jensen, T. Lindel, (University of California) US-A 5,473,057, **1995** [*Chem. Abstr.*, **1996**, *124*, 194297z]; b) T. Lindel, W. H. Fenical, P. R. Jensen, B. H. Long, A. M. Casazza, J. Carboni, C. R. Fairchild, *J. Am. Chem. Soc.* **1997**, *119*, 8744; c) B. H. Long, C. R. Fairchild, A. J. Wasserman, J. Carboni, A. M. Casazza, W. H. Fenical, *Cancer Res.*, **1997**, in press. We thank Professor Fenical for providing us with these papers in advance of publication.
- [4] a) K. C. Nicolaou, F. van Delft, T. Ohshima, D. Vourloumis, J. -Y. Xu, S. Hosokawa, J. Pfefferkorn, S. Kim, T. Li, *Angew. Chem.* **1997**, *109*, 2631; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2520. b) For the total synthesis of sarcodictyin A see: K. C. Nicolaou, J.-Y. Xu, S. Kim, T. Ohshima, S. Hosokawa, J. Pfefferkorn, *J. Am. Chem. Soc.* **1997**, *119*, 11353. c) For synthetic studies in the arabinose section of eleutherobin see: K. C. Nicolaou, J. I. Trujillo, K. Chibale, *Tetrahedron*, **1997**, *53*, 8751.

- [5] X. -T. Chen, C. E. Gutteridge, S. K. Bhattacharya, B. Zhou, T. R. R. Pettus, T. Haskall, S. J. Danishefsky, *Angew. Chem.* **1998**, *110*, 196; *Angew. Chem. Int. Ed.* **1998**, *37*, 185.
- [6] For use of *N*-(5-chloro-2-pyridyl)triflimide as a triflating reagent see: a) D. L. Comins, A. Dehghani, *Tetrahedron Lett.* **1992**, *33*, 6299; b) D. L. Comins, A. Dehghani, C. J. Foti, S. P. Joseph, *Org. Synth.* **1996**, *74*, 77.
- [7] The data provided in references [2] and [3], pertaining to eleuthoside (A and B) and eleutherobin, respectively, do not rigorously establish the absolute stereochemical nature of the sugar domain. The total synthesis (ref. [4]) did not explicitly deal with the *neoeleutherobin* issue raised here.
- [8] By conventions of carbohydrate nomenclature, α and β in the arabinose series correspond to the configurational relationship between C-1 and C-4 of the pyranoside. (For the nomenclature of carbohydrates see: A. D. McNaught *Carbohydr. Res.* **1997**, *197*, 1). In terms of the structures presented here, α would correspond to the equatorial anomer and β to the axial one.
- [9] For an interesting example of metalated [((tetrahydropyran-2-yl)-oxy)methyl] species see: D. K. Hutchinson, P. L. Fuchs, *J. Am. Chem. Soc.* **1987**, *109*, 4930.
- [10] a) W. J. Scott, J. K. Stille, *J. Am. Chem. Soc.* **1986**, *108*, 3033. For reviews see: b) J. K. Stille, *Angew. Chem.* **1986**, *98*, 504; *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 508; c) T. N. Mitchell, *Synthesis* **1992**, 803; c) K. Ritter *ibid.* **1993**, 735.
- [11] a) M. Kosugi, T. Sumiya, T. Ogata, H. Sano, T. Migita, *Chem. Lett.* **1984**, 1225; b) A. Majeed, Ø. Antonsen, T. Benneche, K. Undheim *Tetrahedron* **1989**, *45*, 993; c) G. K. Cook, W. J. Hornback, C. L. Jordan, J. H. McDonald III, J. E. Munroe *J. Org. Chem.* **1989**, *54*, 582; d) J. P. Férézou, M. Julia, Y. Li, W. Liu, A. Pancrazi *Synlett* **1991**, 53.
- [12] For selective alkyl transfer to a vinyl iodide using internal coordination at tin see: E. Vedejs, A. R. Haight, W. O. Moss *J. Am. Chem. Soc.* **1992**, *114*, 6556.
- [13] a) R. J. Ferrier, R. W. Hay, N. Vethaviasar, *Carbohydr. Res.* **1973**, *27*, 5; b) P. J. Garegg, C. Henrichson, T. Norberg, *ibid.* **1983**, *116*, 162; c) H. Lönn, *ibid.* **1985**, *139*, 105, 115.
- [14] D. Seebach, N. Meyer *Angew. Chem.* **1976**, *88*, 484; *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 438. We also approached the synthesis of the stannyl methoxy compounds (**19**, **20** etc.) by a Schmidt-type (R. R. Schmidt, M. Reichrath, *Angew. Chem.* **1979**, *91*, 497; *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 466; R. R. Schmidt, *ibid.* **1986**, *98*, 213 and **1986**, *25*, 212) alkylation of the anomeric hydroxyl with tributylstannylmethyl iodide. For preparation of the alkylating agent see: a) S. L. Buchwald, R. B. Nielsen, J. C. Dewan, *Organometallics* **1989**, *8*, 1593; b) D. E. Seitz, J. J. Carroll, C. P. Cartaya M., S-H. Lee, A. Zapata *Synth. Commun.* **1983**, *13*, 129.
- [15] a) See ref. [1 a]; b) H. Mawlawi, M. C. Monje, A. Lattes, M. Rivière, *J. Heterocycl. Chem.* **1992**, *29*, 1621.
- [16] **1**: $[\alpha]_D^{25} = -73.2$ ($c = 0.17$ in MeOH). Previous reports of $[\alpha]_D^{25}$ for eleutherobin were: -49.3 ($c = 3.0$ in MeOH)^[3b] and -67.0 ($c = 0.2$ in MeOH)^[4a]
- [17] **29**: $[\alpha]_D^{25} = +44.5$ ($c = 0.09$ in MeOH).

Intermolecular Hydrogen Bonding between Water and Pyrazine**

Walther Caminati,* Laura B. Favero, Paolo G. Favero, Assimo Maris, and Sonia Melandri

Hydrogen bonds involving aromatic rings, especially those containing heterocyclic nitrogen atoms, are of fundamental importance in nature. For example, they are essential in base pairing of oligonucleotides, and they determine the tertiary structure and functions of biopolymers. Since all these processes occur in an aqueous environment, the corresponding interactions with water are also of particular interest.^[1]

Although it had been speculated for many years that the π -electron cloud of aromatic rings could act as a hydrogen-bond acceptor, the position of hydrogen was first established unambiguously through rotational spectra from the 1:1 complex of benzene with water obtained in a supersonic expansion.^[2, 3] Thus, it has been shown that the water molecule is located above the plane of the benzene ring, subject to nearly free internal rotation, with both hydrogen atoms pointing toward the π cloud.

Because aromatic nitrogen heterocycles are essential components of proteins and nucleotides, we thought it would be interesting to study the nature of the interactions of such compounds with water. Rotational transitions of pyridine/water have already been described, but that research project has since been abandoned.^[4] Although pyrimidine is the most common six-membered aromatic ring in nature, we chose pyrazine (PRZ) as a prototype, because in this case only the spectrum of the complex is observable in the aromatic-ring/water mixture, since PRZ itself produces no rotational spectrum (the electric dipole moment μ is zero due to symmetry).

Evidence of hydrogen-bond formation between PRZ and water has been obtained from electronic spectra recorded in solution^[5] and in an argon matrix,^[6] but extensive efforts to observe the formation of such complexes in a supersonic expansion were unsuccessful.^[7] The position of the hydrogen atom has not been precisely determined; nevertheless, the blue shift of the $n-\pi^*$ transition strongly suggests that the hydrogen atom is bound to the nitrogen atom. The effects of hydrogen bonding interactions on the electronic molecular spectra of PRZ/water complex and PRZ in solution have been investigated theoretically by Zeng et al.^[8] In all cases the interpretations of experimental spectra rely on the assumption of a linear structure for the $\text{OH} \cdots \text{N}$ bond.

Molecular beam Fourier transform microwave (MBFTMW) spectrometers have frequently been used for the investigation of rotational spectra of molecular complexes of aromatic

[*] Prof. W. Caminati, Prof. P. G. Favero, Dr. A. Maris, Dr. S. Melandri
Dipartimento di Chimica "G. Ciamician" dell'Università
Via Selmi 2, I-40126 Bologna (Italy)
Fax: (+39)51-259-456
E-mail: caminati@ciam.unibo.it
Dr. L. B. Favero
Istituto di Spettroscopia Molecolare del C.N.R.
Via Gobetti 101, I-40129 Bologna (Italy)

[**] We wish to thank Mr. A. Millemaggi for technical help, and the Ministero dell'Università e della Ricerca Scientifica e Tecnologica, as well as the C.N.R., for financial support.