($^2\Pi$) is a pair of vertical transitions, one to the ground state of NH ($^3\Sigma^-$) and the other to the excited singlet state, $^1\Delta$. The extended Franck–Condon contour in our photodetachment spectra with excitation of ring-breathing modes implies that the ground state of the $C_6H_5N^-$ ion is $\tilde{X}\ ^2B_2$ and that much of the charge is delocalized from the N atom onto the phenyl ring. This contrasts with the $\tilde{A}\ ^2B_1$ ion which localizes the extra electron in the $b_2$, nonbonding orbital, on the N atom. Preliminary UHF calculations[10] on both states of the $C_6H_5N^-$ ion in a 6-311++G** basis lead to the $^2B_2$ state being stabilized by about 10 kcal/mol below the $^2B_1$ state. Figure 3 is a symbolic drawing which contrasts the electronic states of NH with those of $C_6H_5N$.

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**Registry No.** $C_6H_5N_3$, 622-37-7; $C_6D_5N_3$, 85770-99-6; $C_6H_5N^-$, 74586-02-0; $C_6D_5N^-$, 143332-33-6; $C_6H_5N$, 2655-25-6; $C_6D_5N$, 143332-34-7.

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## Total Synthesis of the NodRm-IV Factors, the Rhizobium Nodulation Signals

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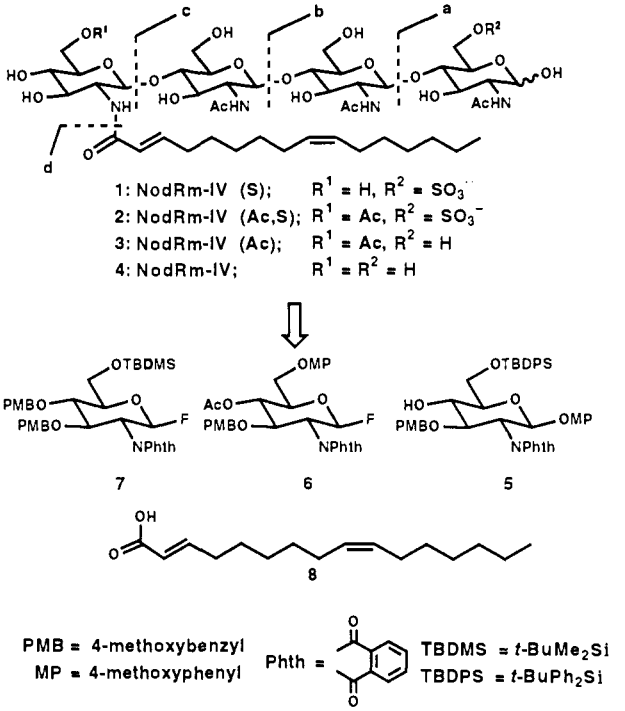
NodRm-IV (S) (**1**) and NodRm-IV (Ac,S) (**2**) are sulfated lipooligosaccharides of *N*-acetyl-D-glucosamine secreted by the microorganism *Rhizobium meliloti*.[1-6] These remarkably specific compounds play a crucial role in the Rhizobium–legume symbiosis by eliciting the formation of nitrogen-fixing root nodules and root hair deformation on alfalfa but not on vetch. Interestingly, the non-sulfated compounds NodRm-IV (Ac) (**3**) and NodRm-IV (**4**) elicit the same organogenesis and root morphology on vetch but not on alfalfa.[5,6] Experiments with mutant strains of *R. meliloti* identified the genes responsible for the sulfation of these lipooligosaccharides.[7] The important actions of these molecules coupled with their fascinating specificity, natural scarcity, and challenging molecular structures prompted us to target them for chemical synthesis. Herein we report the first total synthesis of these substances (**1–4**) in their naturally occurring forms.

**Scheme I.** Structures and Retrosynthetic Disconnections of NodRm-IV Factors (**1–4**)




Despite their repetitive nature in glucosamine units, the structures of NodRm-IV factors (**1–4**) are synthetically quite challenging due to the presence of unsaturation, nitrogen, and sulfur. This variety of functional groups required a carefully designed and executed strategy. Scheme I presents the retrosynthetic analysis on which the synthesis was based. Thus, disconnections at the indicated bonds led to key building blocks **5–8**. The projected construction called for an a, b, c, d sequence of coupling reactions and selective deblocking of hydroxyl groups.

Coupling of glucosamine derivative **5** with glycosyl fluoride **6** under the Mukaiyama–Suzuki[8] conditions led to disaccharide **9** with a β-glycoside linkage as expected from the directing effect of the *N*-phthalimido group (Scheme II). Liberation of the 4′-OH group followed by attachment of a second glucosamine unit **6** as above resulted in the stereospecific formation of trisaccharide **11**. Having performed their function as activating and β-directing groups, the phthalimide moieties were removed with hydrazine, leading to the triamine **12**, which was acetylated to afford the triacetamide **13**. Introduction of the final glucosamine unit was accomplished using derivative **7** and the above mentioned conditions, furnishing tetrasaccharide **14** stereoselectively. Generation of the free amine functionality from **14** as described above allowed the incorporation of the unsaturated fatty acid chain **8** through intermediate **15** and the action of 2-chloro-1-methylpyridinium

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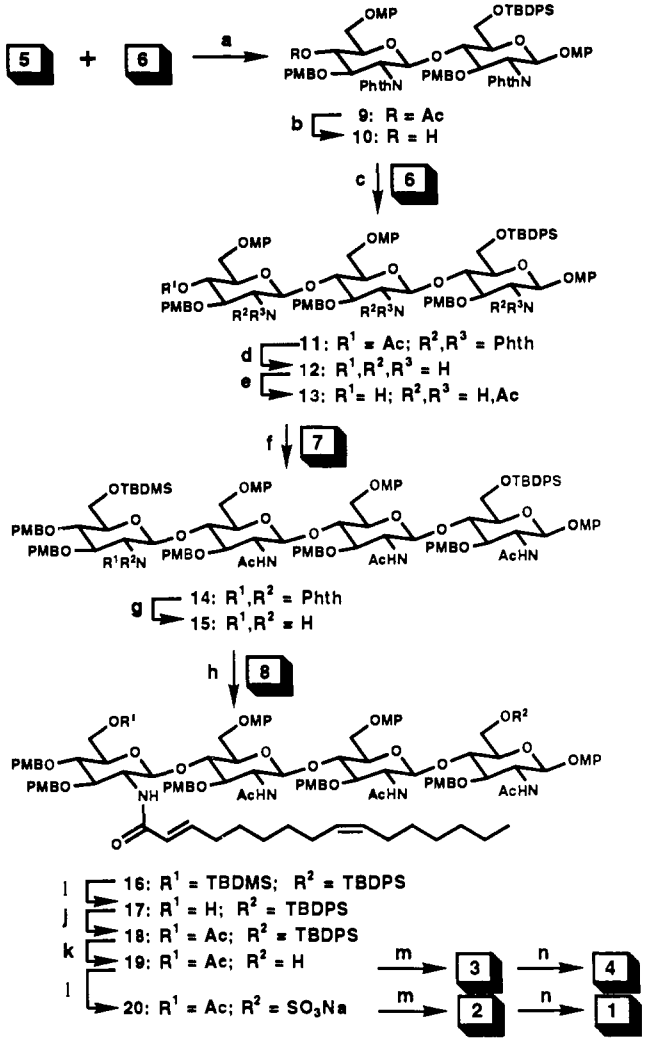
**Scheme II.** Total Synthesis of NodRm-IV Factors[a]




[a] Reagents and conditions: (a) 1.0 equiv of **5**, 1.75 equiv of **6**, 5.0 equiv of AgOTf, 5.0 equiv of $Cp_2ZrCl_2$, 1.0 equiv of 2,6-di-*tert*-butyl-4-methylpyridine, 4-Å molecular sieves, $CH_2Cl_2$, 0–25 °C, 16 h, 56% (plus 36% recovered **5**); (b) 1.0 equiv of $K_2CO_3$, MeOH–THF (1:1), 25 °C, 2 h, 90%; (c) 2.0 equiv of **6**, 5.0 equiv of AgOTf, 5.0 equiv of $Cp_2HfCl_2$, 1.0 equiv of 2,6-di-*tert*-butyl-4-methylpyridine, 4-Å molecular sieves, $CH_2Cl_2$, 0–25 °C, 16 h, 60% (plus 37% recovered **10**); (d) excess of hydrazine hydrate, EtOH–benzene (20:1), 100 °C, 16 h; (e) excess of $Ac_2O$, MeOH–$CH_2Cl_2$ (1:1), 25 °C, 30 min, 72% for two steps; (f) 5.0 equiv of **7**, 5.0 equiv of AgOTf, 5.0 equiv of $Cp_2HfCl_2$, 0.2 equiv of 2,6-di-*tert*-butyl-4-methylpyridine, 4-Å molecular sieves, $CH_2Cl_2$, 25 °C, 16 h, 50% (plus 25% recovered **13**); (g) excess of hydrazine hydrate, EtOH, 100 °C, 6 h, 87%; (h) 3.0 equiv of **8**, 3.0 equiv of 2-chloro-1-methylpyridinium iodide, 3.3 equiv of $Et_3N$, MeCN, 25 °C, 2 h, 73%; (i) 1.3 equiv of pyridinium *p*-toluenesulfonate, EtOH, 25 °C, 16 h; (j) 1.5 equiv of $Ac_2O$, 1.1 equiv of $Et_3N$, DMAP (cat.), $CH_2Cl_2$, 25 °C, 10 min, 72% for two steps; (k) 3.0 equiv of TBAF, THF, 25 °C, 1.5 h, 88%; (l) excess of $SO_3$·$NMe_3$, pyridine, 25 °C, 1 h, 85%; (m) 20.0 equiv of ceric ammonium nitrate (CAN), MeCN–$H_2O$ (4:1), 25 °C, 1 h, 30%; (n) excess of NaOMe, MeOH, 25 °C, 3 h, 75%.

iodide.[9] Selective removal of the *tert*-butyldimethylsilyl group from compound **16** proceeded smoothly on exposure to PPTS[10] to afford **17**. Acetylation of **17** followed by desilylation with $^nBu_4NF$ gave compound **19**. Sequential deprotection of **19** with ceric ammonium nitrate (CAN) and NaOMe led to the targeted NodRm-IV (Ac) (**3**)[11] and NodRm-IV (**4**), respectively. Alternatively, sulfation of **19** with $SO_3$·$NMe_3$ and ion exchange ($Na^+$) gave compound **20**. Sequential deprotection of **20** under the above conditions gave NodRm-IV (Ac,S) (**2**)[11] and NodRm-IV (S) (**1**). Final products **1–4** were purified by reverse-phase HPLC as described in the supplementary material.

The described chemistry renders these scarce bioactive compounds readily available for further biological studies. Molecular design and structure–activity studies are also now feasible, and so is the isolation of the receptors of these compounds.

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**Supplementary Material Available:** Schemes for the synthesis of building blocks **5–8**, including reagents, conditions and yields, and listing of selected physical data for compounds **9**, **11**, **14**, **16**, **19**, **20**, **4**, **3**, **2**, and **1** (12 pages). Ordering information is given on any current masthead page.

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## Kinetic Importance of Conformations of Nicotinamide Adenine Dinucleotide in the Reactions of Dehydrogenase Enzymes

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Suggestions regarding the relationship of cofactor conformation to stereospecificity[1] and to rates[2] of dehydrogenase enzymes have emerged. Our objectives have been to evaluate the potential energies of ground-state conformations and their influence on reaction trajectories and the structures of transition states. To assess the importance of conformational features, we have employed semiempirical (AM1)[3] and molecular dynamics ($CHARM_m$)[4] calculations using single-crystal X-ray structures of both nicotinamides and 1,4-dihydronicotinamides[5] and dehydrogenase enzymes.[6] The virtual angles $X_n$, $X_{am}$, $\alpha_C$, and $\alpha_N$ define the conformations of interest (Charts I and II).

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