consistently larger than those of K_{kin} (Tables I and II). For reactions of R^+ this difference could be due to the spectral measurements being made in highly acidic solutions, whereas the rate measurements are made in dilute alkali, but this explanation seems improbable because the kinetic salt effects due to the arenesulfonates are little affected by added 3 *M* NaCl, and differences between K_s and K_{kin} are less for R^+ than for MG^+ (Tables I and II).

There are several explanations for the different values of K_s and K_{kin}. (i) Our estimation of K_s depends on the assumption that free carbocations are in equilibrium with one species of ion pairs, but there may be a family of ion pairs and the difference spectra may detect only those in which the ions are closely associated. (ii) In addition to the formation of relatively unreactive ion pairs there should be an unfavorable primary kinetic salt effect upon the reactions of oppositely charged ions, although the relatively small effects of salts having small anions, e.g., Cl^-, suggests that these primary effects are not large.[6,7] (iii) The special positive salt effect upon SN1 reactions in nonpolar solvents is explained in terms of an increased rate of dissociation of a solvent separated ion pair,[1] and if ionic recombination in water involves prior formation of an ion pair, e.g., MG^+N^- (cf. ref 4), such a pair could be split unproductively by an arene sulfonate ion, e.g., Scheme II, and this splitting should be more important in reactions of the less reactive MG^+.

Scheme II

$$MG^+ \overset{N^-}{\rightleftharpoons} MG^+N^- \longrightarrow MGN$$

$$ArSO_3^- \uparrow\downarrow N^-$$

$$MG^+ArSO_3^-$$

The carbocations, R^+ and MG^+, have delocalized charge, and they should be polarizable and relatively hydrophobic, and it is these properties which apparently dictate interactions with the aromatic solutes, irrespective of charge (Tables I and II). For a given salt K_s and K_{kin} come closer in magnitude as the binding with the carbocations increases.

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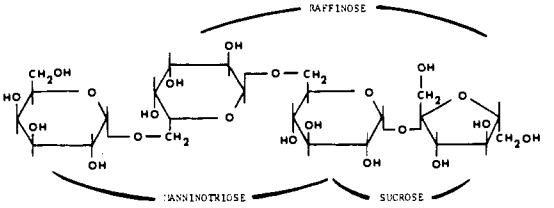
Conformation of the Tetrasaccharide Stachyose

Sir:

Stachyose ($C_{24}H_{42}O_{21}\cdot xH_2O$), *O*-α-D-galactopyranosyl-(1→6)-*O*-α-galactopyranosyl-(1→6)-*O*-α-D-glucopyranosyl (1→2)-α-D-fructofuranoside, is a tetrasaccharide which is widely distributed in the botanical world. It is usually concentrated in plant storage organs (roots, seeds, tubers, etc.), and is often found associated with sucrose and raffinose. These three sugars are the most common plant oligosaccharides. Raffinose is composed of a sucrose portion and one added galactopyranose residue. Stachyose contains an additional galactopyranose ring. Further sequential addition of galactose (1→6) linked residues leads to the relatively rare pentasaccharide, verbascose, and the hexasaccharide, ajugose, whose structures are undetermined.



Stachyose, which crystallizes as a hydrate, represents the first tetrasaccharide structure to be fully characterized by X-ray single-crystal analysis. It crystallizes in the orthorhombic space group $P2_12_12$ with a = 12.801 (6) Å, b = 24.026 (5) Å, and c = 10.856 (6) Å. Crystalline stachyose probably varies in its hydration. Assuming four molecules of stachyose per unit cell, and four water molecules per stachyose molecule, the calculated crystal density is 1.469 g cm^{-3}. With five molecules of water per stachyose molecule, it is 1.505 g cm^{-3}. French et al.[1] reported an experimental crystal density of 1.485 g cm^{-3}, which would correspond to approximately 4.4 water molecules per stachyose molecule. (The commercial sample was labeled as a pentahydrate which might lose water in storage.)

Cu Kα radiation (λ 1.54178) was used to collect 3120 independent reflections with a maximum 2θ of 127.3°. At a later date, 2312 additional independent reflections were collected from the same crystal using Mo Kα radiation (λ 0.71069). The final data set included the full diffracting sphere for Cu radiation and also some reflections available only to Mo radiation. The molybdenum data were put on the same scale as the copper data and used to get normalized structure factor magnitudes $|E|$ which were then used to solve the structure by direct methods. A partial structure was obtained by application of the symbolic addition procedure for noncentrosymmetric crystals.[2] This fragment was then developed into the full structure by the tangent formula refinement and expansion.[3] Full-matrix three-dimensional least-squares refinement[4] (using only the 3120 Cu reflections) is being carried out and difference maps have been calculated to locate the H_2O molecules. The crystallographic R factor, with isotropic thermal factors for all atoms and four water molecules included, is now 0.155. Further difference maps seem to indicate alternative positions for H_2O molecules. There may be a disorder involving two distinct networks of H_2O molecules. The H_2O molecules will certainly play a significant role in packing of the molecules in the crystal. The packing will be described after refinement has been completed.

Figure 1 illustrates the results of the X-ray analysis on stachyose as well as the results of structure studies on sucrose[5] and raffinose.[6] The carbon atoms of the first galactose residue are conventionally numbered, while the numbers on the second galactose, the glucose, and the fructose

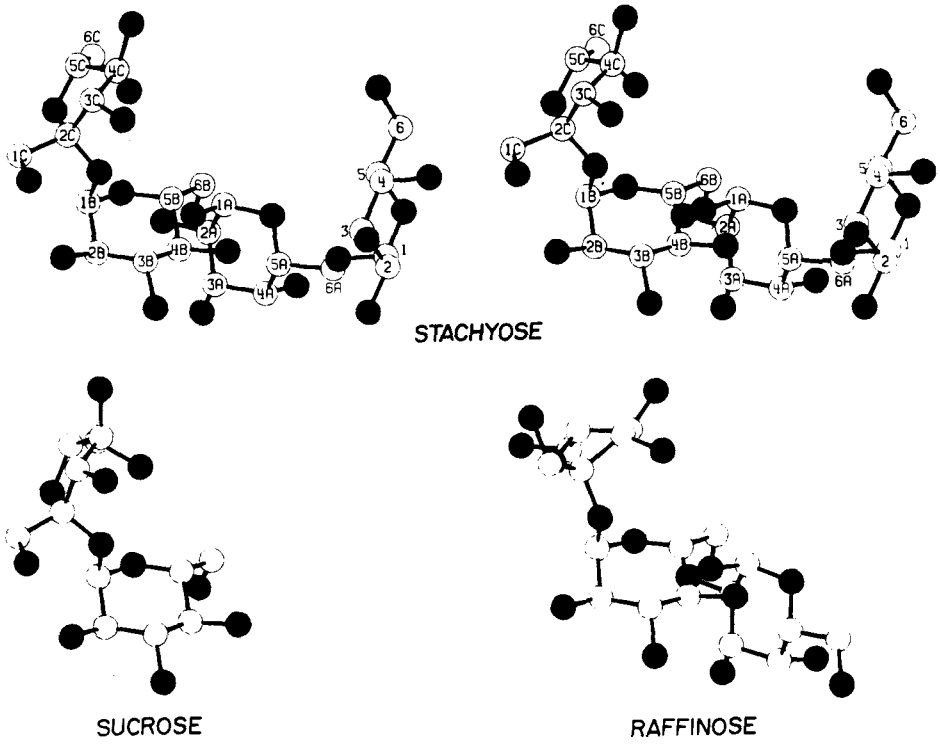


Figure 1. A comparison of the conformations of sucrose, raffinose, and stachyose. Oxygen atoms are blackened to distinguish them from the carbon atoms. The two views of stachyose are suitable for stereo viewing.

Table I. Torsion Angles Describing Ring Linkages

	(1 → 6) Linkages	
	Stachyose	Raffinose
C(2)–C(1)–O(1)–C(6A)	−154.7	
O(5)–C(1)–O(1)–C(6A)	84.4	
C(4A)–C(5A)–C(6A)–O(1)	−154.4	
O(5A)–C(5A)–C(6A)–O(1)	87.2	
C(1)–O(1)–C(6A)–C(5A)	−174.1	
C(2A)–C(1A)–O(1A)–C(6B)	−173.6	−167.6
O(5A)–C(1A)–O(1A)–C(6B)	65.5	71.9
O(1A)–C(6B)–C(5B)–O(5B)	−61.6	−64.8
O(1A)–C(6B)–C(5B)–C(4B)	60.8	58.4
C(1A)–O(1A)–C(6B)–C(5B)	−176.3	−169.5

	(1 → 2) Linkages		
	Stachyose	Raffinose	Sucrose
C(1B)–O(1B)–C(2C)–O(2C)	−50.1	11.4	−44.4
C(1B)–O(1B)–C(2C)–C(3C)	−165.1	−105.5	−159.6
C(1B)–O(1B)–C(2C)–C(1C)	64.7	129.5	73.9
C(2C)–O(1B)–C(1B)–O(5B)	109.6	81.7	107.6
C(2C)–O(1B)–C(1B)–C(2B)	−132.0	−157.5	−129.2

residues bear the suffixes A, B, and C, respectively. The conformations of the three pyranose rings are "normal" chair ($^4C_1$) forms, with ring torsion angles of ~55° magnitude. The fructofuranosyl ring is puckered, with C(3C) exo and C(4C) endo relative to the ring substituents O(1C) and C(6B). The atom labeled C(3C) is 0.38 Å out of the plane passing through C(2C), O(2C), and C(5C); atom C(4C) is 0.20 Å from this plane. Using the suggested nomenclature of Jeffrey and Park,[7] this conformation can be labeled $_3T^4$. The furanose ring pucker in sucrose and raffinose is similar in direction, but in those structures C(4) was displaced further from the plane than C(3).

The overall shape of the stachyose molecule is defined by the torsion angles about the single bonds which link the residues. There are eight such bonds, three in each of the (1→6) linkages and two in the GLU-(1→2)-FRUC linkage. The "hard-sphere" computer calculations of Rees and Scott[8] indicate that the allowed ranges for the torsion angles involved in α-(1→6)-glucans and α(1→6)-galactans are extremely large; i.e., such joints are very flexible. Prior studies of the sucrose moiety have been summarized by Jeffrey and Park,[7] and indicate a considerable flexibility in the (1→2) linkage as well.

Table I lists the linkage torsion angles of stachyose, and compares them with corresponding linkages in sucrose and raffinose. Reference to the table or Figure 1 illustrates that the sucrose moiety in stachyose closely resembles the conformation found in sucrose itself and that raffinose differs considerably in this portion of the molecule. Stachyose is remarkably similar to raffinose in its GAL-(1→6)-GLU linkage; the torsion angles all agree to within 7°. The GAL-(1→6)-GAL linkage conformation has not been previously characterized and differs considerably from the GAL-(1→6)-GLU link, particularly with regard to torsions about the C(5A)–C(6A) and C(5B)–C(6B) bonds, which differ by 140–150 degrees.

Although Rees and Scott list a large "accessible" range of 180 ± 100° for the torsion about the central bond of a (1→6) linkage, the range observed thus far in structure determinations is much smaller. In the two linkages of stachyose involving three single bonds, the central-bond torsions are −174° and −176°; in raffinose,[6] −169.5°; in planteose,[9] where α-D-GAL(1→6)-β-D-FRUC occurs, the angle is 172.5°; in kestose,[7] (β-D-FRUC-(1→2)-β-D-FRUC), the angle is 169.7°. Reducing the magnitude of this torsion generally tends to fold the sugar upon itself, and increases nonbonded repulsions. The effective range for this parameter can probably be safely narrowed to the immediate vicinity of 180° when considering the conformational possibilities for open-chain (1→6) linked oligo- or polysaccharides.

Since this note was first submitted, an independent crystallographic investigation of stachyose came to our attention. Andrews and Jeffrey[10] obtained stachyose coordinates which agree with those obtained in this investigation. Full crystallographic details of both determinations will be published elsewhere in the future.

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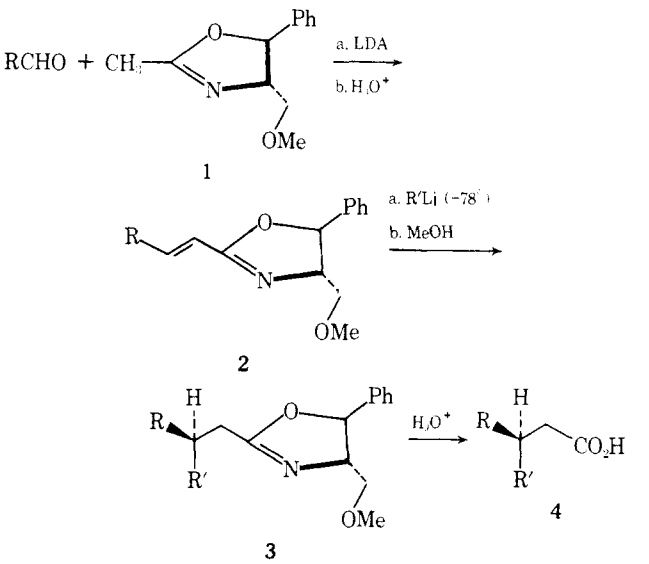
Oxazolines. XIX. An Asymmetric Synthesis of 3-Substituted Alkanoic Acids via Conjugated Addition of Organolithium Reagents to Chiral Oxazolines

Sir:

Lithiated chiral oxazolines have been recently shown to react with various electrophiles generating a new asymmetric center with considerable bias. This process has led to optically active α-alkyl alkanoic acids,[1] α-methoxy acids,[2] β-hydroxy acids,[3] α-substituted butyrolactones,[4] and 2-substituted-1,4-diols.[4] However, the utilization of these chiral oxazolines as electrophilic species has not been previously explored. We now report that (4*S*,5*S*)-2-(*trans*-1-alkenyl)-4-methoxymethyl-5-phenyloxazolines, **2**, undergo 1,4-addition reactions with various organolithium reagents producing, after hydrolysis, 3-substituted alkanoic acids **4** in high enantiomeric purity. Although asymmetric additions to electrophilic olefins (α,β-unsaturated carbonyls,[5-7] vinyl sulfoxides[8]) have been previously described, these results represent the first example possessing substantial generality, allowing recovery of the chiral reagent, and permitting the synthesis of either enantiomer from a common chiral precursor. The requisite alkenyl oxazolines **2** were prepared by condensation of the lithio salt (LDA, THF, −78°) of the commercially available 2-methyloxazoline[9] with the appropriate aldehyde followed by dehydration (TFA, benzene, reflux) of the β-hydroxyethyloxazolines[10] (Table I).



Slow dropwise addition (1-2 hr) of a THF solution (0.25-0.5 *M*) of **2** to 1.5 equiv of the organolithium reagent (diluted with THF) at −78°, under a nitrogen atmosphere, gave the adduct (presumably 6) which, after an additional hour of stirring, was quenched with 5.0 equiv of absolute methanol (−78°). Aqueous work-up and extraction gave crude **3** which was directly hydrolyzed (3-6 *M* H_2SO_4, 3-6 hr reflux) to the 3-substituted alkanoic acid (Table I). The enantiomeric purity of the acids obtained in this manner is exceptionally high in all but one instance (Table I, entry 4) and there is some doubt as to the reliability of the reported rotation in entry 4 (ref i, Table I). Presently, the chemical yields (overall from **2**) are only moderate when allylic protons are present on the alkenyl oxazolines (entries 1-5) due to competing proton abstraction[11] by the organolithium reagents and subsequent addition of 6 to unreacted **2**. Considerable amounts (25-35 wt %) of high molecular weight polymeric material were encountered in these cases. This side process is not a serious problem for the β-styryloxazolines (entries 6 and 7) as the chiral carboxylic acids are formed in 64-66% overall yields. Nevertheless, in all cases the chemical efficiency is overshadowed by the high optical yields, and all compounds are readily prepared in multigram quantities.

That this asymmetric synthesis can give rise to *either enantiomer* of a 3-substituted alkanoic acid from the same *chiral oxazoline* is evidenced by entries 5 and 6 on the table. Both *S*-(+) and *R*-(−) 3-phenylpentanoic acid were

Table I. Optically Active 3-Substituted Alkanoic Acids from 2-(1-Alkenyl)oxazolines

	Oxazolines, 2				Acids, 4				
Entry	R	Yield, %	$[\alpha]^{25}589$	R'Li[c]	Overall yield, %	Obsd $[\alpha]^{25}589$[d]	Lit. $[\alpha]^{25}589$	Optical purity, %	Config
1	Me	53[a]	+38.0° (*c* 10.0)[b]	Et	30	−7.44° (neat)	−8.15° (neat)[f]	92	*R*
2	Me			*n*-Bu	38	+3.84° (neat)	−4.2° (neat)[g]	91	*R*
3	Me			Ph	34	+55.8° (*c* 9.82)[e]	−57.2° (*c* 9.80)[e,h]	98	*S*
4	Et	42	+31.1° (*c* 10.0)[b]	*n*-Bu	49	+2.84° (neat)	+4.69° (neat)[i]	61	*R*
5	Et			Ph	31	+45.8° (*c* 7.05)[e]	−49.66° (*c* 7)[j]	92	*S*
6	Ph	65	122° (*c* 10.0)[b]	Et	66	−48.0° (*c* 9.49)[e]		97	*R*
7	Ph			*n*-Bu	64	−27.8° (neat)	−23.1° (neat)[k]	>95	*R*[l]

[a] Contained ~7% of the cis isomer; yields are based upon the 2-methyl-2-oxazoline. [b] Chloroform solutions. [c] Ethyllithium was used as a 1.22 *M* solution in benzene–ether (70:30); *n*-butyllithium was used as a 2.48 *M* solution in hexane; phenyllithium was used as a 1.53 *M* solution in benzene–ether (70:30). [d] Rotations were measured on a Jasco DIP-180 automatic polarimeter at 25° in a 1-cm^3 (10 cm) cell. [e] Benzene was used as the solvent. [f] C. G. Overberger and I. Cho, *J. Org. Chem.*, 33, 3321 (1968). [g] P. A. Levene and R. E. Marker, *J. Biol. Chem.*, 95, 153 (1932). [h] H. Rupe, *Justus Liebigs Ann. Chem.*, 369, 311 (1909); configuration assigned by V. Prelog and H. Scherrer, *Helv. Chim. Acta.*, 42, 2227 (1959). [i] P. A. Levene and R. E. Marker, *J. Biol. Chem.*, 115, 401 (1936); this is a calculated rotation value and unpublished results from our laboratory tend to indicate that the value is too high. [j] L. Lardicci, R. Menicagli, and P. Salvadori, *Gazz. Chim. Ital.*, 98, 738 (1968). [k] P. A. Levene and R. E. Marker, *J. Biol. Chem.*, 97, 563 (1932). [l] Configuration assigned as *R*(−) by CD curve comparison with *R*-(−)-3-phenylpentanoic acid.