1,4-Dialkoxy-1,3-butadiynes

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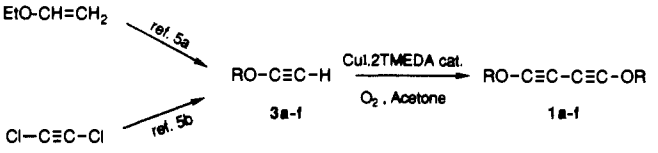
Diacetylenes (1,3-diynes) deserve considerable interest, both from the points of view of their rich chemistry[1] and of the solid-state properties of their homopolymers.[2] Among the 1,4-diheterosubstituted derivatives involving the usual organoelements, only the 1,4-dialkoxy-1,3-butadiynes **1** remain unknown.[3] Our

RO-C≡C-C≡C-OR (**1**) RO-C≡C-OR (**2**) RO-C≡C-H (**3**)

previous experience with the closely related dialkoxyacetylenes **2**[4] indicated that **1** would probably be readily polymerizable substances with a thermal stability modulable as a function of the steric bulk of the substituent alkoxy groups. We report in the present communication on the successful generation of 1,4-dialkoxy-1,3-butadiynes and on the thermal stability of these substances.

The preparation of **1** was planned via the oxidative dimerization of the readily available alkoxyacetylenes **3**.[5] *tert*-Butoxyethyne (**3a**)[5a] was selected to determine the optimal dimerization pro-



cedure. Standard conditions for oxidative dimerization[6-9] showed to be rather inefficient in this case. However, when CuI was used as the catalyst instead of CuCl under the usual Hay[7] conditions (CuCl, TMEDA, acetone, O_2), a 77% yield of **1a**[10] was obtained in a clean way. The better solubility of the CuI·2TMEDA system in acetone is relevant to this result.

Table I. Preparation of 1,4-Dialkoxy-1,3-butadiynes **1** by Oxidative Coupling of Alkoxyacetylenes **3** with Copper Iodide–TMEDA in Acetone under O_2

RO-	**1**	[CuI]:[TMEDA]:[**3**] molar ratio	reaction time,[a] min	yield, %
tert-butoxy	**a**	1:2:20	60	77
1-adamantyloxy	**b**	1:2:20	30	85
decyloxy	**c**	1:2:25	30	78
cyclohexyloxy	**d**	1:2:10	20	95
L-mentyloxy	**e**	1:2:4	35	76
2,6-dimethylphenoxy	**f**	1:2:4	45	65

[a] Reactions performed under vigorous shaking. End point controlled by TLC.

The same reaction conditions applied to **3b-f** allowed the preparation of **1b-f**; the results are summarized in the table. As it can be readily seen, yields are uniformly high; the reactions proceed quickly and very cleanly; and product purification can be readily achieved by simple filtration through a short pad of Al_2O_3.

The thermal behavior of the 1,4-dialkoxy-1,3-butadiynes **1a-f** deserves some comment. The bis(1-adamantyloxy) derivative **1b** is a relatively stable compound, which can be heated to 150 °C without apparent signs of decomposition. The di-*tert*-butoxy derivative **1b**, in turn, is stable at room temperature, but a complete decomposition results when the compound is heated at 50 °C for 14 h in benzene solution. The well-known fragmentation reaction of acetylenic ethers into olefins and ketenes, which takes place with particular ease in the *tert*-butoxy derivatives,[11] is probably relevant to the decomposition process.

The remaining dialkoxybutadiynes **1c-f** possess a much lower stability. The **1e** and **1f** derivatives can be manipulated at room temperature for short periods of time in neat form, but completely polymerize even when stored overnight in CCl_4 at −15 °C. Finally, **1c** and **1d** have to be manipulated at low temperature when neat, since polymerization at room temperature is almost instantaneous.[12]

In summary, a wide range of thermal stabilities can be covered by the 1,4-dialkoxy-1,3-butadiynes on going from bulky tertiary alkoxy groups, which afford thermally stable substances suitable for chemical studies, to primary alkoxy groups, which afford readily polymerizable materials. Although the study of the homopolymers arising from **1** is beyond the scope of the present work, it is suggested that the ready availability of diversely substituted 1,4-dialkoxy-1,3-butadiynes (including those containing

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(10) *Typical experimental procedure*: A mixture of CuI (0.190 g, 1 mmol), TMEDA (0.232 g, 2 mmol), and acetone (20 mL) was stirred for 5 min. *tert*-Butoxyethyne (**3a**; 1.96 g, 20 mmol) in acetone (5 mL) was then added and the system vigorously shaken at room temperature under O_2 for 60 min. The solvent was removed at reduced pressure and the residue dissolved in diethyl ether, washed first with dilute HCl, followed by water, and finally dried with $MgSO_4$, and the solvent was removed. The residue was filtered through a short pad of Al_2O_3 eluting with petroleum ether to afford 1,4-di-*tert*-butoxy-1,3-butadiyne (**1a**; 1.491 g, 77%) as a white solid: mp 62–64 °C dec (from pentane–ether at −15 °C); IR (CCl_4) 2980, 2950, 2190, 1390, 1370, 1270, 1250, 1085, 1030, 860 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 1.42 (s); ^{13}C NMR (50.2 MHz, $CDCl_3$) δ 87.7 (s), 80.2 (s), 29.0 (s), 27.2 (q); mass spectrum (EI), *m/z* (rel intensity) 194 (M^+, 0.1), 138 (1.5), 123 (1.3), 110 (2.1), 95 (5.4), 82 (22), 66 (4), 57 (100). Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.10; H, 9.30.

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(12) The polymeric materials arising from **1c-f** have the appearance of brown viscous oils, soluble in hydrocarbon and chlorinated solvents, and only partially soluble in more polar media (AcOEt, acetone). Their IR spectra exhibit C≡C stretching bands at essentially the same wavenumber as the monomers (ca. 2200 cm^{-1}), although with strongly decreased intensity. This is indicative of 1,2- rather than 1,4-polymerization. The UV-vis spectra, in turn, show strong absorption over a wide range of wavelengths. Thus, the polymer derived from **1e** presents absorption maxima at 248.4, 296 (sh), 440 (sh), and 472.2 nm in isooctane solution.

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chiral alkoxy groups, such as **1e**),[13] together with the use of controlled polymerization techniques,[14] can give rise to materials exhibiting interesting and useful solid-state properties.

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Supplementary Material Available: Physical, spectroscopic, and analytical data for compounds **1a-f** (2 pages). Ordering information is given on any current masthead page.

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Trehalose Conformation in Aqueous Solution from Optical Rotation

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Trehalose (α-D-glucopyranosyl-(1→1)-α-D-glucopyranoside) apparently has several important biological functions. One of the most recently discovered, with potential biotechnological importance, is its effectiveness in stabilizing membrane structure in the dry state and, perhaps, inhibiting biological damage at low temperature.[1-4] The detailed mechanism by which trehalose produces these stabilizing effects has not yet been established. It is known that trehalose binds to the head group of lipids in dry bilayers,[5] but the nature of the important molecular interactions in solution is not yet known.[6-8] We report here a determination of the solution conformation of trehalose based on optical rotation; the relative inflexibility that it displays may prove to be relevant to its cryobiological effectiveness.

Because of its symmetrical chemical structure, the two glucose rings are NMR equivalent; i.e., only one set of ^1H or ^{13}C resonances is observed. Conventional NMR techniques involving the measurement of chemical shifts, relaxation times, coupling constants, or NOEs cannot be applied to deduce the linkage geometry in solution. Attempts to make the two glucose rings distinguishable by NMR, as through isotopic substitution, have not yet been reported.

Chiroptical measurements are very sensitive to saccharide conformation as well as configuration, and a reliable semiempirical calculational model has recently been developed that allows the prediction of optical rotation as a function of disaccharide conformation.[9] We have here applied that model to trehalose with no variation of the model parameters originally reported. Linkage conformations are specified by the dihedral angles ϕ and ψ; because of molecular symmetry the conformation specified as $\phi, \psi = a, b$ can equivalently be specified as $\phi, \psi = b, a$. For a given linkage geometry, we considered four combinations of the exocyclic hydroxymethyl groups, allowing for both *gt* and *gg* conformations in each glucose residue. With statistical weights of 0.67 for the *gt* conformation and 0.33 for the *gg* conformation,[10] the average we require is

$$[\bar{M}]^{calc} = 0.45[M]_{gt,gt} + 0.22[M]_{gt,gg} + 0.22[M]_{gg,gt} + 0.11[M]_{gg,gg}$$

where $[M]$ is the Na_D molar rotation on a disaccharide basis, $0.45 = (0.67)^2$, $0.22 = (0.67)(0.33)$, and $0.11 = (0.33)^2$. Calculated results are displayed in Figure 1 superimposed on a hard-sphere conformational ϕ, ψ map, generated by using the atom-atom contact distances of Rees and Scott.[11] Molecular symmetry leads to the symmetric arrangement of rotations with respect to the diagonal of the figure.

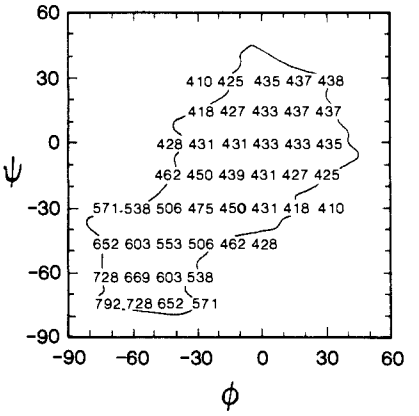

Figure 1. Na_D molar rotations of trehalose calculated as a function of linkage angles ϕ and ψ, superimposed on a hard-sphere conformation map.

The observed trehalose optical rotation[12] of +681 deg cm^2 dmol^{-1} in water is that expected for conformations in the region near $\phi, \psi = -60°, -60°$ (Figure 1). The significant features of conformations in that region are that the C(1)-C(2) bond of each glucose ring is trans to the O(1)-C(1) bond of the other, and the O(1)-C(1) bond of each ring is gauche to the C(1)-O(5) bond of the other.

The solid-state conformation of trehalose ($\phi, \psi = -60°, -59°$)[13] and that of trehalose dihydrate ($\phi, \psi = -58°, -45°$)[14] are located in the same region of the ϕ, ψ map, as is the energy-minimized calculated conformation of Tvaroska and Vaclavik ($\phi, \psi = -61°, -56°$).[15] An earlier, somewhat more empirical, analysis of optical rotation by Rees and Thom[16] led to an averaged solution conformation of $\phi, \psi = -72°, -72°$, indicating a strong preference for the same region of conformational ϕ, ψ space as found by us.

Moreover, the present results indicate that the extent of conformational excursions in aqueous solution is extremely limited, inasmuch as any significant conformational averaging would lead to a substantially reduced optical rotation (Figure 1). Conformations in which either ϕ or ψ is decreased by as little as 30° have molar rotations 100 deg cm^2 dmol^{-1} less than what is observed in aqueous solution. Whether trehalose stabilizes biological membranes through direct binding[17] or indirectly through in-

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