50 ml of absolute ethanol. The suspension was heated at reflux on a steam bath for 1 hr. The catalyst was removed by filtration on a Celite pad and washed with hot ethanol (3 × 15 ml). The combined filtrate and washings were evaporated to dryness, dissolved in the minimum volume of chloroform, and chromatographed on a silica gel column (3.5 × 50 cm) eluting with chloroform–acetone (8.5:1.5). The appropriate fractions were pooled and the solvent was evaporated to yield a colorless foam, 1.80 g (67.0%): $[\alpha]^{25}D$ +2.7° (c 1.0, DMSO); uv λ_{max} (pH 1) 262 nm (ε 10,300); λ_{max} (pH 7) 262 nm (ε 9900); λ_{max} (pH 11) 262 nm (ε 9900); ir λ_{max} (KBr) 1750 cm^{-1} (OAc); pmr (DMSO-d_6) δ 8.05 and 6.50 (doublets for C-7 H and C-8 H, respectively, $J_{7,8}$ = 2 Hz), 8.20 (singlet for C-2 H).

Anal. Calcd for $C_{16}H_{18}N_4O_8 \cdot H_2O$: C, 46.60; H, 4.89; N, 13.59. Found: C, 46.80; H, 4.80; N, 13.49.

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Registry No.—I, 52259-78-6; II, 10299-44-2; III, 28279-62-1; IV, 52259-79-7; V, 52217-05-7; V 5-methyl derivative, 52217-08-0; VI, 52259-80-0; VII, 32817-07-5; VIII, 33037-54-6; IX, 52259-81-1; X, 52217-06-8; XI, 52217-07-9; tetra-O-acetyl-β-D-ribofuranose, 13035-61-5; 2,3,5-tri-O-acetyl-D-ribofuranosyl bromide, 39110-68-4.

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"Octakis-O-(3-aminopropyl)sucrose" as a Bifunctional Catalyst for the Dedeuteration of Isobutyraldehyde-2-d[1]

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"Octakis-O-(3-aminopropyl)sucrose" (OAPS) containing about seven aminopropyl side chains per sucrose moiety has been prepared by reduction of octakis-O-(2-cyanoethyl)sucrose. Measurements of its basicity and equilibrium constant for forming imines with isobutyraldehyde have been made. OAPS is an effective catalyst for the dedeuteration of isobutyraldehyde-2-d in aqueous solution; a pH–rate plot shows a maximum around pH 8.4 at 35°. Under these conditions the catalytic activity is about 14 times that which would be expected if the catalyst were acting only monofunctionally. Hence it is concluded that one amino group on the catalyst transforms the aldehyde to an iminium ion, and then the activated α-deuteron in this isobutyraldiminium ion is removed by another amino group from the same molecule of catalyst. Reasons why this bifunctional catalytic activity is more efficient than that due to polyethylenimines, but less efficient than that due to 8-amino-1-dimethylamino-2-octyne, are discussed.

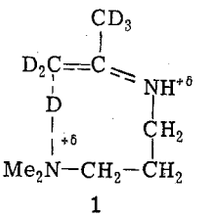
Primary amine salts catalyze α-hydrogen exchange reactions of isobutyraldehyde-2-d, acetone-d_6, and other aldehydes and ketones by transforming them to iminium ions, whose α-hydrogen atoms are much more rapidly removed by bases than are the α-hydrogen atoms of the original carbonyl compounds.[2,3] The monoprotonated forms of

$$Me_2CDCHO + RNH_3^+ \rightleftharpoons Me_2CDCH{=}NHR^+ + H_2O$$

$$Me_2CDCH{=}NHR^+ + B \rightleftharpoons Me_2C{=}CHNHR + BD$$

$$Me_2C{=}CHNHR \xrightarrow{BH} \xrightarrow{H_2O} Me_2CHCHO + RNH_3^+$$

amines of the type $Me_2N(CH_2)_nNH_2$, where n is 2, 3, 4, and 5, show a catalytic activity toward isobutyraldehyde-2-d that increases monotonically with increasing basicity (increasing n),[4,5] but the monoprotonated form of 3-dimethylaminopropylamine is by far the best catalyst toward acetone-d_6.[4,6] These results indicate bifunctional catalysis of the dedeuteration of acetone-d_6 *via* a transition state like **1**. The absence of such catalysis in the case of isobutyraldehyde-2-d was explained in terms of the destabilizing steric interactions between a methyl group from the aldehyde and the NH-bound methylene group from the catalyst that would be present in the analogous transition state for isobutyraldehyde. Such strain may be avoided if the basic group that removes the α-deuteron and the primary amino group that forms the iminium ion are separated by a long enough chain for internal deuteron removal



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to be feasible in the trans form of the intermediate iminium ion. This requirement is met in polyethylenimines[1b,7,8] and 8-amino-1-dimethylamino-2-octyne,[5] which are bifunctional catalysts for the dedeuteration of isobutyraldehyde-2-*d*. The catalytic activity of polyethylenimines is considerably reduced by their tendency to tie up the aldehyde as imidazolidine derivatives, and the understanding of their catalysis is made difficult by the varied and incompletely known structures of these rather random polymers. To avoid these disadvantages but maintain the advantage of having a large number of amino groups in a small space, we decided to prepare octakis-*O*-(3-aminopropyl)sucrose and to study its catalytic activity.

Preparation and Properties of "Octakis-*O*-(3-aminopropyl)sucrose." The material labeled cyanoethyl sucrose used as the starting material fell short of being pure octakis-*O*-(2-cyanoethyl)sucrose in that it contained about 0.8 wt % water, 3.75 wt % bis(2-cyanoethyl) ether, and an average of only about 7.5 cyanoethyl groups per sucrose moiety. Furthermore, about 23% of the disaccharide derivatives had been hydrolyzed to monosaccharide derivatives. Hydrogenation of this material at low pressure using Raney nickel in ammoniacal methanol[9] followed by chromatographic purification gave an off-white, amorphous, hygroscopic solid, which will be called OAPS. This material fell short of being pure octakis-*O*-(3-aminopropyl)sucrose in that it contained about 1.55 molecules of water and 1.35 molecules of carbon dioxide (probably present as carbonate or bicarbonate) per molecule of sucrose moiety. Also there were only about seven 3-aminopropyl groups per sucrose moiety, and there were probably about 0.14 secondary amino groups[10] per sucrose moiety.

Interpretation of the titration curve of OAPS was complicated by the presence of the carbonate impurity. The eight breaks that might be expected if the eight pK values were widely enough separated were not observed. This fact, the impure nature of the material, and the difficulties of estimating activity coefficients for species with as many as eight positive charges discouraged us from trying to calculate the true pK_a values. Instead, pK_{app} values, where K_{app} is defined in eq 1, were calculated at various points

$$K_{app} = \frac{[H^+][Am]}{[AmH^+]} \quad (1)$$

throughout the titration. [Am] and [AmH$^+$] are the concentrations (normalities) of unprotonated and protonated amino groups in the solution. Corrections for the effect of the carbonate impurity on the titration were made by use of the ionization constants of carbonic[11] acid and by using the Davies equation[12] to calculate activity coefficients, with ionic strengths being calculated as if each protonated amino group were an independent unicharged cation. A plot of pK_{app} *vs.* the fraction of amino groups protonated in a titration of 0.0865 N (in amino groups) OAPS with 1.000 M hydrochloric acid is shown in Figure 1. Because of the carbonate impurity 30% of the amino groups were already protonated at the start of the titration; pK_{app} values obtained within 10% of the end point were regarded as too unreliable to plot. The monotonic decrease in pK_{app} that accompanies addition of acid reflects the fact that the amino groups protonated early in the titration have few protonated amino groups in the same molecule whereas those protonated near the end of the titration have many.

The equilibrium "constant" for isobutyraldimine formation, defined as shown in eq 2, in which the concentrations of imine and amine will be expressed as normalities and the

$$K_{Im} = \frac{[Im]}{[i\text{-}PrCHO][Am]} \quad (2)$$

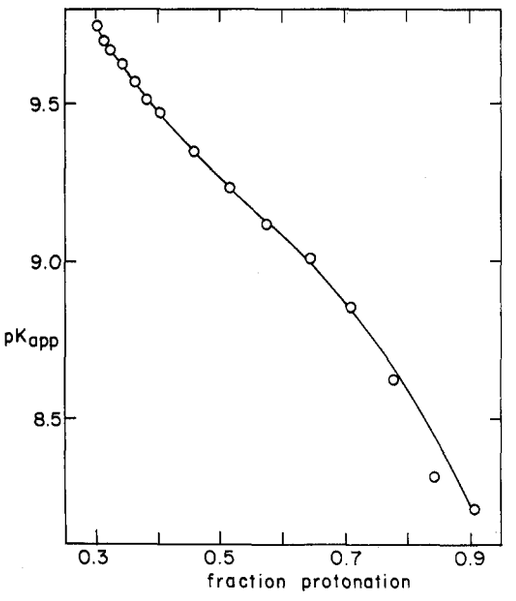

Figure 1. Plot of pK_{app} of OAPS *vs.* fraction protonation in water at 35°.

concentration of aldehyde will include that of the aldehyde hydrate in equilibrium with it, should have a value that depends on the extent of protonation of the OAPS and, to a lesser degree, on the extent of imine formation, since electron-withdrawing substituents are known to decrease equilibrium constants for the formation of imines from isobutyraldehyde.[13] Two independent methods, both used previously,[13] were used to obtain values of K_{Im}. In one method the effect of OAPS on the absorption at the 285-nm maximum of isobutyraldehyde was determined and the imine (and any other products formed) was assumed to have the same absorbance as the amine from which it was formed. In calculating K_{Im}, 1 equiv of amine was assumed to be used up per mole of aldehyde that disappeared. Small corrections also had to be made for the shift in the carbonate–bicarbonate equilibrium brought about by the drop in pH that accompanied addition of aldehyde to the OAPS solution. A K_{Im} value of 46 M^{-1} was obtained using a solution whose equilibrium pH was 10.1 and a value of 21 M^{-1} at a pH of 8.39, where the average amino group has a larger number of electron-withdrawing ammonio substituents in the same molecule with it. Values were also calculated from the magnitude of the drop in pH that accompanied addition of isobutyraldehyde to an OAPS solution. As in the case of monoamines,[13] imine formation causes the pH to drop because the concentration of free amine decreases. In the case of OAPS, however, the introduction of electron-withdrawing aldimino substituents reduces the basicity of free amino groups in the same molecule, thus making the decrease in pH larger than it would otherwise be. Our inability to assess the substituent effect of aldimino groups on the basicity of OAPS decreases the reliability of K_{Im} values determined by the pH method. However, uv measurements support the assumption that an amount of isobutyraldehyde that lowers the pH of an OAPS solution to the same extent that a given amount of strong acid does also lowers its pK_{app} value by about the same amount. This assumption led to K_{Im} values of 24, 25, 36, 35, and 36 M^{-1} at pH's of 7.98, 8.39, 8.68, 8.71, and 9.04, respectively. If small amounts of large-ring aminals are also formed in the reaction of isobutyraldehyde with OAPS, the assumption of 1:1 stoichiometry used in calculating K_{Im} will be in error. Small amounts of this side reaction will have little ef-

Table I
Kinetics of the Dedeuteration of Isobutyraldehyde-2-*d* in Water at 35° [a]

[Catalyst], [b] N [c]	pH	$10^5 k$, sec^{-1}
0.0865[d]	9.82	8.55
0.0863[d]	9.33	14.20
0.0862[d]	9.04	16.22
0.0861[d]	8.71	17.60
0.0858	8.39	20.02
0.0856	7.98	17.50
0.0855	7.64	13.01
0.0854	7.25	7.11
0.0859	8.68	19.22
0.0959	8.53	21.5
0.0482	8.62	15.8
0.0241	8.42	7.38
0.189	8.54	35
0.086[e]	9.09	1.60

[a] $[Me_2CDCHO]_0$ = 0.046. [b] OAPS, unless otherwise noted. [c] Normalities in total amine (protonated, unprotonated, or in the form of imine). [d] Using 3-week-old catalyst solutions. [e] 2-Methoxyethylamine.

fect on the K_{Im} values calculated from uv data; they will make the K_{Im} values calculated from pH measurements somewhat larger than they should be. When the logarithms of the K_{Im} values reported here are placed in the plot of log K_{Im} for monoamines *vs.* pK[13] the average deviation (0.06) is not much larger than that observed with the monoamines of the type RCH_2NH_2, where R contains an sp^3-hybridized carbon atom at its point of attachment (0.05). This suggests that our values refer very largely to imine formation.

Catalysis by OAPS. Catalysis of the dedeuteration of isobutyraldehyde-2-*d* in aqueous solution at 35° was studied in the presence of 0.0860 ± 0.0006 *N* (in total amine) OAPS at a number of pH's and at pH 8.52 ± 0.10 in the presence of several different concentrations of OAPS, with the results shown in Table I. All the runs were carried out with fresh catalyst solutions except the first four, in which solutions that were about 3 weeks old were used. The fact that the rate constant obtained in the fourth run is 8% smaller than that obtained in the ninth run, which is almost a duplicate of it, suggests a small amount of deterioration of the catalyst solution on standing. However, correction for such deterioration would not significantly change any conclusions drawn from the plot of *k vs.* pH shown in Figure 2.

The plot, in Figure 3, of *k vs.* the concentration of catalyst at pH 8.5, including a point for 0.086 *N* catalyst interpolated from Figure 2 and one for no catalyst calculated from the catalysis constants for water and hydroxide ions, suggests that the rate may level off at higher concentrations, but the amount of catalyst available was not sufficient to test this suggestion. This tendency for the rate to level off as the catalyst concentration increases resembles that observed with polyethylenimines[1b,7,8] and is explained in the same way. Most of the reaction proceeds *via* the rapid reversible transformation of isobutyraldehyde-2-*d* to a complex, which is mainly imine, with much smaller amounts of iminium ion. The rate-controlling step is a first-order reaction of the complex, in which the iminium form is attacked by an amino group present in the same ion. The rate of reaction by this mechanism would have to

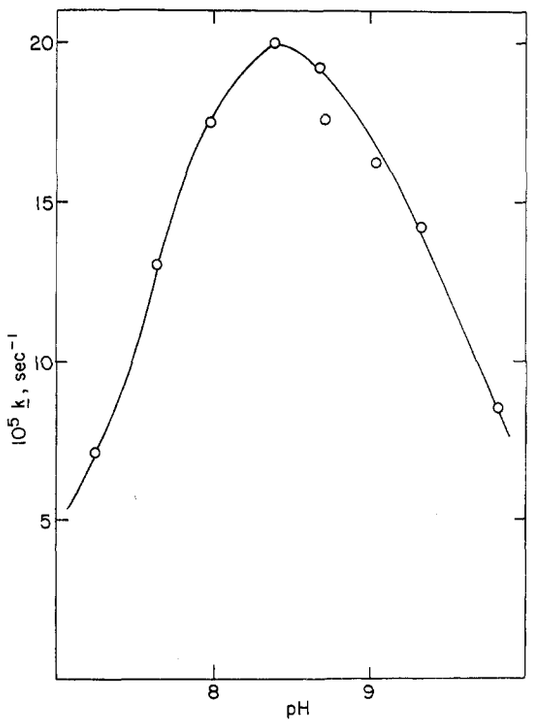

Figure 2. Rate constants for dedeuteration of 0.0546 *M* isobutyraldehyde-2-*d* by 0.086 *N* OAPS at various pH's in water at 35°.

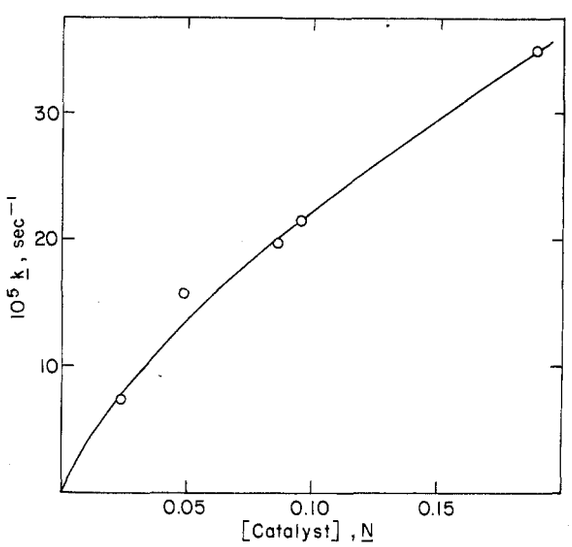

Figure 3. Rate constants for dedeuteration of 0.0546 *M* isobutyraldehyde-2-*d* at pH 8.5 in the presence of various concentrations of OAPS in water at 35°.

level off when there is enough catalyst to transform all the aldehyde to complex. Since ultraviolet measurements show that 0.086 *N* catalyst complexes about 30% of the aldehyde at pH 8.5, the first-order rate constant for reaction of complexed aldehyde must be about $(20 \times 10^{-5}/0.3)$, or 7×10^{-4} sec^{-1}.

The pH–rate profile shows a clear maximum around pH 8.4. The principal reason for this maximum is that at lower pH there are not enough unprotonated amino groups to provide the required internal basic catalysis, and at higher pH not enough of the complexed aldehyde is in the protonated active iminium form. The location of the maximum may be rationalized as follows. Take the rate-controlling step as being a reaction between the isobutyraldiminium

$$v = k[\mathrm{Am}][\mathrm{ImH^+}] \quad (3)$$

ion (ImH^+) and amine (Am) with rate as shown in eq 3. Let the equilibrium constant for the formation of the iminium ion from aldehyde and primary ammonium ion be K_I. This gives eq 4, which may be compared with eq 5 for the observed first-order rate constant k_1 to give eq 6. The species

$$v = kK_I[\mathrm{Am}][\mathrm{AmH^+}][\mathrm{RCHO}] \quad (4)$$

$$v = k_1[\mathrm{RCHO}]_{total} \quad (5)$$

$$k_1 = kK_I[\mathrm{Am}][\mathrm{AmH^+}][\mathrm{RCHO}]/[\mathrm{RCHO}]_{total} \quad (6)$$

Am and AmH^+ are not constant species; the average Am in an acidic solution, for example, is in a molecule with more positively charged ammonio substituents and so it is more weakly basic than the average Am in a more basic solution. Hence k and K_I are pH dependent. However, it is known from studies of catalysis of the dedeuteration of isobutyraldehyde-*2-d* by various primary ammonium salts in the presence of pyridine buffers that when Am is held constant and AmH^+ is varied a plot of log (kK_I) *vs.* pK_{AmH} has a slope of about −0.40.[14] Similarly, a study of catalysis by methylammonium ions in the presence of various tertiary amines shows that a plot of log (kK_I) *vs.* pK_{AmH} has a slope of about 0.42.[15] Hence, when both Am and AmH^+ are varied, with the decrease in the basicity of the former being equal to the increase in acidity of the latter, the product kK_I should not change very much. The product $[Am][AmH^+]$ would have a maximum value at the pH at which the amine and ammonium concentrations are equal if the sum of these two concentrations were kept constant. However, this sum increases somewhat with decreasing pH because of the concomitant decrease in the equilibrium constant for imine formation (K_{Im}), which also causes the ratio $[RCHO]/[RCHO]_{total}$ to increase with decreasing pH. Therefore the rate maximum is expected to occur at a pH somewhat lower than the pH at which OAPS is half protonated. This pH is 9.27 in the absence of isobutyraldehyde but it would be somewhat lower in the presence of the aldehyde, which lowers the basicity of the OAPS. Hence the occurrence of the rate maximum at pH 8.4 is consistent with the proposed mechanism.

Like any amine, OAPS must have the ability to act as a monofunctional catalyst in the dedeuteration of isobutyraldehyde-*2-d*. Bifunctional catalysis will be observable only if it is as important as monofunctional catalysis or more so. (Monofunctional catalysis can lead to rate eq 4 if the amine and ammonium groups are in different catalyst molecules.) We have estimated the efficiency to be expected of monofunctional catalysis in two ways. We have studied the catalytic activity of 2-methoxyethylamine, a compound whose steric requirements near the reaction center resemble those of OAPS and whose basicity (pK_a = 9.09) is about the same as that of half-neutralized OAPS (pK_{app} = 9.27). At pH 9.09, where its catalytic activity *via* the iminium-ion mechanism should be nearly maximal, 2-methoxyethylamine is seen (from the last entry in Table I) to be only about one-tenth as good a catalyst as is OAPS under the same conditions. We also used the extensive previous work on amine catalysis of the dedeuteration of isobutyraldehyde-*2-d* to estimate the monofunctional catalytic activity, employing linear free energy relationships as described in more detail in several other cases.[5,6,16] Application of this method to the run with 2-methoxyethylamine gave a k of 1.7×10^{-5} sec^{-1}, in good agreement with the value shown in Table I. Application to the run on OAPS at pH 8.39 gave the value 1.4×10^{-5} sec^{-1}. According to this estimate 92.7% of the reaction at pH 8.39 arises from bifunctional catalysis, 5.5% from the attack of an amino group from one OAPS molecule on an isobutyraldiminium ion derived from another OAPS molecule, 1.7% from attack of an amino group on free isobutyraldehyde-*2-d*, and 0.1% from all other mechanisms combined. From these figures it follows that the average effective concentration of the amino groups in the same molecule with an isobutyraldiminium ion is 0.28 *N*.

On a normality basis the catalytic activity of OAPS is about three times that of PEI-50,000[1b] (polyethylenimine with an average molecular weight of 50,000, the most active of the PEI catalysts studied) at concentrations around 0.1 *N;* furthermore, aldehyde complexed to OAPS is about three times as reactive as that complexed to PEI-50,000, at the optimum pH's of about 8.5 and 7.5, respectively. One advantage of OAPS over PEI is that it gives less nonproductive binding; much of the aldehyde bound by PEI is held as imidazolidine derivatives. Also, nearly all the amino groups of OAPS are primary and hence suitable for imine formation as well as basic catalysis, whereas about three-fourths of the amino groups in PEI are rather hindered secondary and tertiary amino groups, which probably give negligible amounts of iminium ion formation and considerably less basic catalysis than they would if they were less hindered. On the other hand, PEI has a lower equivalent weight than OAPS and is almost as good a catalyst on a weight basis. The activity of OAPS is only about one-third that of the monoprotonated form of 1-dimethylamino-8-amino-2-octyne,[5] which has an unhindered tertiary amino group, the most effective type of basic catalyst.[15,17] In general, it seems that the "shotgun" approach of using catalysts such as OAPS and PEI's can give bifunctional catalysis, but that carefully designed bifunctional species offer more promise for highly effective bifunctional catalysis.

Experimental Section

"Octakis-*O*-(2-cyanoethyl)sucrose." Eastman cyanoethylsucrose [ir (neat) 3480 (OH), 2950 and 2900 (CH), 2260 (C≡N), and 1100 cm^{-1} (C–O); nmr ($CDCl_3$) τ 7.35 (t, 16.1, J = 6 Hz, CH_2CN), 6.27 (m, 29.1, OCH_2C and $OCHC_2$), 4.68 (d, 0.16, J = 3 Hz, O_2CHC), and 4.40 ppm (d, 0.9, J = 3 Hz, O_2CHC)] was ordinarily used without further treatment.

Anal. Calcd for $C_{36}H_{46}N_8O_{11}$: C, 56.39; H, 6.05; N, 14.61. Found (average of four analyses with standard deviations): C, 55.34 ± 0.09; H, 6.18 ± 0.04; N, 14.06 ± 0.10.

The doublets at τ 4.40, 4.68, and 5.42 ppm were attributed to C-1 hydrogen atoms of the glucose moiety of cyanoethylsucrose, cyanoethylated α-glucose, and cyanoethylated β-glucose, respectively. This attribution was supported by the increasing size of the τ 4.68 and 5.42 ppm peaks (the latter being a doublet with a coupling constant of 6.4 Hz) and the decreasing size of the τ 4.40 ppm peak in samples that had been hydrolyzed with acidic aqueous methanol for increasing lengths of time. It is also supported by observing that the corresponding doublets of sucrose, α-glucose, and β-glucose fall at τ 4.53 (J = 3 Hz), 4.70 (J = 3 Hz), and 5.30 ppm (J = 7 Hz), respectively.[18] From the relative peak areas and the assumption that cyanoethylated fructose (whose pmr spectrum would be obscured by that of cyanoethylsucrose) was present in the same amount as cyanoethylated glucose, it was calculated that 77% of the sucrose moieties were intact and 23% had been hydrolyzed to monosaccharide derivatives. By a method analogous to that described in more detail in connection with octa(aminopropyl)sucrose, the average number of cyanoethyl groups per sucrose moiety (whether the sucrose moiety exists in the unhydrolyzed form or not) was calculated so as to give the best possible agreement with the elemental analysis of the material. The value 7.36 [plus the amounts of water and bis(2-cyanoethyl) ether known to be present] gave calculated carbon, hydrogen, and nitrogen contents within 0.14 of the average experimental values. This value is within the experimental uncertainty of the value 7.6, which was calculated from the integrated nmr spectrum.

The water content of this material was found to be 0.8 wt % by Karl Fischer titration. Attempts at molecular distillation were unsuccessful but small foreruns of bis(2-cyanoethyl) ether were obtained. High-pressure liquid chromatography using a Porosil C

(silica gel) column showed that a solution of 2.69 g of the cyanoethylsucrose in enough ethyl acetate to give a volume of 10 ml was 0.0814 *M* in bis(2-cyanoethyl) ether. This corresponds to a bis(2-cyanoethyl) ether content of 3.75% by weight.

"Octakis-O-(3-aminopropyl)sucrose." Reduction of octacyanoethylsucrose with hydrogen over Raney nickel[19] in acetic anhydride gave material that may well have been the acetyl derivative of the desired product. However, attempts at basic hydrolysis gave either too little reaction or dark brown syrups. Attempted reduction using a rhodium catalyst gave no reaction in twice the time reported for complete reduction of several 3-alkoxypropionitriles.[20] Reduction with diborane[21] gave material whose nmr spectrum showed the presence of little, if any, of the desired product. The method finally adopted used activated Raney nickel (W. R. Grace Co.) at about 60 psi of hydrogen pressure.[9] In a typical run 10.0 g of cyanoethylsucrose and about 40 g of Raney nickel in 250 ml of methanol saturated with ammonia at 10° gave complete reduction in 4 hr at 54°. Three filtrations, the last through 2.0-μ Millipore Polyvic, and solvent removal *in vacuo* gave a viscous green syrup that was dissolved in water, centrifuged, filtered again through Polyvic, and freeze dried, leaving 8.8 g (85%) of pale green semisolid material.

Chromatography of material prepared as described on basic alumina, Florisil, and activated charcoal using water–methanol mixtures gave various combinations of little or no material eluted from the column and products of decomposition. Gel permeation chromatography using 0.0100 *M* aqueous sodium chloride as the eluent, monitored by optical rotation measurements, gave only one peak with an elution volume only slightly greater than the void volume when Sephadex G-10 was used. Sephadex G-25 gave slower elution but shoulders on the single peak as the only evidence of separation. With Sephadex G-15 on a 2.75 × 53 cm column, two peaks were obtained, the larger with the same relative elution volume as a mol wt 400 ethylene glycol telomer and the smaller (more rapidly eluted) with the same relative elution volume as a mol wt 800 ethylene glycol telomer. Preparative scale chromatography was carried out with 4–5-g samples of material using a 5 × 92 cm column and in some runs a third fraction, with apparent molecular weight about 1100, was observed. The mol wt 800 fraction comprised about 15% of the material put on the column and its nmr spectrum indicated the presence of about 65% sucrose derivative. Rechromatography gave in 4% overall yield a mol wt 800 fraction that appeared to be chromatographically homogeneous: nmr (D_2O) τ 8.10 (quintet, 15.9, J = 6.5 Hz, $CH_2CH_2CH_2$), 7.10 (t, 15.5, J = 7 Hz, CH_2N), 6.15 (m, 29.7, OCH_2C and $OCHC_2$), 5.25 (s, DOH), and 4.35 ppm (0.9, O_2CHC). A number of batches of doubly chromatographed OAPS were combined to give the one homogeneous sample that was used for the analyses and kinetic studies.

Anal. Calcd for $C_{36}H_{78}N_8O_{11}$: C, 54.11; H, 9.84; N, 14.02. Found: C, 48.12, 48.29; H, 8.54, 8.55; N, 11.46, 11.30.

When this material stood in deuterium oxide containing hydrochloric acid, the τ 4.31 ppm peak, which was attributed to a sucrose derivative, gradually disappeared, and peaks at τ 4.50 and 5.20 ppm, which were attributed to the α and β forms of a glucose derivative, appeared and grew. The τ 5.20 peak was about 20% larger than the 4.50 ppm peak. The maximum possible area of a τ 4.50 ppm peak in the purified OAPS corresponded to the presence of no more than 15% fructose and glucose derivatives, assuming a 1:1 ratio of fructose to glucose and a 1:1.2 ratio of α- to β-glucose derivative.

Titration with standard hydrochloric acid gave a sharp end point, from which an equivalent weight of 119.9 was calculated. The carbonate content was determined by acidification of an aqueous solution to the titration end point and injection on a 6 ft × 0.25 in. Poropak QS column at 70°. Peak areas were calibrated using carbon dioxide solutions prepared by acidifying standard aqueous sodium bicarbonate solutions. Manipulations were carried out so as to prevent premature loss of carbon dioxide from the aqueous solutions, and 0.192 mol of carbon dioxide per equivalent of base was found.

The Van Slyke analysis method used gave 99.9% of the theoretical amount of nitrogen, with a standard deviation of 0.7%, for fractionally distilled 3-methoxypropylamine. For bis(3-aminopropyl) ether that was 99.3% pure by glpc and contained 98.7% of the expected amount of base by titration, 99.5 ± 0.9% of the theoretical amount of nitrogen was obtained. Four determinations on the OAPS used for kinetic studies gave 0.0848 ± 0.0010 *N* for the primary amine concentration of solutions that were 0.0865 *N* in total base. This corresponds to 0.98 equiv of primary amine per equivalent of base.

The absence of a nitrile band from the infrared spectrum and blank experiments on bis(2-cyanoethyl) ether showed that less than 1% of the nitrile groups in the reactant escaped reduction.

The elemental analysis was used to calculate the water content and the average number of hydroxy groups per sucrose moiety that had been transformed to $H_2NCH_2CH_2CH_2O$ or $RNHCH_2CH_2CH_2O$ groups. Let n be the number of aminopropylated hydroxy groups, w the number of water molecules, c the number of carbon dioxide molecules, and s the number of secondary amino groups per sucrose moiety (including those that have been hydrolyzed to glucose and fructose derivatives).[22] The carbon, hydrogen, and nitrogen contents may then be expressed as shown in

$$\%C = 96.38(12.011)(12 + 3n + c)/m \quad (7)$$

$$\%H = 96.38(1.008)(22 + 7n + 2w - 3s)/m \quad (8)$$

$$\%N = 96.38(14.007)(n - s)/m \quad (9)$$

$$m = 342.30 + 57.096n + 18.015w + 44.013c - 17.031s \quad (10)$$

eq 7–9, in which the term 96.38 arises from the presence of 3.62% sodium chloride and m is an apparent molecular weight, which is defined in eq 10. The equivalent weight, Van Slyke determination, and carbon dioxide analysis show that s and c are equal to $0.0196n$ and $0.1882n$, respectively. Substitution of these values into eq 7–10 and determination of the values of n and w that permitted calculation of %C, %H, and %N with the smallest sum of the squares of the deviations gave values of 7.16, 1.55, 0.14, and 1.35 for n, w, s, and c, respectively. This corresponds to 6.88 3-aminopropyl groups per sucrose moiety. Most of the 1.55 molecules of water may be accounted for as carbonate if the carbon dioxide is present in this form (rather than as carbamates) and much of the remainder may be that which has gone into the hydrolysis of ~15% of the sucrose moieties.

The Carbobenzoxy Derivative of "Octakis-O-(3-aminopropyl)sucrose." In hope of obtaining a crystallizable product OAPS was carbobenzoxylated.[23] To 1.0 g of crude OAPS and 1.94 g of sodium bicarbonate in 50 ml of 85:15 methanol–water was added 2.22 g of recrystallized benzyl chloroformate with stirring during 1 hr. After stirring overnight the solution and a white syrup were separated from white crystals of sodium salts. Addition of 50 ml of water to the solution precipitated a syrup that was combined with the syrup that had separated during the reaction. Three more precipitations by water from methanol gave 2.20 g (94%) of the carbobenzoxy derivative: ir (neat) 3340 (N–H), 3075 and 3040 (aromatic C–H), 2950 and 2880 (aliphatic C–H), 1700 (C=O), 1135, and 1080 cm^{-1} (C–O); nmr τ 8.5 (m, 17.2, CCH_2C), 7.0 and 6.6 (m, 44.0, CCH_2N and OCH–), 5.1 (s, 15.8, $PhCH_2O$), and 2.9 ppm (s, 39.3, Ph). Theoretical integrals are 16, 45, 16, and 40, respectively. The material gave a negative ninhydrin test. It could not be crystallized, but a methanol solution deposited some white flakes when cooled to −78°. Hydrogenolysis of these flakes and of the material remaining in solution was carried out in methanol using 5% palladium on charcoal. The nmr spectra and gel permeation chromatograms of the OAPS produced showed some differences but not enough to promise a useful method of purification.

Kinetics. The rate of dedeuteration of isobutyraldehyde-2-*d* was followed by extracting the acid-quenched reaction mixture with chloroform and making nmr measurements on the extracts.[2,17] The pH of an OAPS solution was adjusted by addition of hydrochloric acid and measured again after the addition of aldehyde. The change in pH caused by addition of aldehyde was the basis of one of the two methods used for calculating K_{Im}. On the average, six points were taken per kinetic run.

Registry No.—Octakis-*O*-(2-cyanoethyl)sucrose, 18304-13-7; octakis-*O*-(3-aminopropyl)sucrose, 52341-49-8; isobutyraldehyde-2-*d*, 4303-51-9.

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Synthesis of α-Ylidene-γ-butyrolactones Using an α-Phosphono-γ-butyrolactone Carbanion

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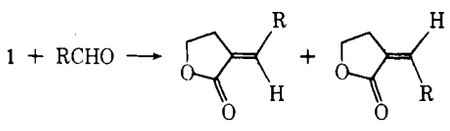
Reactions of an α-phosphono-γ-butyrolactone carbanion with aldehydes, ketones, heterocumulenes, and nitrosobenzene gave α-ylidene-γ-butyrolactones and α-anilino-γ-crotonolactone in good yields.

Phosphono carbanions bearing an electron-withdrawing substituent on the carbon α to the phosphorus function are useful reagents for olefin synthesis.[1] As an extension of this phosphonate olefin synthesis, we have investigated the reactions of an α-(*O,O*-diethylphosphono)-γ-butyrolactone carbanion (**1**)[2] with aldehydes, ketones, heterocumulenes, and nitrosobenzene.

The phosphonate carbanion **1** easily reacted with benzaldehyde to give only α-*trans*-benzylidene-γ-butyrolactone (**2**) in almost quantitative yield, regardless of the reaction temperatures employed. The structure of **2** was determined as follows. The nmr spectrum ($CDCl_3$) of **2** shows β-methylene (d–t, 2 H), γ-methylene (t, 2 H), phenyl (s, 5 H), and olefinic protons (t, 1 H) at δ 3.10, 4.45, 7.30, and 7.40, respectively. Although it is anticipated that the olefinic proton of the trans isomer would be observed downfield from the corresponding proton of the cis isomer, with the above data alone we cannot determine whether **2** is the trans or cis isomer. However, a change of solvent from $CDCl_3$ to benzene-d_6 produced a downfield shift of 0.20 ppm for the olefinic proton of **2**, whereas other protons suffered upfield shifts of 0.30–1.10 ppm. This result suggests that the olefinic proton is situated at the cis position to the carbonyl group.[3] Therefore, the structure was determined to be α-*trans*-benzylidene-γ-butyrolactone.

Reactions of **1** with *p*-nitrobenz-, cinnam-, and trichloroacetaldehyde similarly gave α-*trans*-(*p*-nitrobenzylidene)- (**3**), α-cinnamylidene- (**4**), and α-*trans*-(2,2,2-trichloroethylidene)-γ-butyrolactone (**5**) in 71, 55, and 100% yields, respectively.



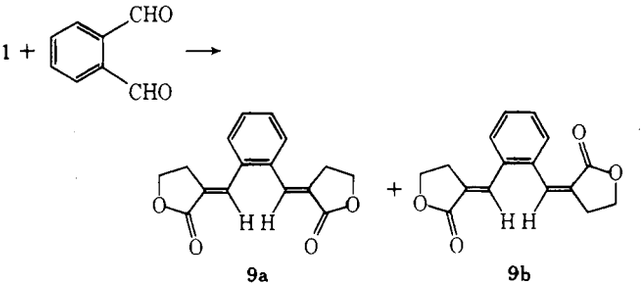
trans cis

2, R = Ph **6b**, R = *i*-Pr
3, R = *p*-$NO_2C_6H_4$ **7b**, R = Et
4, R = Ph_2CH=CH
5, R = CCl_3
6a, R = *i*-Pr
7a, R = Et

In contrast, the reactions with isobutyr- and propionaldehyde resulted in the formation of the mixtures of the corresponding α-*trans*- (**6a** and **7a**) and α-*cis*-(substituted ylidene)-γ-butyrolactones (**6b** and **7b**), ratios of which were approximately 1:1 and 3:2 by nmr, in good yields. Although separation of individual α-*trans*- (**6a**) and α-*cis*-(isobutylidene)-γ-butyrolactone (**6b**) was unsuccessful, their structural assignments rested upon nmr data and hydrogenation of the mixture over a platinum/carbon catalyst to α-isobutyl-γ-butyrolactone (**8**).

Thus, in the cases using aldehydes containing bulky substituents such as the phenyl, styryl, and trichloromethyl groups, only trans olefins were obtained, but use of aldehydes having rather small substituents such as the isopropyl and ethyl groups yielded mixtures of trans and cis olefins.

Interestingly, the reaction with *o*-phthalaldehyde gave a mixture of α,α′-bis(*trans,trans-o*-xylidene)- (**9a**, 47%) and α,α′-bis(*cis,trans-o*-xylidene)-γ-butyrolactone (**9b**, 7.3%).



9a **9b**

In the reaction with *p*-phthalaldehyde, α,α′-bis(*trans,trans-p*-xylidene)- (**10a**) and α,α′-bis(*cis,trans-p*-xylidene)-γ-butyrolactone (**10b**) were likewise obtained in 67 and 4.4% yields. No corresponding α,α′-bis(*cis,cis*-xylidene)-γ-butyrolactones could be detected in either reaction. Although the formation of the trans,trans isomers, **9a** and **10a**, in both reactions is in accord with the results ob-