View Article Online / Journal Homepage / Table of Contents for this issue

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102. *Light-scattering and Viscosity Studies of Two Synthetic Non-ionic Detergents in Aqueous Solution.*

By P. H. ELWORTHY and C. B. MACFARLANE.

Nonaoxyethylene glycol monohexadecyl ether (Hn_9) and dodecaoxyethylene glycol monohexadecyl ether (Hn_{12}) have been prepared by the Williamson ether synthesis from hexadecyl bromide and the appropriate glycol. These detergents have been studied in aqueous solution by light-scattering and viscosity techniques. The results for Hn_9 have been analysed statistically to determine the errors in c/T, dn/dc, and ρ. The overall error in these determinations of molecular weight by light scattering was $\pm 10\%$. Hn_9 gave 140,000 and Hn_{12} gave 117,000 for the micellar weight; the micelles appeared to be reasonably spherical.

Viscosity results were interpreted in terms of micellar hydration, giving $0{\cdot}69_5$ g. of water per g. of Hn_9 and 0·95 for Hn_{12}. Calculation of the radii of the micelles indicated that the length of the monomers was far less than their extended length, suggesting that the polyoxyethylene chains are curled in the micelle.

THE micelle size of non-ionic detergents containing polyoxyethylene groups has been studied by several workers.[1,2,3] In general it has been shown that the micelles are

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[1] Becher, *J. Colloid Sci.*, 1961, **16**, 49.

[2] Kushner and Hubbard, *J. Phys. Chem.*, 1954, **58**, 1163; Kushner, Hubbard, and Doan, *ibid.*, 1957, **61**, 371; Stauff and Rasper, *Kolloid Z.*, 1957, **151**, 148; Kuriyamo, *J. Colloid Sci.*, 1960, **15**, 268.

[3] Elworthy, *J. Pharm. Pharmacol.*, 1960, **12**, 260T.

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reasonably spherical and considerably hydrated. The hydrating water appears to be trapped in the polyoxyethylene chains. No clear picture has yet been obtained of how the hydration is affected by the length of the polyoxyethylene chains, or of the possible structure imposed on the micelle by curling or kinking of these chains. Becher[1] has shown that the micelle size decreases as the length of the polyoxyethylene chain is increased.

Commercial materials have generally been used in determinations of micelle size. Kushner, Hubbard, and Doan,[2] and Stauff and Rasper,[2] used molecular distillation as a means of fractionation, while Kelly and Greenwald[4] fractionated a polyoxyethylene-iso-octylphenol condensate by chromatography. Long-chain oxyethylene glycols have been synthesised by Fordyce *et al.*,[5] using the Williamson ether synthesis to condense the mono-potassium derivative of a glycol with an αω-dihalide. Non-ionic detergents have been synthesised by the same general reaction with an alkyl halide and in the place of the dihalide.[6,7] We have used this procedure to prepare nona- and dodeca-oxyethylene glycol, and to condense these materials with hexadecyl bromide. Some of the errors present in the light-scattering method of measuring molecular weight have been investigated by using these materials.

EXPERIMENTAL

Syntheses of Glycols and Detergents.—3,6,9,12,15,18,21,24-*Octaoxahexacosane*-1,26-*diol* (*Nona-oxyethylene Glycol*, n_9). Sodium (46 g.) was dissolved slowly at a temperature not exceeding 75° in redistilled triethylene glycol (1200 g.; b. p. 134°/2 mm., n_D^{20} 1·4553; cf. ref. 8) by stirring under a layer of light petroleum (b. p. 100—120°). αω-Dichlorotriethylene glycol (187 g.) was added, and stirring continued at 115° until the reaction mixture was neutral (4 hr.). Precipitated salt was filtered off, and the excess of triethylene glycol removed by distillation under reduced pressure. The residue was distilled in a short-path still, giving *nonaoxyethylene glycol* (185 g.), m. p. 16°, n_D^{38} 1·4612 (Found: C, 52·0; H, 9·1; OH, 8·1. $C_{18}H_{38}O_{10}$ requires C, 52·2; H, 9·2; OH, 8·2%).

3,6,9,12,15,18,21,24,27,30,33-*Undecaoxapentatriacontane*-1,35-*diol* (*Dodecaoxyethylene Glycol*, n_{12}).—Hexaoxyethylene glycol and its αω-dichloro-derivative were synthesised by the method of Fordyce *et al.*[5] The dodecaoxyethylene glycol was prepared from sodium (23 g.), redistilled triethylene glycol (600 g.), and αω-dichlorohexaoxyethylene glycol (159·5 g.) by the method described above. Short-path distillation gave 123 g. of *product*, m. p. 24°, n_D^{38} 1·4615 (Found: C, 52·6; H, 9·4; OH, 6·1. $C_{24}H_{50}O_{13}$ requires C, 52·7; H, 9·2; OH, 6·2%).

3,6,9,12,15,18,21,24,27-*Nonaoxatritetracontan*-1-*ol* (*Nonaoxyethylene Glycol Monohexadecyl Ether*, Hn_9).—Sodium (2·3 g.) was dissolved in the nonaoxyethylene glycol (166 g.) as before, hexadecyl bromide (30·7 g.) (redistilled B.D.H. material; m. p. 14°, n_D^{20} 1·4622; cf. ref. 9) added, and the mixture stirred at 135° until neutral (1 hr.). After cooling it was extracted with ether (3 × 150 ml.), and the residue after evaporation of the ether re-extracted with warm dry light petroleum (b. p. 60—80°; 3 × 50 ml.). This procedure removed the unchanged glycol present in the original extract. The residue (21 g.) obtained on evaporation of the petroleum was recrystallised from ether.

This material (1·5 g.) was adsorbed from benzene on alumina (25 g.), and the column washed with 1 : 4 acetone–benzene until no further material was eluted (200 ml.). About 15% of the initial column load was removed in this step, the eluate being a water-insoluble fraction, possibly the dihexadecyl ether of the nonaoxyethylene glycol. Further elution with acetone–methanol–benzene (300 ml.; 25 : 1 : 24) gave the *monohexadecyl ether* (0·9 g.) which, recrystallised from ether, had m. p. 40·5° (Found: C, 63·4; H, 10·9; OH, 2·7. $C_{34}H_{70}O_{10}$ requires C, 63·9; H, 11·0; OH, 2·7%).

3,6,9,12,15,18,21,24,27,30,33,36-*Dodecaoxadopentacontan*-1-*ol* (*Dodecaoxyethylene Glycol Monohexadecyl Ether*, Hn_{12}).—Sodium (1·15 g.), dodecaoxyethylene glycol (110 g.), and hexadecyl

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[4] Kelly and Greenwald, *J. Phys. Chem.*, 1958, **62**, 1096.
[5] Fordyce, Lovell, and Hibbert, *J. Amer. Chem. Soc.*, 1939, **61**, 1905.
[6] Gingras and Bayley, *Canad. J. Chem.*, 1957, **35**, 599.
[7] Mulley, *J.*, 1958, 2065.
[8] Curme and Johnston, "Glycols," p. 170, Reinhold Publ. Corpn., New York, 1952.
[9] Flaschenträgen and Wannschaff, *Ber.*, 1934, **67**, 1121.

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bromide (15·35 g.) gave, by the method described as for Hn_9, a *product* (11 g.) that, crystallised and chromatographed in the same way, had m. p. 43·5° (Found: C, 62·1; H, 10·5; OH, 2·0. $C_{40}H_{82}O_{13}$ requires C, 62·3; H, 10·7; OH, 2·2%).

Light-scattering Measurements.—The apparatus described by Elworthy and McIntosh [10] was used. After calibration with Ludox solutions, turbidities of $27·2 \times 10^{-5}$ and $9·6 \times 10^{-5}$ cm.$^{-1}$ were obtained for benzene and carbon tetrachloride, respectively; also the observed molecular weights were within 2% of the known molecular weights for some polystyrene fractions. Great care was taken to exclude dust from the solutions; a seasoned no. 5 porosity sintered-glass gas-filter tube was found to be an excellent filter. Measurements on water, which had been slowly redistilled from permanganate, gave Rayleigh's ratios between 1·0 and $1·1 \times 10^{-6}$ cm.$^{-1}$, indicating that very little stray light was present in the apparatus, and that dust had been effectively removed from the water.

Specific Refractive Index Increments (dn/dc).—These were determined on a Hilger–Rayleigh interference refractometer, by Bauer's technique [11] for monochromatic light.

Viscosities.—Viscosities of solutions relative to water were determined in a suspended-level dilution viscometer, giving ±0·2% error in relative viscosity.

Densities.—Densities were determined by displacement of pure dry n-hexane. Small corrections were applied to the results for the amounts of Hn_9 and Hn_{12} which dissolved in the hexane. Owing to the tendency of the compounds to dissolve, density measurements were made at 20° while all other measurements were made at 25°. The temperature control in the light-scattering measurements was ±1°, and ±0·01° in all other measurements. The densities of Hn_9 and Hn_{12} were $0·978 \pm 0·001$ and $1·037 \pm 0·001$ g. ml.$^{-1}$, respectively.

RESULTS AND DISCUSSION

The micellar weights were calculated from Debye's equation: [12]

$$H(c - c_0)/(T - T_0) = 1/M + 2Bc$$

where T is turbidity, T_0 the turbidity at the critical micelle concentration (c_0), and c the concentration in g. ml.$^{-1}$. The optical constant, $H = 32\pi^3 n_0^2 (dn/dc)^2/3N\lambda^4$, where n_0 is the refractive index of the solvent, and λ the wavelength of the light used (5461 Å). The values of c_0 were obtained from large-scale plots of c against T, and were 0·0002 and 0·00018 g. ml.$^{-1}$ for Hn_9 and Hn_{12}, respectively. Fig. 1 gives plots of $(c - c_0)/(T - T_0)$ against $(c - c_0)$. In the case of Hn_9 a large number of solutions were measured (cf. Table 1) to enable the results to be analysed statistically. We considered three of the five most probable sources of error in a determination of a micellar weight by light scattering, namely, errors in the measurement of c/T, of depolarisation, ρ, and of dn/dc. As large dissymmetries were not observed, giving only a small correction to $H(c - c_0)/(T - T_0)$, the error in these measurements was not assessed. The remaining error lies in the evaluation of the calibration constant of the apparatus, which is being studied.

TABLE 1.

Depolarisations of Hn_9 solutions.

$10^3(c - c_0)$ (g. ml.$^{-1}$) ……	1·101	1·790	1·905	2·187	2·351	2·617	2·777	2·995
ρ ……	$0·015_2$	$0·006_4$	$0·023_1$	$0·051_2$	$0·010_8$	$0·012_5$	$0·026_9$	$0·017_2$
$10^3(c - c_0)$ (g. ml.$^{-1}$) ……	3·165	3·178	3·283	3·860	3·895	4·595	4·790	6·384
ρ ……	$0·005_2$	$0·011_0$	$0·022_2$	$0·020_2$	$0·012_4$	$0·007_6$	$0·017_0$	$0·086_0$

The apparatus had been tested and good agreement with literature figures obtained for the depolarisations of Ludox solutions, toluene, and benzene.[10] The intensies of both vertical and horizontal components at c_0 were subtracted from those of the solutions.

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[10] Elworthy and McIntosh, *J. Pharm. Pharmacol.*, 1961, **13**, 663.

[11] Bauer, in " Physical Methods of Organic Chemistry," ed. Weissberger, Vol. I, p. 1211, Interscience, Publ. Inc., New York, 1960.

[12] Debye, *Ann. N.Y. Acad. Sci.*, 1949, **51**, 575; *J. Phys. Chem.*, 1949, **53**, 1.

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The results in Table 1 were tested for correlation between concentration and depolarisation; the calculated correlation coefficient, $r = 0{\cdot}27$, while the theoretical $r = 0{\cdot}50$. No correlation exists between ρ and $(c - c_0)$. The mean value of ρ was $0{\cdot}016_7 \pm 0{\cdot}004_8$ $(P = 0{\cdot}95)$.

TABLE 2.

Values of dn/dc for Hn_9 solutions.

$10^3(c - c_0)$ (g. ml.$^{-1}$)	1·624	1·842	2·460	2·613	2·944	3·884	4·398	4·852	5·425	6·384
dn/dc* (ml. g.$^{-1}$)	0·1386	0·1341	0·1351	0·1340	0·1367	0·1350	0·1347	0·1344	0·1337	0·1366

* The refractive index at c_0 was subtracted from the refractive index of each solution in the calculation of dn/dc.

A test (cf. Table 1) showed that there was no correlation between dn/dc and $c - c_0$ ($r = -0{\cdot}23$; theor. $r = 0{\cdot}63$ at $P = 0{\cdot}95$). The mean value of dn/d$c = 0{\cdot}1353 \pm 0{\cdot}0011$ ml. g.$^{-1}$.

When the plots of $(c - c_0)/(T - T_0)$ against $(c - c_0)$ for Hn_9 were considered (cf. Fig. 1), a significant correlation was obtained between the two quantities. Robinson and Saunders[13] have also assessed the error in c/T for lysolecithin sols, obtaining limits of error of ±7%. It is necessary to assess the variance of both the means value of $(c - c_0)/(T - T_0)$ and that of the slope of the graph in obtaining the error in $(c - c_0)/(T - T_0)_{c=0}$. We obtained $3{\cdot}506 \pm 0{\cdot}284$ for the mean values and limits of error $(P = 0{\cdot}95)$ of this intercept.

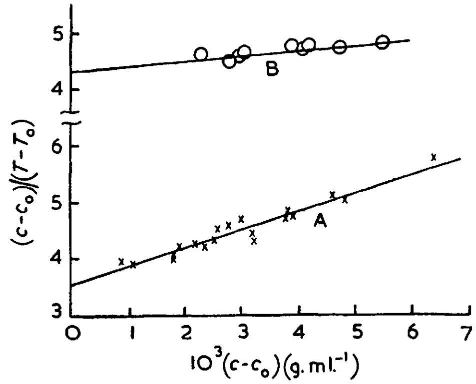

FIG. 1. Plot of $(c - c_0)/(T - T_0)$ against $(c - c_0)$. For symbols see text. A = Hn_9; B = Hn_{12}.

Combining these results in the calculation of M, we have $H = 2{\cdot}008 \pm 0{\cdot}032 \times 10^{-6}$, and the Cabannes factor $= 0{\cdot}964 \pm 0{\cdot}011$. There is roughly ±8% error in the assessment of $(c - c_0)/(T - T_0)_{c=0}$, ±1·6% in H, and ±1% in the Cabannes factor. The observed dissymmetry (Z_{45}) was 1·03, giving $M = 140{,}000 \pm 14{,}000$. This error was much larger than expected, and the main part of it comes from the measurement of turbidity of the detergent solutions. In spite of the great care taken in cleaning cells and filters, and in filtering the solutions, traces of dust may be responsible for this variation but there was certainly not an excessive amount present, as the observed dissymmetries were close to unity. It is possible that the tendency of the detergent to suspend dust, and also its completely non-ionic character, may be responsible for the variations in $(c - c_0)/(T - T_0)$; Stacey[14] states that aqueous solutions containing salt are relatively easy to clarify, and it may be that errors of this size are inherent in the study of this class of compound by light scattering.

For Hn_{12}, dn/dc = 0·1342 (ml. g.$^{-1}$), $\rho = 0{\cdot}008_5$, and $Z_{45} = 1{\cdot}03$, giving $M = 117{,}000$.

For polyoxyethylene dodecyl and nonyl phenyl derivatives, Becher[1] has observed that the micellar size decreases as the ethylene oxide chain lengthens. Our results on

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[13] Robinson and Saunders, *J. Pharm. Pharmacol.*, 1959, **11**, 115T.

[11] Stacey, " Light Scattering in Physical Chemistry," Butterworths, London, 1956, p. 79.

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Hn_9 and Hn_{12} show the same effect; also a commercially produced member of the hexadecyl series (containing 22 ethylene oxide units) gave[3] a micellar weight of 101,000 by light scattering (97,000 by diffusion). The origin of this effect probably lies in the increasing affinity of the monomer for water as the hydrophilic chain length increases, the hydrophobic part of the molecule remaining constant.

The observed dissymmetries indicate that no dimensions of the micelles exceed $\lambda/20$ (270 Å); the depolarisations are possibly a better guide to the asymmetry of the micelles than the Z values. The values of ρ show that the micelles are very nearly spherical. Fig. 2 gives the viscosity results: the limiting values of $(\eta_{sp}/\phi)_{\phi=0}$ are 4·20 and 4·97 for Hn_9 and Hn_{12}, respectively, where η_{sp} is specific viscosity and ϕ is the volume fraction of the solute. At the present state of this work we assume that the micelles are spherical, and interpret the viscosity results in terms of micellar hydration. Unhydrated spheres should give $(\eta_{sp}/\phi)_{\phi=0} = 2{\cdot}5$; Oncley[15] gives $(\eta_{sp}/\phi)_{\phi=0} = 2{\cdot}5\ (1 + w/\bar{v}\rho_1)$ where $\bar{v}$ is the specific volume of solute, ρ_1 the density of solvent, and w the weight of water hydrating one g. of material: $w = 0{\cdot}69_5$ g. per g. of Hn_9 and 0·95 g. per g. of Hn_{12}. (The commercial Hn_{22} gave $w = 1{\cdot}96$ g./g.) There appears to be a steady increase in the micellar hydration as the series is ascended. As the hydration of this class of detergent is probably a trapping of water within the mesh of the polyoxyethylene chains, a greater degree of hydration is to be expected as the chain length increases.

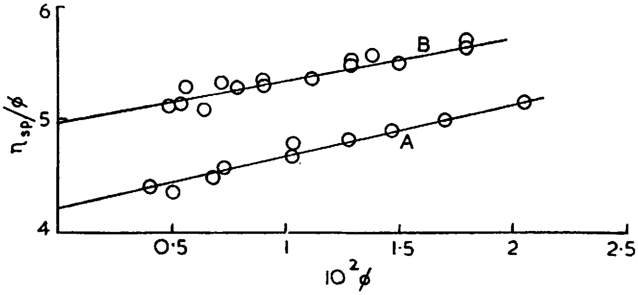

FIG. 2. Plot of η_{sp}/ϕ against ϕ. For symbols see text. A = Hn_9; B = Hn_{12}.

The micellar volumes of Hn_9 and Hn_{12} can be calculated from the number of monomers present in the micelle, and the degree of hydration, giving 398,000 Å^3 and 374,000 Å^3, respectively. The radii of the micelles will be 47 and 45 Å, while Hn_{22} gave 48 Å. These radii are far smaller than the extended length of the monomers (56 Å for Hn_9, 67 Å for Hn_{12}, and 101 Å for Hn_{22}, from molecular models). It appears that considerable curling of the monomer occurs when incorporated in the micelle. This effect may take place in the polyoxyethylene chain, giving a mesh-like structure suitable for trapping the hydrating water. The radius of the Hn_9 micelles appears to be anomalous, as it is larger than that of Hn_{12}. This may be due either to the large error in the light-scattering determination of micellar weight, or to assigning the deviation of $(\eta_{sp}/\phi)_{\phi=0}$ from 2·5 solely to hydration. A small amount of asymmetry may be present in the micelle, so that the smaller amount of hydration is required to give an intercept of $(\eta_{sp}/\phi)_{\phi=0}$ of 4·20; hence the calculated micellar volume may be too large. We are investigating the lower members of the series, *e.g.*, hexaoxyethylene glycol monohexadecyl ether, to try to elucidate this problem.

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SCHOOL OF PHARMACY,
ROYAL COLLEGE OF SCIENCE AND TECHNOLOGY,
GLASGOW, C.1.

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[15] Oncley, *Ann. N.Y. Acad. Sci.*, 1940, **41**, 121.