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A NEW STEROIDAL PROBE

Frederic MENGER
Department of Chemistry, Emory University, Atlanta, Georgia, 30322 U.S.A.
Bernard BOYER
Laboratoire de Chimie Organique Physique, U.S.T.L. 34060 Montpellier Cédex, FRANCE.

Abstract : The ORD of 17 α-hydroxy-5 α-pregnan-20-one is shown to respond to changes in solvent polarity ; the steroid is thus useful as an environmental probe. Several examples are given in the micelle area.

In 1965 Danilewicz and Klyne[1] noted that the ORD spectra of 17 α-hydroxy-5 α-pregnan -20-one 1 manifest a dramatic change in extrema and amplitudes when the solvent is change from methanol to heptane. The large differences in molecular rotation were ascribed to the presence or absence of intramolecular hydrogen bonding. It occured to us that this behavior could be exploited to probe the polarity of environments in which the steroid is embedded.

Although we have recently shown that (+) -trans-2-chloro-5-methyl cyclohexanone serves as a useful ORD probe[2], the steroid seemed to present certain advantages : it is extremely water-insoluble and hence prone to enter micelles, vesicles and other molecular aggregates, its molecular rotation (ϕ) is so large that relatively small amounts are required (typically 2×10^{-4} M), and finally the permeability and stability of both natural and synthetic membranes are affected by incorporation of steroids ; development of a steroidal probe seemed, therefore, potentially important.

Figure 1 shows the ORD spectra of 1 in six solvents. There are clearly two classes of solvents : large positive Cotton effect solvents (methanol, DMSO and dioxane) and low positive Cotton effect solvents (heptane, trichloroethylene and CCl_4). The magnitude of the difference is illustrated by a ϕ_{328} = + 5752 for methanol compared with a ϕ_{300} = - 3180 for heptane. Thus, the probe should be able to detect water if it is present in a hydrophobic binding site.

Figure 2 presents the ORD of 2×10^{-4} M steroidal probe solubilized in 0.10 M hexadecyltrimethylammonium bromide (curve B) and 0.10 M sodium dodecyl sulfate (curve C). There is no doubt that the probe enters the micelles because dissolution of the steroid in water lacking surfactant is impossible even with prolonged sonication. Curves B and C are seen to resemble that of methanol (curve A) as opposed to that heptane (curve E). These results show that the binding sites of HTAB and SDS micelles contain water, in complete agreement with results obtained by us[3,4] and others[5] using a variety of methods.

Figure 2 also demonstrates that the steroidal probe in a water pool system consisting of water, heptane and sodium dioctylsulfosuccinate[6] manifests a heptane-like ORD spectrum (curve D). No doubt the steroid is present in the heptane solvent that separates the succinate-encased water pools. This microemulsion does not appear to "drag" water into a normally non-aqueous environment ; water is abundantly present in water pool system where the probe able to solvent sort.

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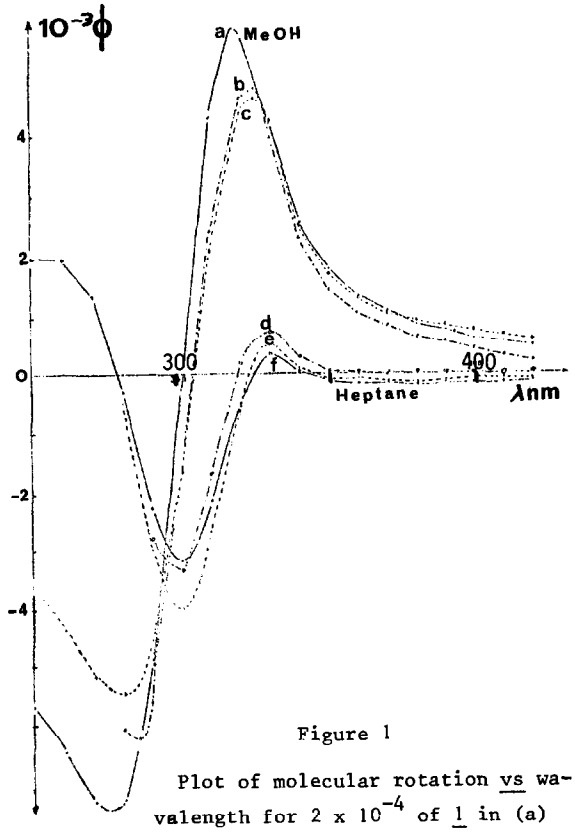

Figure 1

Plot of molecular rotation vs wavelength for 2 x 10^{-4} of 1 in (a) methanol, (b) DMSO, (c) dioxane, (d) trichloroethylene, (e) CCl_4 and (f) heptane .

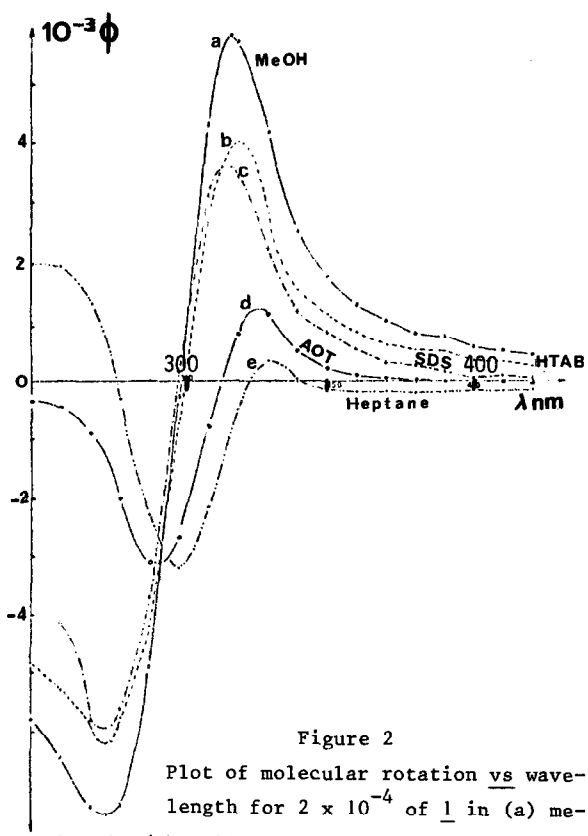

Figure 2

Plot of molecular rotation vs wavelength for 2 x 10^{-4} of 1 in (a) methanol, (b) 0.10 M aqueous HTAB, (c) 0.10 M aqueous SDS, (d) heptane containing 0.10 M AOT and 4.0 M water and (e) heptane .

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