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Circular dichroism spectra of opium alkaloids in the solid state

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Hercules Chemical Co.), and a derivatized epichlorohydrin polymer (DECH, North American Rockwell). All of the polymers were used directly and none contained significant levels of antioxidant. Table I shows the equivalent weight values obtained using the three analysis methods described. Each value is the mean of at least three replicate determinations and differences were considered statistically significant at the 95% confidence level.

Analysis of the Table I data indicates that for HTPB₂ the AA/PY vs. AA/NMIM and the AA/PY vs. PA/PY values are different whereas the PA/PY vs. AA/NMIM values are not different.

Samples of HTPB₂ under gaseous nitrogen were heated on the steam bath for 4 h after which the equivalent weight was determined using the AA/NMIM method. The Table I data indicate that the 4-h esterification period required for the AA/PY method causes significant degradation of this polymer.

No significant bias is apparent for a linear saturated polymer such as PEG; however, the PA/PY data for PECH and DECH are obviously different compared to the other methods. Both of the latter polymers are initiated from a trifunctional alcohol (e.g., glycerol) and the chain length of a specific branch is not controllable. Cohen and Fong (4) concluded that, in addition to the steric nature of the anhydride, variation in equivalent weight values between methods may also be due to steric or electronic properties of the hydroxyl compound. The presence of the chlorine atom on PECH or a similar group adjacent to the hydroxyl group may alter the properties of the polymer sufficiently to cause the observed differences. *N*-Methylimidazole was also used to

catalyze the esterification of HTPB₂ with phthalic anhydride but no significant reaction occurred.

Although the interference of phenols with equivalent weight determinations using acetic anhydride is recognized, the AA/NMIM method described herein is more generally applicable to different hydroxyl terminated polymers than either the AA/PY or PA/PY methods which were compared.

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Circular Dichroism Spectra of Opium Alkaloids in the Solid State

Sir: We wish to demonstrate that analytical distinction among compounds of similar molecular structure is possible using a method which is not usually considered capable of such a level of individuation.

The experimental procedure itself is not new. The novelty was to take two well established and conceptually unconnected procedures and to combine them into what appears to be a definitive method of identification, albeit limited at this time to only seven members of the family of opium alkaloids in their pure states.

The method applies the technique of circular dichroism (CD) ultraviolet spectropolarimetry to the study of compounds in the solid state. More specifically, the compounds are pressed in KBr pellets formed in the usual way. This use of a KBr matrix in CD studies is not commonly encountered (1, 2), although other solid state media have been investigated (3) using either CD or ORD. None have been used for analytical purposes of the kind described here.

Other innovative experimental uses of polarized spectroscopy include magnetocircular dichroism (4) (MCD) and liquid crystal CD (5). Our interest in the analytical distinction of the opiates by the latter method led us directly into an investigation of the spectra of the compounds pressed into dry KBr pellets. This correspondence contains our preliminary results, which hold considerable promise for qualitative, and perhaps with development of the technique, even quantitative analyses.

EXPERIMENTAL

All samples and the analytical grade KBr were dried at 140 °C for at least 48 h prior to their use in preparing specimens. The opiates studied were morphine, morphine sulfate, codeine, 3-

acetylmorphine, 6-acetylmorphine, 3,6-diacetylmorphine (heroin) hydrochloride, thebaine, and hydrocodone. Salts and free bases can be investigated with equal ease.

Spectra were taken on a Cary 61 spectropolarimeter operating in the normal mode. Samples consisted of an approximate 1:100 dilution with 80 mg KBr. Specimens must be thin (ca. 0.2 mm) for adequate UV transmission. The sample holder was constructed to fit both the pellet press and the carriage in the sample compartment of the Cary 61 so that damage to the fragile specimen could be avoided. Tests for the existence of linear dichroism components to the signal were made by rotating the specimen 90° and 120° and repeating the spectrum. Samples were dissolved in ethanol or water and the UV and isotropic solution CD spectra obtained for comparison.

RESULTS AND DISCUSSION

The solid state CD spectra of the seven compounds are shown in Figures 1 and 2. There are two morphine spectra, one for the free base, the other for the sulfate. Similarities exist in the spectra of codeine, 3-acetylmorphine, and morphine sulfate, all of which show negative ellipticities at the ¹L_b absorption band around 286 nm, and positive ellipticities at the ¹L_a band around 248 nm. These are qualitatively consistent with the more familiar ethanol CD spectra of these compounds (6). Semiquantitatively, the ellipticities increase in the order 3-acetylmorphine, morphine sulfate, and codeine, respectively.

Spectra of the other compounds are uniquely different. The morphine free base spectrum bears no resemblance even to that of morphine sulfate, which is perhaps the most startling result. Liberation of the free base brings about the spectral change anticipated from these data. This is an interesting distinction from the viewpoint of the forensic analyst in that

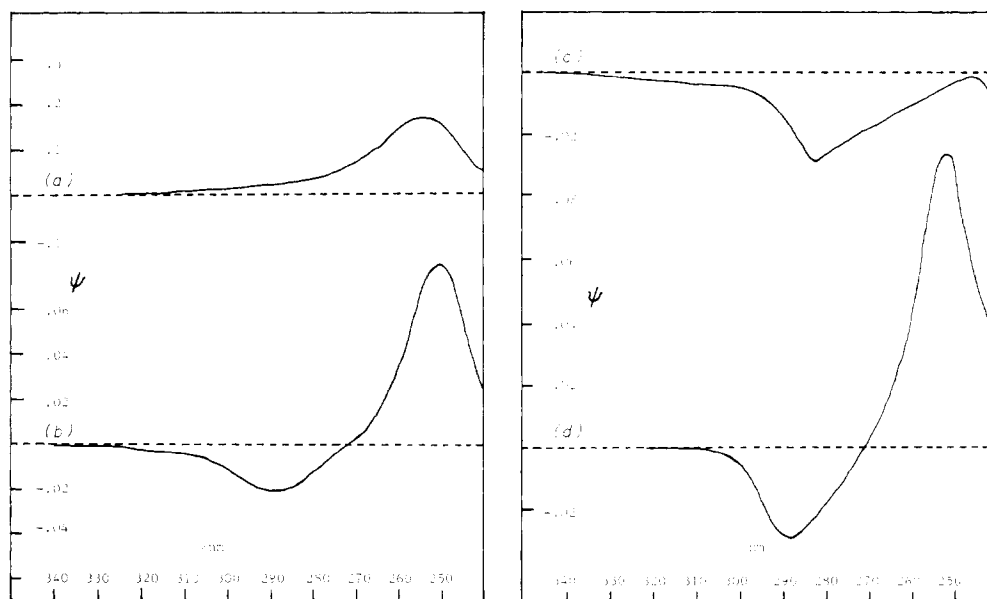


Figure 1. CD spectra of (a) morphine, (b) morphine sulfate, (c) heroin, and (d) codeine. Ordinate ψ is the experimentally measured ellipticity in degrees. Samples are all 0.8 mg/80 mg KBr

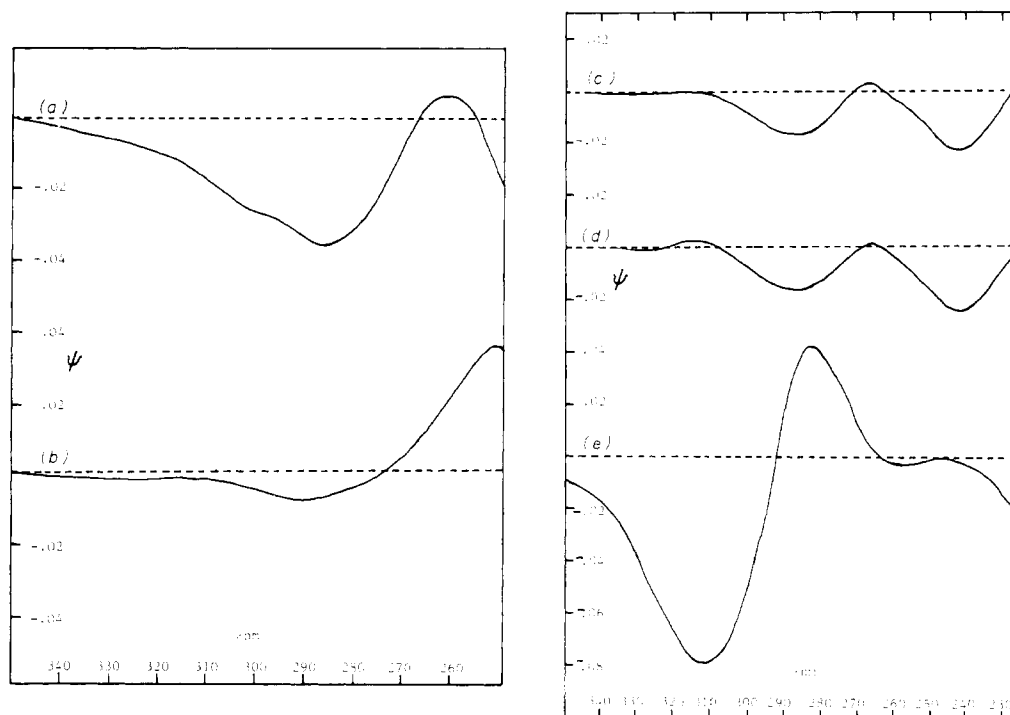


Figure 2. CD spectra of (a) 6-acetylmorphine, (b) 3-acetylmorphine, (c) thebaine, (d) thebaine (sample rotated 90°), (e) hydrocodone. Ordinate ψ is the experimentally measured ellipticity in degrees. Samples are all 0.8 mg/80 mg KBr

the sample can be identified in its original form without the risk of its being altered by an extraction procedure. Nothing that is different in the solid state structure, as seen by X-ray diffraction (7, 8), appears to account for the changes in the spectra. Both the free base and the hydrochloride salt hydrates (no structure is reported for the sulfate) crystallize with the morphine molecules arranged around a screw axis of the same handedness with evidence for strong intermolecular hydrogen bonding.

Heroin is easily distinguishable by its all negative ellipticity spectrum and a unique asymmetric band structure for the 1L_b transition. The spectrum for 6-acetylmorphine, the principal metabolite of heroin, differs from the previously discussed spectra in that it shows broadening of the 1L_b band and its separation into two components, presumably a consequence

of crystal forces. There is also a significant change in the ratio of the ellipticity maxima. For thebaine and hydrocodone, additional chromophores in the C-ring introduce new features to the spectra to aid in the identification process.

Linear dichroism components in the CD spectra appear to be minimal but real. Typical of the small changes are those shown for thebaine (Figure 2), which can be seen by comparing the spectra obtained on rotation of the sample. A quantitative study may require that sample orientation be carefully monitored. There is good reason to believe that better uniformity can be obtained by first sizing the KBr crystals by careful separation in a set of standard sieves.

In some cases there is a strong resemblance between these spectra and those taken of the same compounds in a cholesteric liquid crystalline solvent (9). Distinction is a conse-

quence of substantial and very specific crystal (anisotropic) forces.

Quantitative aspects of solid state CD are being pursued and the data base is being extended to include other controlled substances and some poisons.

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Isotopic Effect in Gas Chromatographic Analysis of Argon for Trace Oxygen

Sir: When using a very sensitive gas chromatograph (properties according to ASTM E260 (1) definitions: sensitivity, 3.34×10^5 mV·mL/mmol for nitrogen; detection limit, 8.98×10^{-7} mmol/mL for nitrogen) for measuring trace impurities in argon used as an inert blanket over liquid sodium, it was observed that the presence or absence of a small apparent oxygen peak correlated with changes in source of carrier gas, which was either vapor from liquid argon stored in a 114 m³ (3000 gal.) Dewar or cylinder argon. Both were purified over Ti at 800 °C. The fact that argon and oxygen are not separated on a 5A Molecular Sieve under the operating conditions used suggested examination of isotopic ratios of the different sources of argon. Mass spectrometric measurements of isotope ratios indicated there was indeed a difference. The isotopic ratios measured on a Nuclide 6-60 SGA were:

	liquid argon system	cylinder argon
38/40	0.000621	0.000615
36/40	0.00322	0.00315

The cylinder gas as carrier and system argon as sample gave an apparent oxygen peak equivalent to 9.6 ppm oxygen. If we assume that the difference in thermal conductivity of argon and oxygen times the concentration of oxygen is equal to the difference in thermal conductivity of the argon isotopes times the apparent concentration of ³⁶Ar + ³⁸Ar, we can calculate an effective concentration change of ³⁶Ar + ³⁸Ar that would

produce the change measured by the chromatograph. Carrying out these calculations after estimating the thermal conductivity of ³⁶Ar + ³⁸Ar from the measured value for natural argon and the fact that it changes as $1/\sqrt{m}$ indicated a difference in concentration of ³⁶Ar of 83 ppm.

This is an example of sample vacancy chromatography (2) where the katharometer senses the difference in thermal conductivity of the argon sample and carrier.

Therefore, if one is using a chromatograph to measure trace levels of oxygen in argon, one should take precautions to compensate for the isotopic effect. In the present work, this was done by using the same source of argon for carrier and system application (sodium cover gas) in which trace oxygen was sought.

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