Helix Sense of Poly-β-benzyl-L-aspartate

Sir:

It has been shown that poly-β-benzyl-L-aspartate (PBLA) forms left-handed α helices in chloroform solution.[1,2]

It has also been shown that copolymers of benzyl-L-aspartate with other aspartate esters (such as ethyl, propyl, and isopropyl esters) as well as homopolymers of the latter or of para-substituted L-benzylaspartate esters are able to assume in the same solvent the right-handed α-helical conformation depending upon temperature and composition.[3-8]

These results have demonstrated the importance of the side chain–side chain and/or side chain–main chain interactions in stabilizing one of the α helices.

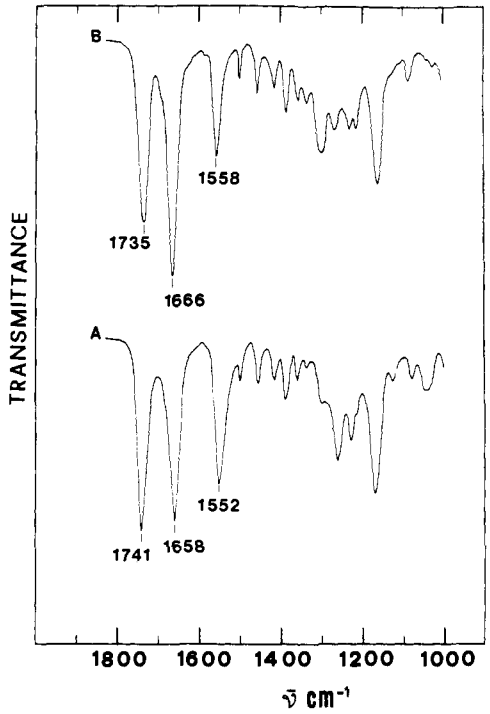

Figure 1. Ir spectra of PBLA films cast: A, from TMP; B, from chloroform.

Recently, Malcolm has reported that PBLA is capable of assuming a right-handed α helix in the solid state.[9] He obtained a monolayer of PBLA by spraying a chloroform solution of the polymers over water, and recorded X-ray reflections and ir spectra of such a layer.

These results have prompted us to find solvents for PBLA in which the polymer would be capable of assuming the right-handed α-helical conformation.

(1) R. H. Carlson, K. S. Norland, G. D. Fasman, and E. R. Blout, *J. Amer. Chem. Soc.*, **82**, 2268 (1960).
(2) E. M. Bradbury, A. R. Downie, A. Elliot, and W. E. Hanby, *Proc. Roy. Soc., Ser. A*, **259**, 110 (1960).
(3) E. M. Bradbury, B. G. Carpenter, and H. Goldman, *Biopolymers*, **6**, 837 (1968).
(4) M. Hashimoto and J. Aritomi, *Bull. Chem. Soc. Jap.*, **39**, 2707 (1966).
(5) M. Hashimoto, *ibid.*, **39**, 2713 (1966).
(6) M. Goodman, F. Boardman, and L. Litowski, *J. Amer. Chem. Soc.*, **85**, 2491 (1963).
(7) M. Goodman, C. M. Deber, and A. M. Felix, *ibid.*, **84**, 3773 (1962).
(8) M. Goodman, A. M. Felix, C. M. Deber, A. R. Brause, and G. Schwartz, *Biopolymers*, **1**, 371 (1963).
(9) R. B. Malcolm, *Nature (London)*, **219**, 929 (1968).

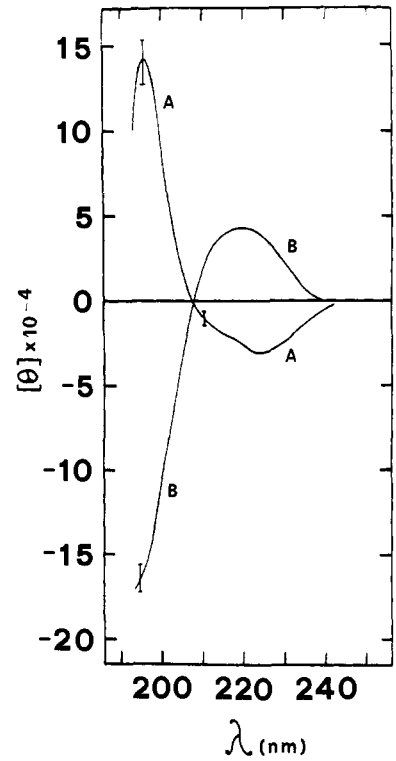

Figure 2. CD spectra of PBLA solution in: A, TMP; B, chloroform.

When trimethyl phosphate (TMP) is added to a chloroform solution of PBLA the polymer precipitates. The ir spectrum of the solid obtained in such a way is shown in Figure 1. For comparison, in the same figure is shown the ir spectrum of PBLA films obtained from chloroform solutions. The positions of the amide I band (1658 cm^{-1}), that of the amide II (1552 cm^{-1}), and that of the carbonyl ester (1741 cm^{-1}) are characteristic for a right-handed α helix as reported by Bradbury, *et al.*,[10] for other poly-L-aspartates. It has to be noted that the ir spectra for the two senses of spiralization of PBLA are different also in the 1200-cm^{-1} region.

PBLA dissolves in TMP when the temperature is raised to 130–140°. On cooling these solutions, the polymer may precipitate depending on its molecular weight.

High molecular weight polymers remain in solution indefinitely when the concentration is low ($\leqslant 10^{-3}$ *M*), whereas low molecular weight samples give rise to phase separation. Ir spectra recorded on the solid precipitated at room temperature from TMP as well as on films obtained by evaporating the solvent from TMP solutions of PBLA gave bands corresponding to the right-handed α helix.

The CD spectrum of high molecular weight PBLA ($\sim 10^5$) dissolved in TMP and recorded at room temperature is shown in Figure 2 together with the spectrum obtained on a chloroform solution of the sample (the latter spectrum was obtained with a 0.01-mm cell to minimize the absorption of the solvent).

The spectra are important for the following reasons: (i) the n–π* and the parallel π–π* bands are not well resolved in the PBLA spectrum in chloroform; (ii) PBLA in TMP has a CD spectrum opposite to that in

(10) E. M. Bradbury, B. G. Carpenter, and R. M. Stephens, *Biopolymers*, **6**, 905 (1968).

chloroform, *i.e.*, the polymer is a right-handed α helical; (iii) the spectrum of PBLA in TMP has a lower intensity especially in the parallel $\pi-\pi^*$ band. The perpendicular $\pi-\pi^*$ band lies at 196 nm.

All these peculiarities may find their origin in structures slightly distorted with respect to that of a regular α helix. A contribution of the side chains to the rotatory properties of PBLA cannot be excluded.

If CD spectra of PBLA in TMP are recorded at temperatures higher than 100° the dichroic bands are characteristic of a coil conformation having a negative maximum at ~200 nm.

PBLA dissolves readily in DMSO. ORD measurements on these solutions gave b_0 values around -100, which is the value found for PBLA in the random coil conformation.[11]

Also the films that we obtained from PBLA solutions in DMSO by evaporating the solvent gave ir spectra similar to those reported in Figure 1 for a right-handed α helix.

All these results point out the importance of the solvent in stabilizing the overall conformation of a polypeptide and in making one sense of spiralization energetically more favorable than the other, at least when the difference in internal potential energy between the two is not large, as appears to be the case for PBLA chains.[12]

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(11) E. M. Bradbury, C. Crane-Robinson, V. Giancotti, and R. M. Stephens, *Polymers*, in press.

(12) J. F. Yan, G. Vanderkooi, and H. A. Scheraga, *J. Chem. Phys.*, 49, 2713 (1968).

V. Giancotti, F. Quadrifoglio, V. Crescenzi*
Istituto di Chimica, Università di Trieste
Trieste, Italy
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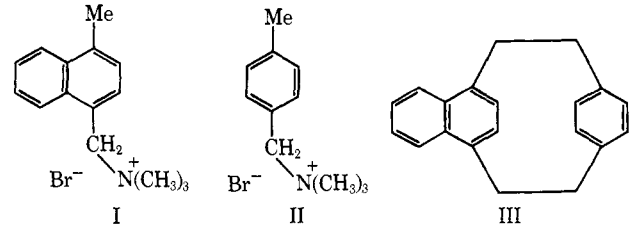
The Reaction of Benzo[2.2]paracyclophane with Singlet Oxygen

Sir:

We have recently described the reactions of singlet oxygen with [2.2](2,5)-furanophane,[1] [2.2](2,5)-furanoparacyclophane,[2] and *anti*-[2.2](1,4)naphthalenophane.[3,4] In the above cases, initial oxygen uptake was followed by a second-stage intramolecular Diels–Alder addition forming cagelike oxygenated derivatives. We now report that the reaction of singlet oxygen in methanol with the cyclophane III results in oxygenation of the naphthalene ring accompanied by a rearrangement to the metaparacyclophane system.

Benzo[2.2]paracyclophane (III),[5] prepared by a pyrolytic route,[6] was subjected to photooxidation in the standard way, using a 150-W (G.E.) floodlamp as light source, methylene blue as sensitizing dye, and a



I II III

mixture of methanol and benzene (1:1) as solvent. After bubbling oxygen through this mixture for 12 days, the solvent was removed, yielding a mixture of materials containing mostly III and two new products (*ca.* 15%), a solid (A), and an oil (B).[7]

Product A is a crystalline material. The mass spectrum contains a weak parent peak at *m/e* 288, and strong peaks at 184, 169, and 154 as well as a weak peak at 104. The appearance of peaks at *m/e* 184 and 104 corresponding to the rupture of the ethylene bridges is typical of the fragmentation observed in the cyclophane series,[4,10] and clearly shows that the methoxyl group is located on the naphthalene ring. The infrared spectrum contains no hydroxyl band, but absorption (cm^{-1}, KBr) at 1610, 1385 (strong), and 1103. The ultraviolet spectrum has $\lambda_{max}^{95\%\ EtOH}$ at 296 (ϵ 5190) and 236 nm (ϵ 45,200). The nmr spectrum ($CDCl_3$) contains peaks at τ 2.02, (m, 2 H), 2.5 (m, 2 H), 2.77 (m, 2 H), 4.48 (s, 1 H), 4.49 (q, 2 H, J = 8 Hz), 6.04 (s, 3 H), and a multiplet centered at 7.3 (8 H). *Anal.* Calcd for $C_{21}H_{20}O$: C, 87.46; H, 6.99. Found: C, 87.37; H, 6.84.

The above spectroscopic evidence is in complete agreement with the assignment of structure IX to the methoxylated product A. Its formation is outlined in the sequence IV → IX (Scheme I). Of particular importance in distinguishing between IX and the alternative system X is the appearance of the low-field nmr spectrum of A which corresponds in detail remarkably closely to the spectrum of 1-methoxy-2,4-dimethyl-

(1) H. H. Wasserman and A. Doumaux, *J. Amer. Chem. Soc.*, **84**, 4611 (1962).

(2) H. H. Wasserman, A. Doumaux, and R. E. Davis, *ibid.*, **88**, 4517 (1966).

(3) H. H. Wasserman and P. M. Keehn, *ibid.*, **88**, 4522 (1966).

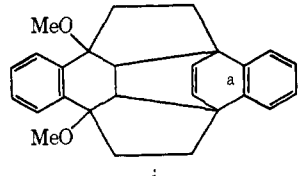
(4) P. M. Keehn, Ph.D. Dissertation, Yale University, 1969.

(5) A previous preparation of III was reported by D. J. Cram, C. K. Dalton, and G. R. Knox (*J. Amer. Chem. Soc.*, **85**, 1088 (1963)) through a route involving annelation of the benzo ring to a [2.2]paracyclophane nucleus. Our product gave a satisfactory C and H analysis and exhibited spectroscopic properties identical with those described by the above workers.

(6) By heating a mixture of quaternary ammonium bromides I and II in boiling xylene for 10 hr, followed by chromatography on silica gel.

(7) Compound B has an nmr spectrum showing aromatic absorption in the region τ 2.85, and sharp singlets at 3.64 (2 H), 4.47 (2 H), and 7.14 (6 H). This material was quite labile, and on warming, underwent rapid change to an unstable product which did not exhibit the sharp nmr singlets at τ 3.64 and 4.47. On treatment with HI, it readily reverted to III. Based on the nmr evidence and analogies with related reactions,[3] we have assigned structure V to the labile compound, B. This product appears to result from the transannular peroxide, IV, by solvolysis in methanol followed by an internal Diels–Alder reaction (see Scheme I).[8]

(8) The stability of i[3] relative to V may be associated with the presence of the aromatic ring in the place of a double bond at position a. Compound V most probably undergoes a ready thermal reversal of the intramolecular Diels–Alder reaction.



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