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Low temperature photochemistry in the daunomycin - DNA intercalation complex

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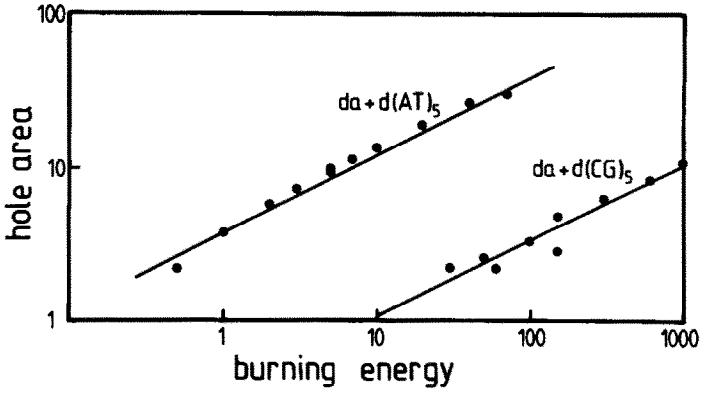
It is well known that the molecule quinizarin (1,4-dihydroxy-anthraquinone) exhibits a photochemical reaction at low temperatures [1]: upon absorption of visible light, an intramolecular hydrogen bond is broken and an intermolecular one to a nearby solvent molecule is formed This photoreaction can be monitored by the technique of photochemical hole burning (PHB) described below.

The anticancer drug daunomycin (da) shows similar optical properties as quinizarin. In 1985, it has been demonstrated [2] that in da a photoreaction can be induced as well. Our aim was to investigate the photoreaction in the intercalated state and to compare our results to those of conventional absorption and fluorescence spectroscopy.

The PHB technique allows to initiate site-selective photochemical bleaching of the dye molecules at low temperatures [3].We irradiate the sample with a narrow-band laser beam of low intensity. Only the dye molecules absorbing at the laser frequency will be able to undergo the photochemical reaction. As a result, they will change the spectral position of their absorption line so that the number of molecules absorbing at the laser frequency decreases. We then can observe a small photochemical "hole" in the absorption spectrum the shape of which is determined by physical properties of the dye. The efficiency of the photochemical conversion is, like in NMR, dependent on the molecular environment.

comparison of hole areas of two
daunomycin – DNA systems



From the figure, we see the dependence of the holes on burning energy. There is a striking difference between the two DNA systems used, $d(AT)_5$ and $d(CG)_5$, of a factor 13 in favour of the former complex. Since the hole area is indicative of the number of molecules that undergo the photoreaction, it can be considered as a photochemical quantum yield.

The scale factor shows up also in fluorescence quantum yield experiments. Since the fluorescence spectrum of the dye, upon intercalation, remains unchanged in spectral distribution, the quantum yields can be derived directly from the fluorescence intensity. Here also, we observe a 13 times larger quantum yield for da + $d(AT)_5$ than for da + $d(CG)_5$. This difference is connected with a change in fluorescence lifetime: the former complex has an excited state lifetime of 1.7 ns, whereas the latter shows a decay time of 0.7 ns.

We suggest that the described experimental results have the same cause: a difference in intermolecular coupling. In the da + $d(CG)_5$-complex, the vibrational energy, into which an optical transition decays, can dissipate much faster than in an $d(AT)_5$- complex, so that we find a larger internal conversion rate in the former case. This increase in decay rate (for da + $d(CG)_5$) leads to a larger solvent shift in the absorption spectrum, shorter decay time of the fluorescence intensity, smaller fluorescence and smaller photochemical quantum yield. (Here it is assumed that the photoprocess goes through the triplet state of the molecule)

Looking for hydrogen bond acceptors, which are, as we know, a prerequisite for the photochemical process, we find that no solvent molecule is close enough to form a hydrogen bond, but there is one acceptor inside the DNA: according to the x-ray analysis of Wang et al. [4] it is the O2 - oxygen atom of thymine/cytosine provided that the molecular structures of our helices are comparable with the hexamer considered in [4]. A similar H - bonding configuration has been proposed by Arora for the related drug steffimycin [5]. This explanation seems to fit best to our experimental results.

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