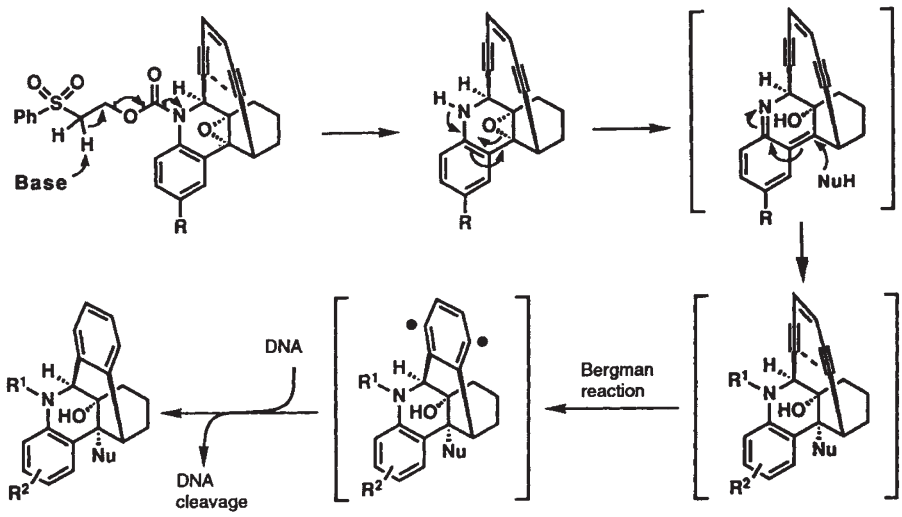

FIG. 3. Enediyne design, synthesis and biological action.

products all possess an enediyne unit as part of an overall structure which also contains a delivery system (carbohydrate or intercalating group), and a triggering device. The molecules are in effect prodrugs, in that the two triple bonds are held apart until after the triggering mechanism has taken place. The Bergman reaction can then occur, and a benzene diradical is formed, leading to damage of the DNA.

A number of groups are active in this area, but Nicolaou and coworkers have probably made the greatest contributions to our knowledge of the chemistry and modes of action of these intriguing molecules[7,8]. In their latest contribution[1], they report the first total synthesis of calicheamicin γ_1 (**2**) in stereochemically pure form. The synthesis is highly convergent and should provide access to gram quantities of the natural product and structural analogues.

In addition, Nicolaou *et al.* have also recently provided details of the synthesis of much of the dynemicin molecule, as well as of the syntheses of several simplified diynes[9,10]. Several of these, most notably (**7**), possess quite staggering anti-tumour activity (see table), and Nicolaou proposes that the mechanism of action is as shown in Fig. 3. The enediyne is held apart in the rigid parent structure, but following abstraction of a proton, and migration of electrons, the epoxide is opened thus effecting relaxation of the rigid structure, and precipitating the Bergman reaction.

This is clearly not the end of the story. Bergman could surely not have predicted that his 'innovative' chemistry had already been invented in the natural world, and this research provides yet another illustration of the wealth of chemistry and pharmacology associated with natural products, and just waiting to be discovered. □

CYTOTOXICITIES OF DESIGNED ENEDIYNE **7** AGAINST 19 TUMOUR CELL LINES (TOP) AND FOUR NORMAL CELL LINES (BOTTOM)

Cell type	Cell line	IC_{50} (M)	Cell type	Cell line	IC_{50} (M)
Melanoma	SK-Mel-28	3.1×10^{-6}	Lung carcinoma	UCLA P-3	9.8×10^{-8}
Melanoma	M-14	1.6×10^{-6}	Pancreatic carcinoma	Capan-1	3.1×10^{-9}
Melanoma	M-21	1.6×10^{-6}	T-cell leukaemia	TCAF	1.1×10^{-9}
Colon carcinoma	HT-29	1.6×10^{-6}	Multidrug resistant T-cell leukaemia	TCAF-DAX	1.7×10^{-9}
Ovarian carcinoma	Ovcar-3	7.8×10^{-7}			
Astrocytoma	U-87 UG	7.8×10^{-7}	Myeloma	RPMI-8226	7.7×10^{-9}
Glioblastoma	U-251 MG	3.9×10^{-7}	Mouse leukaemia	P-388	4.6×10^{-9}
Breast carcinoma	MCF-7	7.8×10^{-7}	Mouse leukaemia	L-1210	1.3×10^{-9}
Lung carcinoma	H-358	2.0×10^{-7}	Promyelocytic leukaemia	HL-60	3.6×10^{-11}
Lung carcinoma	H-522	9.8×10^{-8}	T-cell leukaemia	Molt-4	2.0×10^{-14}
Bone marrow	HNBM	5.0×10^{-5}	Normal human dermal fibroblast	NHDF	5.0×10^{-6}
Human mammary epithelial cells	HMEC	6.3×10^{-6}			
			Chinese hamster ovary	CHO	3.1×10^{-6}

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DAEDALUS

That inward eye

SOME forms of brain surgery are conducted under purely local anaesthetic. When the surgeon touches the conscious brain with an electrode, the patient is often overwhelmed by some vivid memory. Different regions of the brain trigger different memories. Daedalus now proposes a less invasive method of exploring our mental world.

He points out that a changing magnetic field can induce a strong but diffuse ring current in an electrical conductor. To give a more concentrated ring current, he has devised an electromagnet whose two pole pieces are tubular. The field between them is hollow, less intense in the middle than at the periphery. Increase the current in the electromagnet, and the strong annular field expands into the central region. A conductor in that region experiences a small, localized ring current. Two such magnets at right angles, their fields intersecting in quadrupolar fashion, define an even tighter ring current at the point of intersection.

Centred on a human head, and given a suitable sudden step-increase in its current, Daedalus's quadrupolar magnet should induce a ring current in a small specific area of the brain. The local neurons would be fired. The subject would carry out whatever action, experience whatever sensation, or recall whatever memory was triggered by those neurons.

DREADCO volunteers are now trying this out in practice. For safety's sake, they operate the whole machine themselves. They choose the region of their brain to be activated, and slowly increase the intensity of the current pulses of the magnet until they start to feel the effects. If these are too disconcerting, they can back off or move to another region; if the effects are interesting or pleasant they can increase the intensity further. Each volunteer can thus explore his brain, and produce a crude 'map' of its contents.

The results will be fascinating, particularly for Daedalus's more absent-minded volunteers. Will they find all sorts of mislaid memories, quite beyond conscious recall? Does the brain, like some obsessive bureaucracy, really file copies of everything? Do some people pack a lot more memory into a given space, by efficient coding? If so, what is the code? Daedalus suspects that information on a particular topic (like animals or faces) may well be coded in the form of an archetype, with specific examples being economically stored as perturbations of that archetype. The DREADCO encephalomagnet may reveal at last the primitive elements from which we construct our image of the world.

David Jones