through enzymology, as nature conducts reactions through a relatively restricted set of procedures.

The examples quoted by Pryce and Roberts permit us to make direct comparison of the 'state of the art' in the respective areas. Indeed, four of their five flagships for biotransformation are resolutions of racemic compounds by enzymes and not asymmetric syntheses! The fifth is an epoxidation (enzyme catalyst not specified) affording the β-blocker (*S*)-atenolol, carried out by the Shell subsidiary IBIS. By comparison, chemical asymmetric epoxidation is being carried out on a multi-ton scale by the Sharpless titanium-tartrate method (see p.632 of our review) to produce related glycidols. Other examples of asymmetric synthesis used on a large scale in industry are current; we cite the rhodium catalyst-based isomerization which is the key step in the Takasago process for the synthesis of the ubiquitous flavour ingredent menthol, competing with a cheap and abundant natural source. Consequently, we stand by our views expressed in our article, which we believe to be fair and accurate.

There is ample scope for both chemical and biochemical methods in asymmetric synthesis. To some extent these will be provided by healthy competition which will sharpen the development of new science. We welcome the opportunity to participate in this competition with our friends in the biotechnology community.

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Toxic oil disaster

SIR—The events that took place in the Madrid area of Spain in 1981 probably represent the worst recorded outbreak of food-borne chemical intoxication ever documented. Between May 1981 and March 1983, 340 deaths and more than 20,000 cases were registered[1]. Subsequent research on the causes of the outbreak, however, has been singularly unrewarding[2].

Epidemiological evidence has implicated the consumption of aniline-degraded, and subsequently reprocessed, rapeseed oil as the causative agent, but attempts to reproduce the chemical composition of suspect samples of oil have been unsuccessful. Furthermore, the pathology seen in the affected patients was previously unknown and no comparable animal model response has been demonstrated.

We report here progress in addressing these two fundamental inhibitions to successful examination of the mechanisms of this syndrome: the production of oil of comparable chemical composition to case-related oils; and the development of a discriminating *in vitro* bioassay. Our results show that the necessary tools for the mechanistic study of the Spanish toxic oil syndrome are available. Further work now has a reasonable prospect of resolving this eight-year-old mystery.

Samples of crude rapeseed oil, including one of the *Jet Neuf* variety believed to have been used to produce the original toxic oil, were adulterated with aniline, stored and then processed under conditions mimicking as closely as possible the conditions that pertained in the 1981 incident. Figure 1 shows HPLC traces of these adulterated oils and of similarly processed control oil not denatured with aniline. For comparison, case-related and control oils of known provenance (supplied by the *Fondo de Investigaciones Sanitarius de la Seguridad Social*) are also shown. Several compounds are present in the aniline-treated oils, and radiochemical studies show that these are aniline-derived.

In vitro toxicological studies using mouse neuroblastoma and rat liver epithelial cells successfully discriminated between aniline-adulterated oils and controls, and some HPLC fractions from each, when the test material was presented to the cells in a predigested form. Without this pretreatment, nonspecific toxic effects were seen in all cases. Figure 2 shows examples of the effects of exposing cells to extracts of control and aniline-treated oil samples.

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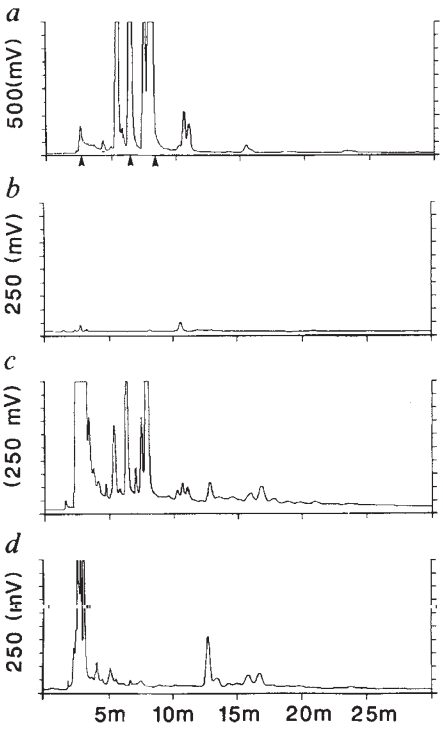

FIG. 1 HPLC traces of *a*, ^{3}H-aniline-adulterated and then processed French rapeseed oil, compared with: *b*, its appropriate processed control; *c*, genuine case related oil KM489; and *d*, an appropriate control of similar age. Column C18 ODS, solvent methanol:water 95:5 by volume. Monitor absorbance at 254 nm. Main radioactive peaks marked.

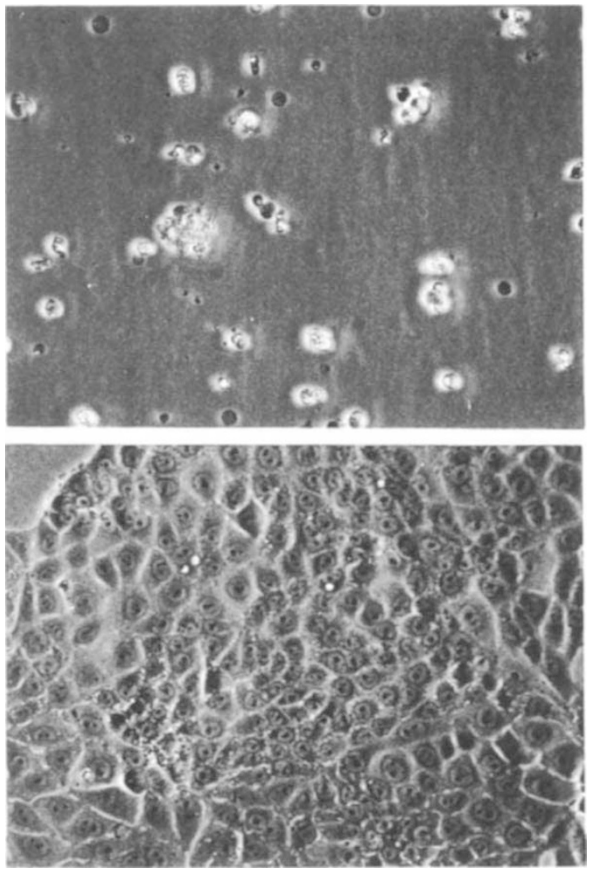

FIG. 2 Effect of extracts from aniline-treated rapeseed oil (top) and an appropriate control oil (bottom) on rat liver epithelial cells. Magnification, × 300.

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