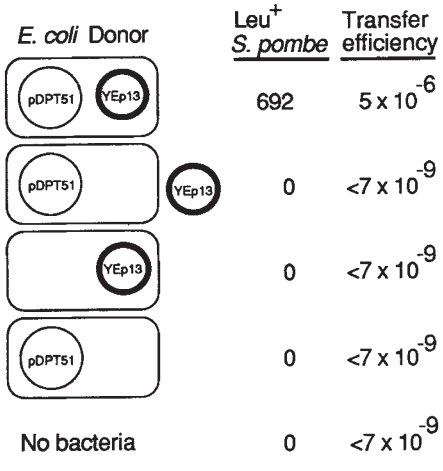
based plasmid YEp13 to *S. pombe* was obtained by mixing bacteria and yeast and selecting Leu$^+$ yeast prototrophs. The results of a typical experiment are shown in the figure. We observed production of Leu$^+$ *S. pombe* at frequencies comparable to those reported using *S. cerevisiae* as the recipient[2]. The absolute requirement for the helper plasmid, which provides essential mobilization and transfer functions for *E. coli*/*E. coli* conjugation, strongly suggests that a conjugal mechanism is used in the *E. coli*/*S. pombe* DNA transfer. Furthermore, a transformation mechanism is unlikely as exogenous DNA is completely ineffective under these conditions.

Analysis of five independent Leu$^+$ yeast 'transconjugants' yielded results expected of *S. pombe* strains harbouring an episome. All five isolates grew slowly under selection and exhibited mitotic instability for the Leu$^+$ phenotype such that on average only 22 per cent of cells in such a culture retested as Leu$^+$. In addition, Southern blot analysis of genomic DNA showed that all had inherited YEp13 DNA sequences: three carried intact YEp13 and two carried plasmids that had undergone rearrangements (data not shown). The level of mitotic instability and the frequency of rearrangements are both typical of YEp13 plasmids introduced into *S. pombe* by transformation[4].



Transfer of plasmid-encoded information from *E. coli* to *S. pombe*. The *E. coli* strain SB21 (ref. 2) containing the broad-host-range 'helper' plasmid pDPT51 or a transformant of this strain which also contained YEp13 were mixed with a *leu1 S. pombe* strain and plated directly on yeast medium lacking leucine. YEp13 contains a functional *ori-T*, replicates autonomously in *S. pombe* and contains the *S. cerevisiae LEU2* gene, which complements the *S. pombe leu1* mutation. Requirements for the transfer process were investigated by manipulating the *E. coli* genotype (shown schematically) or by providing exogenous YEp13 DNA. Transfer efficiency is the number of Leu$^+$ colonies per potential yeast recipient.
METHODS. *S. pombe* strain Sp659 (h^-/h^- *leu1-32/leu1-32 ura4/ura4 ade6/ade6*) and the various *E. coli* donor stains were grown separately to saturation in YE (0.5 per cent yeast extract) and LB (plus antibiotics), respectively. The antibiotics trimethoprim (200 μg ml^{-1}) for pDPT51 or tetracycline (12.5 μg ml^{-1}) for YEp13 were added to LB as required for plasmid selection. Cultures were washed once and resuspended in TNB (50 mM Tris, pH 7.6, 0.05 per cent NaCl). Routine transfer experiments were performed by mixing 200 μl 5× concentrated Sp659 (~10^8 cells) with 200 μl 10× concentrated bacteria (~10^9 cells). The mixtures were immediately pelleted, resuspended in 200 μl TNB and plated to SD medium[2]. To provide exogenous YEp13, 10 μg CsCl-purified plasmid DNA was added directly to TNB and plated with the cells.

The finding that DNA can be transferred directly from *E. coli* to *S. pombe* is significant for several reasons. Fission-yeast geneticists may find applications for this 'conjugation' method as an alternative to DNA-mediated transformation for introducing cloned genes into *S. pombe*. DNA manipulated on most pBR322 derivatives will be suitable for conjugation-mediated transfer since pBR322 carries a functional *ori-T*. Furthermore, given the great evolutionary distance between budding and fission yeasts, one may be encouraged to test other eukaryotes as potential recipients in the laboratory. The prevalence and significance of trans-kingdom conjugation in nature remains to be determined. In this regard, we note that unexpectedly significant similarities have recently been reported between a yeast and a bacterial alcohol dehydrogenase[5], between a retroviral and a bacterial RNase H (ref. 6), and between fungal and bacterial isopenicillin N synthetases[7]. Could sexually promiscuous bacteria have grafted these unusual limbs onto the evolutionary tree?

ROBERT S. SIKORSKI
WILLIAM MICHAUD
HENRY L. LEVIN
JEF D. BOEKE
PHILIP HIETER
Department of Molecular Biology and Genetics,
The Johns Hopkins University School of Medicine,
Baltimore, Maryland 21205, USA

1. Zambryski, P., Tempe, J. & Schell, J. *Cell* **56**, 193–201 (1989).
2. Heinemann, J. & Sprague, G.F. *Nature* **340**, 205 (1989).
3. Stachel, S.E. & Zambryski, P.C. *Nature* **340**, 190 (1989).
4. Heyer, W.-D., Sipiczki, M. & Kohli, J. *Molec. cell. Biol.* **6**, 80–88 (1986).
5. Williamson, V.M. & Paquin, C.E. *Molec. gen. Genet.* **209**, 374–381 (1987).
6. Doolittle, R.F., Feng, D.-F., Johnson, M.S. & McClure, M.A. *Q. Rev. Biol.* **64**, 1–30 (1989).
7. Ramon, D., Carramolino, L., Patino, C., Sanchez, F. & Penalva, M.A. *Gene* **57**, 171–181 (1987).

Capable biocatalysts

SIR—In their recent review on asymmetric chemical synthesis[1], Brown and Davies commented that ". . . the methods of biotechnology are most suited to the production of natural molecules or closely related homochiral compounds and . . . by contrast potentially all homochiral compounds are accessible . . by chemical asymmetric synthesis". We believe this conclusion undermines the already demonstrated capabilities of biotransformations.

A few examples of the preparation of homochiral compounds by biotransformations that are either operating on the multitonne scale now, or are sufficiently highly developed processes awaiting commercial-scale operation, should set the record straight. All the processes described below produce compounds of high optical purity, greater than or equal to 95 per cent enantiomeric excess.

(1) (*S*)-Naproxen ((*S*)-6-methoxy-α-methyl-2-naphthaleneacetic acid) by esterase resolution of racemic Naproxen (International Bio-Synthetics, BV-IBIS).

(2) L-2-chloropropionic acid by halohydrolase treatment of the racemic chloro acid (ICI).

(3) (*R*)-(-)-2,2-dimethyl-1, 3-dioxolane-4-methanol by bio-enantioselective oxidation of the racemic compound (IBIS).

(4) (*R*)-Glycidyl butyrate by lipase resolution of the racemic ester (Genzyme).

(5) (*S*)-Atenolol ((*S*)-(-)-4-(2-hydroxy-3-isopropylaminopropoxy) - phenylacetamide) via enantioselective bio-epoxidation of the prochiral methyl-4-(2-propenyloxy)-phenylacetate (IBIS).

These selected examples, together with the increasing number of enantioselective biotransformations being discovered in an extremely broad range of organic chemical structural types, clearly show the versatility of asymmetric synthesis using enzymes or whole-cell systems. We believe that asymmetric synthesis using natural catalysts is a highly attractive proposition for the preparation of novel, optically pure organic compounds. Reviews and textbooks (refs 2–5, for example) are available to encourage organic chemists to measure the attributes of these methods against the use of man-made asymmetric catalysts and reagents.

R. J. PRYCE
Shell Research Ltd,
Sittingbourne, Kent ME9 8AG, UK
S. M. ROBERTS
Department of Chemistry,
University of Exeter, Devon EX4 4QD, UK

BROWN AND DAVIES REPLY—The needs of both the chemical and pharmaceutical industries for pure organic compounds with a high specificity of action will ensure rapidly expanding application of asymmetric synthesis over the next several years. In our article[1] we endeavoured to stress the approaches devised by synthetic organic chemists. We drew a distinction between the use of homochiral catalysts and reagents, as defined, and more classical approaches, including resolution of racemates and use of the 'chiral pool'. We touched on the alternative possibility of using the methods of biotechnology, acknowledging the 'spectacular selectivity' of enzymes. We stressed a potential advantage of the chemical approach in that the range of asymmetric transformations available through organic chemistry is far wider than the range available