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ASYMMETRICAL REDUCTION OF PERFLUOROALKYLATED KETONES, KETOESTERS AND VINYL COMPOUNDS WITH BAKER'S YEAST

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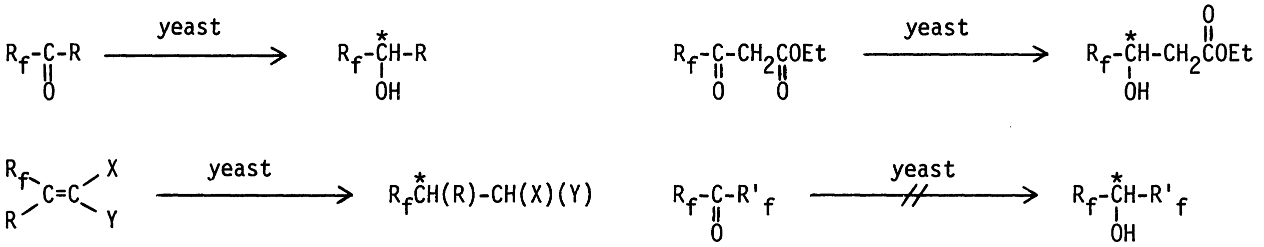
Reduction of perfluoroalkylated ketones, ketoesters and vinyl compounds with baker's yeast was studied. The ketones and β-ketoesters were asymmetrically reduced to give optically active perfluoroalkylated carbinols and hydroxyesters, while the vinyl compounds were reduced to perfluoroalkylated alkanes.

The importance of the biological transformation of halogen-containing organic compounds in life cycle has been recognized in recent years.1) As far as fluorine compounds are concerned, Tonomura and his co-workers have isolated an enzyme which is able to decompose a carbon-fluorine bond.2,3) From the synthetic point of view, however, none of biological research has been reported except a few approaches to transformation of monofluoroorganic compounds and to reduction of aryl trifluoromethyl ketones with baker's yeast.4-7)

The background above encouraged us to study the biological differentiation of various types of perfluoroalkylated organic compounds, especially those bearing long perfluoroalkyl chains and we now wish to report on the reduction of (perfluoroalkyl) alkyl ketones, β-(perfluoroalkyl)-β-ketoesters and (perfluoroalkyl)vinyl compounds with the baker's yeast.

Although the reactions were sluggish particularly in the case of compounds with long perfluoroalkyl chains, all of these types of compounds were asymmetrically reduced to give optically active alcohols and alkanes. The reactions were traced by ^{19}F NMR to check their ends. Bis(perfluoroalkyl) ketones, however, were strongly resistant to the action of the yeast, and none of carbinols were obtained.



$$R_f\text{-}\underset{\underset{O}{\|}}{C}\text{-}R \xrightarrow{\text{yeast}} R_f\text{-}\underset{\underset{OH}{|}}{\overset{*}{C}H}\text{-}R \qquad R_f\text{-}\underset{\underset{O}{\|}}{C}\text{-}CH_2\underset{\underset{O}{\|}}{C}OEt \xrightarrow{\text{yeast}} R_f\text{-}\underset{\underset{OH}{|}}{\overset{*}{C}H}\text{-}CH_2\overset{\overset{O}{\|}}{C}OEt$$

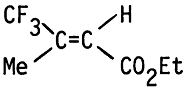
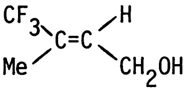
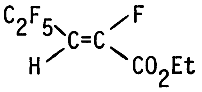
$$\begin{matrix}R_f & & X\\ & C{=}C & \\ R & & Y\end{matrix} \xrightarrow{\text{yeast}} R_f\overset{*}{C}H(R)\text{-}CH(X)(Y) \qquad R_f\text{-}\underset{\underset{O}{\|}}{C}\text{-}R'_f \xrightarrow{\text{yeast}}\!\!\!\!\!\!\!\!\!\!\!/\!/\;\;\;\;\; R_f\text{-}\underset{\underset{OH}{|}}{\overset{*}{C}H}\text{-}R'_f$$

Results shown in Table 1 indicate that methyl ketone or β-ketoester carrying a bulky perfluoroalkyl group such as C_7F_{15} are reduced by the yeast to give optically active carbinols. It is remarkable that even the carbon-carbon double bond of perfluoroalkylvinyl compounds is rather easily reduced to saturated alkanes. Optical purities of the products were determined by ^{19}F NMR after conversion of the carbinols to their diastereomeric esters by optically active perfluorocarboxylic acids, which have been developed by our group.8)

The present biological approach is considered to be the most convenient one-step process for preparing optically active perfluoroalkylated compounds, and it offers a possibility for biological transformation of polyfluoroorganic compounds to versatile substances.

In a typical procedure, ethyl trifluoroacetoacetate (5 g) was added to a suspension of baker's dry yeast (Oriental Yeast Co. Ltd., 50 g) and soluble starch (Wako's 1st grade, 75 g) in water (500 ml), and the mixture was stirred at room temperature. After 5 days of the fermentation with stirring, the mixture was subjected to centrifugal separation, and an oily material was extracted with diethyl ether. The ethereal extract was dried over magnesium sulfate, and then the solvent was removed. Distillation gave the corresponding alcohol in a 92% yield, bp 88 - 90 ^{o}C/21 mmHg.

Table 1 Reduction with Yeast

Substrate	Reaction Time (day)	Product[a]	B.p. (^{o}C/mmHg)	$[\alpha]^{25}_{D}$ (neat; l=1)	Optical Purity (%)	Yield (%)
$n\text{-}C_3F_7C(O)Me$	10	$n\text{-}C_3F_7\overset{*}{C}H(OH)Me$	101-103	-18.30	87	68
$n\text{-}C_7F_{15}C(O)Me$	14	$n\text{-}C_7F_{15}\overset{*}{C}H(OH)Me$	90-91/25	-17.59	91	74
$n\text{-}C_4F_9C(O)CF_3$	-	———	———	———	—	0
$n\text{-}C_8F_{17}C(O)CF_3$	-	———	———	———	—	0
$CF_3C(O)CH_2CO_2Et$	5	$CF_3\overset{*}{C}H(OH)CH_2CO_2Et$	88-90/21	+11.68	96	92
$n\text{-}C_7F_{15}C(O)CH_2CO_2Et$	7	$n\text{-}C_7F_{15}\overset{*}{C}H(OH)CH_2CO_2Et$	121-123/2	+14.86	93	87
	7	$CF_3\overset{*}{C}H(Me)CH_2CO_2Et$	143-145	+10.61	76	68
	7	$CF_3\overset{*}{C}H(Me)CH_2CH_2OH$	83-85/15	+15.13	67	61
	7	$C_2F_5CH_2\overset{*}{C}HFCO_2Et$	91-93/26	-16.52	78	72

a) Each structure was determined by means of IR, NMR and Mass spectral data.

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