Hydroxylation of Diamantan-1- and -4-ol with the Fungus *Rhizopus nigricans*

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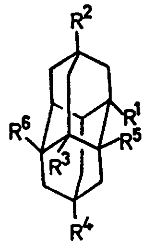
Summary Diamantan-1- and -4-ols are hydroxylated by *Rhizopus nigricans* in a highly regioselective manner, yielding diols which are mostly inaccessible by presently available chemical methods.

The 1-position of diamantane is favoured over the 4-position in kinetically controlled ionic substitution reactions,[1] but 4-substituted derivatives have lower enthalpies than their 1-substituted counterparts and separable mixtures of the two can be obtained readily through the application of thermodynamic control.[2] The regioselective introduction of two bridgehead substituents into diamantane poses considerably greater synthetic problems since there are several arrangements possible for a disubstituted derivative. The possibility of being able to introduce functional groups by the use of micro-organisms seemed to us an attractive alternative to chemical methods.

Incubation[3] of diamantan-1-ol (**1**) (1 g) with *Rhizopus nigricans* for 2 days yielded diamantane-1,7-diol (**3**) (0·93 g), m.p. 334—336°, of *ca.* 97% isomeric purity.† Diamantan-4-ol (**2**) (1 g) and *Rhizopus nigricans* produced a 5:1 mixture (0·75 g) of diamantane-1,9-diol (**4**), m.p. 264—266°, and diamantane-4,9-diol (**5**), m.p. 290—292°, which were separable on alumina. Of the six possible tertiary diamantanediols, (**3**)—(**8**), isomers (**5**),[2b] (**6**), and (**7**) were already in hand, the latter two from hydrolysis of the corresponding dibromides.[1b] The structures of the two new diols were assigned on the evidence that the isomer produced on hydroxylation of diamantan-1-ol (**1**) did not display intramolecular hydrogen bonding, thereby eliminating the 1,2-isomer (**8**), and direct comparison (m.p.s. and g.l.c. analysis) eliminated isomers (**6**) and (**7**), which left the 1,7-isomer (**3**). The preponderant product of hydroxylation of the apical alcohol (**2**) was also different from the 1,4-isomer (**6**); therefore it must be the 1,9-isomer (**4**).



	R¹	R²	R³	R⁴	R⁵	R⁶
(**1**)	OH	H	H	H	H	H
(**2**)	H	OH	H	H	H	H
(**3**)	OH	H	OH	H	H	H
(**4**)	OH	OH	H	H	H	H
(**5**)	H	OH	H	OH	H	H
(**6**)	H	OH	H	H	OH	H
(**7**)	OH	H	H	H	H	OH
(**8**)	OH	H	H	H	OH	H

These assignments were substantiated by the close agreement between the measured n.m.r. chemical shifts of the dichlorides, prepared from the individual diols and hydrochloric acid, and those calculated for 1,7- and 1,9-dichlorodiamantane using shift additivities[4] derived from the spectra of the monochlorodiamantanes.[2b]

Clearly *Rhizopus nigricans* is a most effective reagent in diamantane methodology in respect of both its efficiency

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† Measured by g.l.c. analysis of the corresponding dichloride using a 20 m capillary Carbowax 20 M column.

and selectivity of hydroxylation. Ionic bromination[1b] and chlorination,[2a] the only published chemical procedures for introducing more than one bridgehead substituent into diamantane, reveal the importance of inductive effects, and their limitations, inasmuch as the second substituent is preferentially introduced at positions as far removed as possible from the first substituent. It is of particular interest therefore that the substitution patterns produced by *Rhizopus nigricans* are largely those presently inaccessible by chemical methods.

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[1] (a) T. M. Gund, M. Nomura, V. Z. Williams, jun., P. von R. Schleyer, and C. Hoogzand, *Tetrahedron Letters*, **1970**, **4875**; (b) T. M. Gund, P. von R. Schleyer, and C. Hoogzand, *ibid.*, **1971**, **1583**.

[2] (a) D. Faulkner, R. A. Glendinning, D. E. Johnston, and M. A. McKervey, *Tetrahedron Letters*, **1971**, **1671**; (b) T. Courtney, D. E. Johnston, M. A. McKervey, and J. J. Rooney, *J.C.S. Perkin I*, **1972**, **2691**.

[3] The incubation conditions were similar to those described by J. W. Blunt, I. M. Clark, J. M. Evans, E. R. H. Jones, G. D. Meakins, and J. T. Pinhey, *J. Chem. Soc.* (*C*), **1971**, **1136**.

[4] See R. C. Fort, jun., and P. von R. Schleyer, *J. Org. Chem.*, **1965**, **30**, 789; F. W. van Dursen and P. K. Korver, *Tetrahedron Letters*, **1967**, **3923**; F. W. van Dursen and A. C. Udding, *Rec. Trav. chim.*, **1968**, **87**, **1243**.