

Enantioselective Reduction of Ketones in Optically Active Host Compounds with a BH_3 -Ethylenediamine Complex in the Solid State

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Treatment in the solid state of inclusion compounds of ketones in optically active host molecules with a BH_3 -ethylenediamine complex gave optically active alcohols.

Some solid-solid reactions of substrate and reagent, such as Baeyer-Villiger oxidation,¹ NaBH_4 reduction,² and pinacol rearrangement,³ have been reported. However, an enantioselective solid-solid reaction has not been reported. Recently, we found that enantioselective reduction of ketones to alcohols can easily be achieved in the solid state.

Enantioselective reduction of ketones to alcohols has received much attention over the years.⁴ However, until now all reactions were carried out in solution. We now report an enantioselective solid-solid reaction of ketones in inclusion compounds with chiral hosts and a BH_3 -ethylenediamine complex which give optically active alcohols.

The host-guest inclusion compounds (**10**) and (**11**) of ketones (**1**), (**3**), and (**5**) with (*R,R*)-(-)-1,6-di(*o*-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol (**7**)⁵ and (*R,R*)-(-)-*trans*-2,3-bis(hydroxydiphenylmethyl)-1,4-dioxaspiro-

[4.4]nonane (**8**),⁵ respectively, were prepared according to a reported procedure.⁵ Melting points of (**10**) and (**11**) are shown in Tables 1 and 2, respectively. In all inclusion compounds, the host : guest ratio is 1 : 1 except in the case of a 1 : 2 ratio for the complex of (**7**) and (**1a**).

Solid-solid reaction of (**10**) and (**11**) with (**9**) was carried out by the following method. A mixture of finely powdered (**10**) or (**11**) and (**9**) was kept under N_2 at room temperature for 24 h by occasional stirring. The reaction mixture was decomposed with water and extracted with ether. The ether solution was washed with dilute HCl, dried, and evaporated to give crude alcohols. Distillation of the crude alcohols *in vacuo* gave pure alcohols in the yields shown in Tables 1 and 2. Optical purity and absolute configuration of the alcohols were determined by comparison of the $[\alpha]_D$ values and their signs with those reported (see footnotes of Tables 1 and 2).

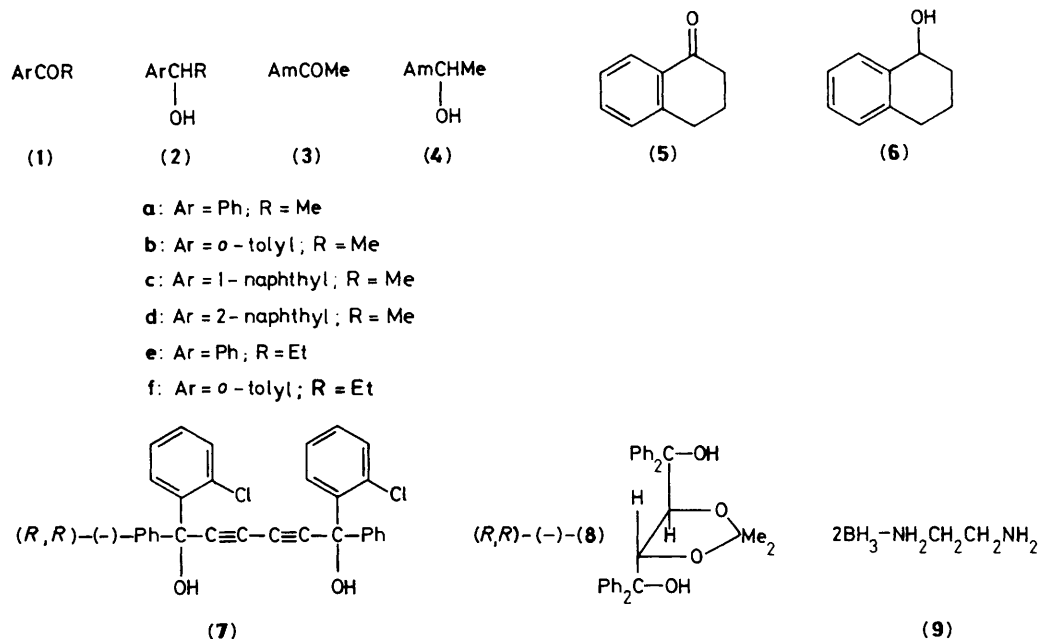


Table 1. Melting point of (10), and yield, optical purity, and absolute configuration of the alcohol obtained by solid-solid reaction of (10) with (9).^a

Ketone in (10)	M.p. of (10)/°C	Alcohol		
			Yield/%	Optical purity ^b / enantiomeric excess
(1a)	107—109	(<i>R</i>)-(+)-(2a)	96	44
(1b)	104	(<i>R</i>)-(+)-(2b)	57	59
(1c)	94—95	(<i>R</i>)-(+)-(2c)	20	22
(1d)	90—91	(<i>R</i>)-(+)-(2d)	29	5
(1e)	111—112	(<i>R</i>)-(+)-(2e)	55	42
(1f)	100—102	(<i>R</i>)-(+)-(2f)	64	42
(3)	88—91	(±)-(4)	60	0
(5)	104—105	(<i>R</i>)-(-)-(6)	34	6

^a Reactions were carried out in a 1:1.5 molar ratio of (10) and (9) except in the case of (10) of the ketones (1c), (1d), and (1e) [a 1:3 ratio of (10) and (9)]. ^b Optical purity and absolute configuration of (2a),⁶ (2b),⁷ (2c),⁸ (2d),⁹ (2e),¹⁰ (2f),⁷ and (6)¹¹ were determined by comparison of their data with those reported.

Table 2. Melting point of (11), and yield, optical purity, and absolute configuration of the alcohol obtained by solid-solid reaction of (11) with (9).^a

Ketone in (11)	M.p. of (11)/°C	Alcohol		
			Yield/%	Optical purity ^b / enantiomeric excess
(1a)	78—80	(<i>R</i>)-(+)-(2a)	26	1
(1c)	75—77	(<i>R</i>)-(+)-(2c)	32	22
(1e)	80—85	(<i>R</i>)-(+)-(2e)	46	5
(5)	93—97	(<i>R</i>)-(-)-(6)	32	34

^a Reactions were carried out in a 1:1.5 ratio of (10) and (9). ^b Optical purity and absolute configuration of (2a),⁶ (2c),⁸ (2e),¹⁰ and (6)¹¹ were determined by comparison of their data with those reported.

It is interesting that enantioselective reductions were achieved by the solid-solid reaction, although enantioselectivities were not very high. In the case of the dialkyl ketone (3), however, no enantiocontrol was observed. In all cases of the enantioselective reactions, (*R*)-alcohols were produced. With the inclusion compounds of ketones and host compounds of (*R*)-configuration, (9) would attack the ketones from the direction which gives (*R*)-alcohols selectively. This will be clarified by *X*-ray structural studies of (10) and (11) in the near future. Furthermore, since host compounds of (*S*)-configuration are also easily available,⁵ one can control the reduction pathway in order to produce (*S*)-alcohols.

It is very clear that the enantioselective reduction described above is a real solid state reaction rather than one involving prior dissociation of the complex to yield free borane, since treatment of the inclusion compounds with gaseous borane B₂H₆ at room temperature for 12 h recovered the inclusion compounds unchanged.

Received, 25th January 1989; Com. 9/00420C

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