Asymmetric Ring Transformation of *meso*-7-Substituted Bicyclo[3.3.0]octanones into Chiral Bicyclo[3.2.1]octene Derivatives

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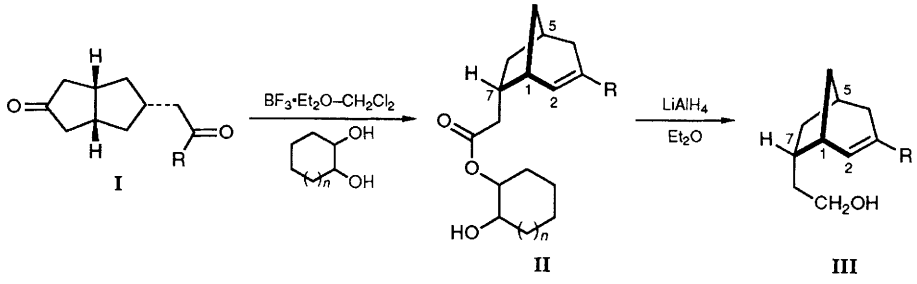
Asymmetric ring transformation of *meso*-7-(2-oxoalkyl)bicyclo[3.3.0]octan-3-ones into chiral bicyclo[3.2.1]oct-2-ene derivatives is accomplished by treatment with chiral cyclic (six- or seven-membered ring) 1,2-diols–BF_3–Et_2O.

Generally, the conversion of *meso*-compounds into chiral compounds seems to be difficult, although this conversion can rarely be accomplished by an enzymatic[1] or chemical[2] procedure. In this communication, we describe the asymmetric ring transformation from *meso*-substrates into chiral compounds, by a method based on the drastic ring transformation reaction developed by our group.[3–5]

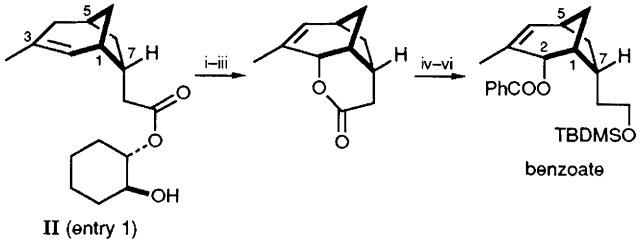
meso-Substrates, 7-substituted bicyclo[3.3.0]octanones **I**[5] can be prepared by the conventional method from bicyclo[3.3.0]octane-3,7-dione. Treatment of *meso*-substrates (1 equiv.) with BF_3–Et_2O (3–5 equiv.) and chiral (*R*,*R* or *S*,*S*)-cyclic-1,2-diols[6] (2 equiv.) in CH_2Cl_2 at room temperature for 12–24 h afforded the ring transformation products,[5] in fair to good yields, as an inseparable mixture† of diastereoisomers (Table 1). As shown in Table 1, in all cases, the ring transformation reaction proceeded in a diastereoselective manner, *i.e.* the substrate with R = Me (entries 1 and 2) was transformed by (*S*,*S*)-cyclohexane-1,2-diol or (*R*,*R*)-cycloheptane-1,2-diol into the corresponding bicyclo[3.2.1]octene derivatives with 26% diastereoisomeric excess (d.e.) or 27% d.e., respectively. Similarly the substrate with R = Bu^n (entries 3 and 4) was converted into the ring transformation product with 44% d.e. or 36% d.e. In the cases where R = cyclohexyl (entries 5 and 6) and R = Ph (entries 7 and 8), the diastereoselectivity was remarkably improved to afford products with 81–93% d.e. The best result (93% d.e.) (entry 7) was obtained in 63% yield by a combination of substrate (R = Ph) and (*S*,*S*)-cyclohexane-1,2-diol. In conclusion, this asymmetric ring transformation seems to be remarkably affected by the bulkiness of substituent (R). There is no precedent for the diastereoselective conversion from *meso*-compounds into chiral compounds, on the basis of drastic ring transformation. The absolute configuration of the ring transformation product **II** in entry 1 was determined from

† The d.e. of the products in entries 1–6 was estimated directly from the ^{13}C NMR spectra, the products in entries 7 and 8 were determined by ^{13}C NMR spectra after conversion into (+)-MTPA ester of the alcohol obtained by $LiAlH_4$ reduction. [MTPA = α-methoxy-α-(trifluoromethyl)phenylacetic acid].

Table 1 Ring transformation of *meso*-7-substituted bicyclo[3.3.0]octanones into chiral bicyclo[3.2.1]octene derivatives



Entry	R	Diol (*n*)	Yield (%)	D.e. (%)	Abs. config **II**	$[\alpha]^{25}_{D}$ ($CHCl_3$) of **III**
1	Me	*S*,*S* (1)	66	26	1*R*,5*R*,7*R*	−29.3
2	Me	*R*,*R* (2)	70	27	1*S*,5*S*,7*S*	+42.1
3	Bu^n	*S*,*S* (1)	52	44	1*R*,5*R*,7*R*	−33.8
4	Bu^n	*R*,*R* (2)	66	36	1*S*,5*S*,7*S*	+33.3
5	Cyclohexyl	*S*,*S* (1)	71	81	1*R*,5*R*,7*R*	−54.7
6	Cyclohexyl	*R*,*R* (2)	65	81	1*S*,5*S*,7*S*	+54.4
7	Ph	*S*,*S* (1)	61	93	1*R*,5*R*,7*R*	−54.4
8	Ph	*R*,*R* (2)	60	83	1*S*,5*S*,7*S*	+47.7



Scheme 1 *Reagents*: i, 5% aq. KOH; ii, PhSeCl; iii *m*-chloroperbenzoic acid (*m*CPBA); iv, $LiAlH_4$; v, *tert*-butyldimethylsilyl chloride (TBDMSCl)–pyridine (Py); vi, PhCOCl–Py

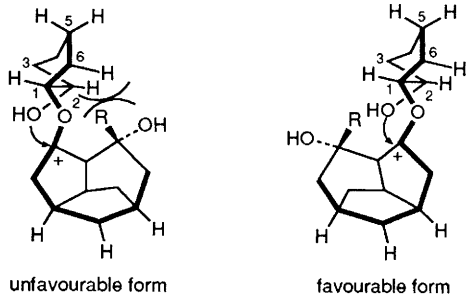


Fig. 1

the circular dichroism spectrum of the benzoate‡ derived from **II** by a sequence of reactions (Scheme 1). Its negative Cotton effect [$\Delta\varepsilon = -1.25$ (231 nm)] indicated that the absolute configuration of the benzoate is 1*R*,2*S*,5*R*,7*R*,[7] *i.e.* the absolute configuration of **II** (entry 1) could be concluded to be 1*R*,5*R*,7*R*. The absolute configuration of the other products was determined on the basis of the preliminary finding that, in the ^{13}C NMR spectrum of **II** (entry 1), the chemical shift of C-1 with the *R* configuration appeared at a lower field than that of the *S* configuration. The stereochemical course of this asymmetric induction is assumed to be as follows. This ring transformation seems to proceed *via* three steps; (*i*) intramolecular aldol condensation; (*ii*) acetalization; (*iii*) Grob fragmentation.[5] Acetalization of intermediary enantiomeric aldols by chiral cyclic diol is considered to be a kinetic resolution process (Fig. 1), in which one enantiomer yields preferentially the acetal having the desirable orientation to cause the Grob fragmentation.

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‡ The benzoate was prepared as follows. By conventional base-catalysed hydrolysis, selenolactonization using PhSeCl followed by oxidation with *m*CPBA[8] and reduction with $LiAlH_4$, product in entry 1 was converted into the diol. The benzoate was obtained from the diol *via* the protection of primary alcohol with TBDMSCl and subsequent benzoylation of the secondary alcohol.

References

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