CHEMISTRY LETTERS, pp. 1865-1868, 1991.

Regiochemistry of Boron Trifluoride Mediated Hydrolysis of Glycidyl Benzoates

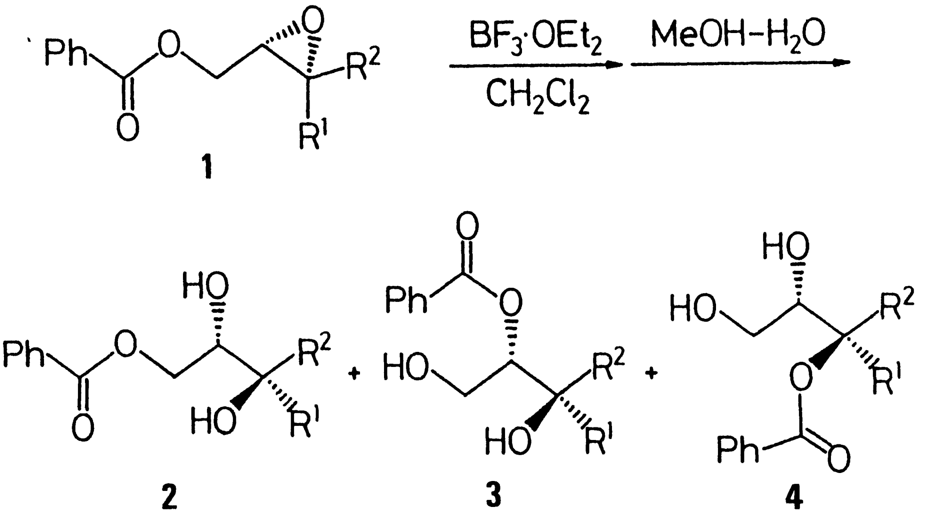
Makoto YOSHITAKE,† Hiroyuki KOBAYASHI, Makoto YAMAMOTO,*
Shigeo KOHMOTO, and Kazutoshi YAMADA
Department of Materials Science, Faculty of Engineering,
Chiba University, Chiba 260
† Graduate School of Science and Technology, Chiba University, Chiba 260

Hydrolysis of glycidyl benzoates in the presence of $BF_3 \cdot OEt_2$ in CH_2Cl_2 affords regioisomeric triol mono benzoates, their ratios remarkably change depending on the temperature particularly in the reaction of 3,3-dimethylglycidyl benzoate.

Acyloxy group transfer in acid catalyzed hydrolysis of glycidyl esters is well-known and the intervention of cyclic acyloxonium ions is proposed via neighboring carbonyl group participation in epoxide ring cleavage.[1,2] However, such reactions were limited to those of structurally restricted cyclic or a few acyclic substrates, and the studies on regiochemistry of acyclic systems have not been explored in detail.[2] We present herein the first example of the temperature dependent regiochemical control of acyloxy group transfer in the $BF_3 \cdot OEt_2$ mediated hydrolysis of acyclic glycidyl esters.

Among various glycidyl esters, Lewis acids ($BF_3 \cdot OEt_2$, $TiCl_4$, $(i\text{-}PrO)_4Ti$, and $EtAlCl_2$),[3] and solvents examined (CH_2Cl_2, Et_2O, and MeCN), the reactions of glycidyl benzoates in the presence of $BF_3 \cdot OEt_2$ in CH_2Cl_2 provided the most successful results. Other esters (acetates, propionates, and phenylacetates) resulted in lower yields and selectivities than the corresponding benzoates.

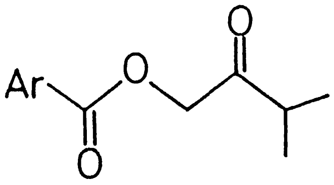
After a treatment of glycidyl benzoate **1** with $BF_3 \cdot OEt_2$ (1 equiv.<) in CH_2Cl_2, the resulting mixture was stirred in various sequence of reaction temperature. By slowly adding aqueous MeOH at the final reaction temperature, the regioisomeric mixture of hydrolyzed products was obtained. Although unsubstituted glycidyl benzoate ($R^1 = R^2 = H$) was unreactive in this condition, the reactions of **1a**, **b**, and **c** gave triol mono benzoates in good yields. The regioisomers were assigned by ^1H NMR[4] and inversion of stereochemistry of the epoxides was comfirmed by the delivation to known acetonide alcohols.[5)] The products ratios varied depending on the reaction conditions. Particularly remarkable change of selectivity was observed in the reaction of **1a**.



	R^1	R^2	Condition$^{a)}$ Temp/℃ (Time/min)	Yield/%	Ratio$^{b)}$ **2**	:	**3**	:	**4**
a	Me	Me	-78(30)	98	87	:	-	:	13
a	Me	Me	-78(30)→ 0(60)	95	12	:	86	:	2
a	Me	Me	-78(30)→ 0(60)→ -78(30)	89	14	:	85	:	3
b	Me	H	-78(30)	73(85)$^{c)}$	22	:	62	:	16
b	Me	H	-78(30)→ 0(60)	93	8	:	56	:	36
b	Me	H	-78(30)→ 0(60)→ -78(30)	86	6	:	57	:	37
c	H	Me	-78(30)	76(86)$^{c)}$	34	:	59	:	7
c	H	Me	-78(30)→ 0(60)	84	24	:	58	:	18
c	H	Me	-78(30)→ 0(60)→ -78(30)	81	22	:	58	:	20

a) Two equimolar amounts of $BF_3 \cdot OEt_2$ was used. b) Product ratios determined by ^{1}H NMR spectroscopy. c) Conversion yield.

A conventional acid catalyzed hydrolysis of **1a** in aqueous media ($HClO_4$ / H_2O / MeCN) gave **2a** along with a small amount of **1a**. The reaction of 3,5-dinitrobenzoate exclusively afforded a rearrangement product **5**. These results suggest that the $BF_3 \cdot OEt_2$ promoted hydrolysis of **1** proceeds via cyclic acyloxonium ion intermediates.

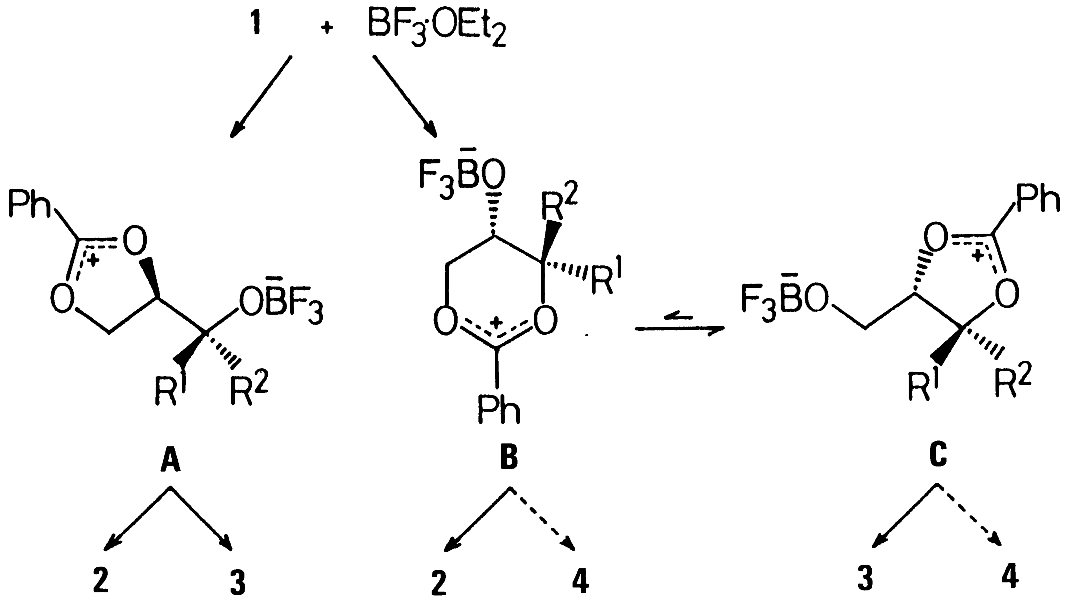


Ar = 3,5-dinitrophenyl

5

The perfect inversion of stereochemistry at epoxy carbons indicates that hemi-orthoesters are formed as intermediates by hydration of the cyclic acyloxonium ions.[6)]

The dramatic change of regiochemistry in the reaction of **1 a** depending on the temperature could be well explained to be attributed to the interconversion between two possible cyclic acyloxonium ion intermediates. In this case, the six-membered ring intermediate **B** is initially formed via a specific bond cleavage of the epoxide between the more substituted carbon and the oxygen atoms. Since this intermediate is stable under the non-equilibrium condition at -78 ℃, the aqueous quench at this temperature affords **2 a** and **4 a**. At 0 ℃, the interconversion among the cyclic acyloxonium ions could give rise to the thermodynamically favored distribution biased to more stable five-membered ring intermediate **C** which was directly trapped with allyltributylstannane to give the allylated dioxolane.[7,8)] Then **3 a** is selectively formed[9)] and its ratio does not change after re-cooling of the reaction mixture. On the contrary, the reactions of symmetrically substituted epoxides **1 b** and **c**, in which the lower regioselectivities and poor temperature dependence of them were observed, could cause competitive directions to **A** and **B** at the initial stage.[9)]



Our present observation suggests an unknown interconversion among cyclic acyloxonium ion intermediates derived from glycidyl benzoates and $BF_3 \cdot OEt_2$. Aqueous quenching of them under kinetically or thermodynamically controlled condition allows the regioselective formation of triol mono esters. Attempts on versatile nucleophilic trapping of these cyclic acyloxonium ion intermediates are in progress.[8)]

References

1) "Selective Organic Transformations," ed by B.S.Thyagarajan, John Wiley & Sons, INC, New York (1972).

2) W.R.Roush, R.J.Brown, and M.DiMare, J.Org.Chem., 48, 5083 (1983).

3) Utilization of metal chloride such as $TiCl_4$, $SnCl_4$, and $EtAlCl_2$ caused side-reaction to form chlorohydrins. Titanium tetraisopropoxide was ineffective to the present hydrolysis reactions.

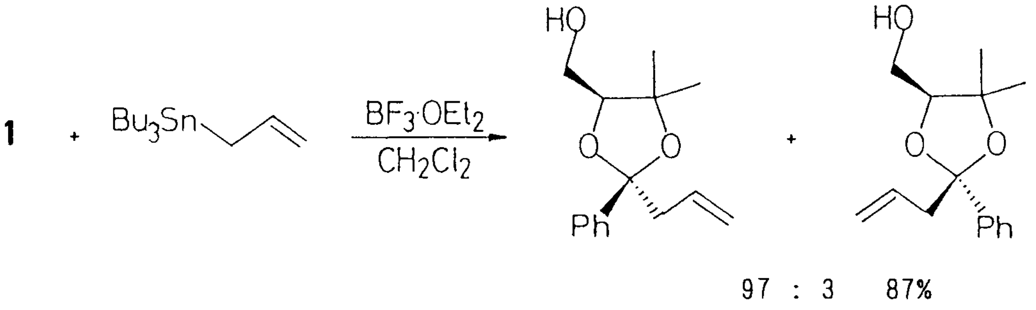
4) Greater downfield shifts of benzoyloxy substituted methylene or methine protons substantiated the assignment of regiochemistry. Derivation to known acetonide alcohols also supported the regiochemistry. see: Ref.5.

5) R.Dumont and H.Pfander, Helv.Chim.Acta, 66, 814 (1983).

6) Formations of hemi-orthoesters as intermediates by hydration of acyloxonium ions have been well studied, see: "Stereoelectronic Effects in Organic Chemistry," ed by P.Deslongchamps, Pergamon Press, Oxford (1983).

7) Since acyloxonium ions favor to be planar, the six-membered rig structure is less stable than the alternative five-membered one; see: H.Paulsen, Pure Appl.Chem., 49, 69 (1975); H.Paulsen and R.Dammeyer, Chem.Ber., 109, 1837 (1976).

8) The reaction of **1a** with allyltributylstannane at 0 ℃ exclusively gave 2-allyl-4-(hydroxymethyl)-2-phenyl-1,3-dioxolane in high stereoselectivity. This suggests the intervention of intermediate **C** but not **A**. Details of the results will be reported elsewhere.



9) The regioselective bezoyloxy group transfer is accomplished by the selective cleavage of C-O bond in the hemi-orthoester. The fact that simple cyclic or acyclic hemi-orthoester afforded a mixture of regioisomers (see Ref.6) strongly suggests the contribution of the hydroxy group outside the ring to the regiochemistry. However, it is difficult to explain the complicated results of reactions of **1b** and **c**.

(Received July 5, 1991)