H.; Park, Y. C.; Yun, M.; Kim, S. *Tetrahedron Lett.* **1994**, *35*, 129. (c) Lee, E.; Park, C. M. *J. Chem. Soc. Chem. Comm.* **1994**, 293.
6. Lee, E.; Kang, T. S.; Joo, B. J.; Tae, J. S..; Li, K. S.; Chung, C. K. *Tetrahedron Lett.* **1995**, *36*, 417.
7. Hanessian, S.; Sahoo, S. P. *Tetrahedron Lett.* **1984**, *25*, 1425.
8. The *cis* isomer **7** was assigned as the major product following the results of the closely related studies reported in the reference 6. The assignment was confirmed by the synthesis of the final products **1** and **2**.
9. Formation of **13** probably involves intramolecular hydrogen abstraction of the intermediate primary radical.
10. They were identified by comparing with the known physical and spectroscopic data from the literature.

Selective Conversion of 4,5-Epoxypentanoic Acids Esters to the Corresponding γ-Ketoesters Using Tetrabutylammonium Dihydrogentrifluoride

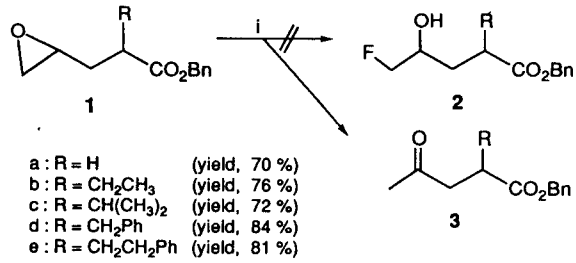
Soo-Suk Lee and Dong H. Kim*

Center for Biofunctional Molecules and Department of Chemistry, Pohang University of Science and Technology, San 31 Hyojadong Pohang 790-784, Korea

Received October 11, 1995

Oxiranes constitute an important class of compounds to synthetic chemistry:[1] They are easily prepared and very reactive. Furthermore, they bear very versatile chemical reactivity. Thus, a large variety of carbon[1c,d] as well as oxygen,[1a] sulfur,[1a] nitrogen[1c] and halogen[1f] nucleophiles can cleave oxirane rings, generating a diverse nature of functionalities. This unusual chemical property of epoxides has made oxiranes as one of the most frequently used intermediates for organic synthesis.

Recently, Landini and his associates reported that tetrabutylammonium dihydrogentrifluoride is a readily available, convenient, and highly efficient catalyst for the regioselective hydrofluorination of many epoxides to afford fluorohydrins when used in conjunction with a molar excess of potassium hydrogen difluoride under solid-liquid phase transfer conditions.[2] The fluorohydrins thus obtained are thought to be of considerable importance as versatile intermediates for the preparation of diverse fluorine-containing compounds of medicinal interest. In connection with other project, we were interested in obtaining fluoromethyl ketones and we thought that these compounds may be prepared by simple oxidation of fluorohydrins which are obtainable from appropriate epoxides using the reagent of Landini.[2] However, when we carried out the reaction with benzyl ester of 2-benzyl-4,5-epoxypentanoic acid under the conditions of Landini, hoping to obtain the ester of 2-benzyl-5-fluoro-4-hydroxypentanoic acid, there was obtained an unexpected product of a methyl ketone instead. We wish to report preliminary results of this regioselective isomerization reaction of epoxyesters to the corresponding methyl ketoesters under unusual conditions.



(i) $Bu_4N^+H_2F_3^-$ (0.1 equiv.), KHF_2 (2 equiv.), 120 °C, 5 h

Scheme 1.

The 4,5-epoxyesters were readily prepared by epoxidating the corresponding olefines with *m*-chloroperbenzoic acid. The epoxides thus obtained were treated with the hydrofluorinating agent[3] as described by Landini *et al.*[2] Thus, a heterogeneous mixture of epoxide **1**, catalytic amount of tetrabutylammonium dihydrogentrifluoride and an excess of potassium hydrogen difluoride was heated at 120 ℃ until the epoxide is no longer detectable by TLC. It took about 5 h. The reaction mixture was then dissolved in methylene chloride and the solution was filtered on celite. The crude product obtained by concentration of the filtrate was purified by column chromatography, giving the corresponding γ-ketoester[4] in satisfactory yield (Scheme 1).[5] Structural assignments for the products was supported by the spectral data: two carbonyl absorption bands (e.g., 1717 and 1731 cm^{-1} for **3d**) in their IR spectra and a characteristic singlet magnetic resonance signal for methyl protons in the region of δ 2.0-2.1 ppm in the NMR spectra. The mass spectral data and results of microelemental analyses were in agreement with the structures.

It is worthy noting that the present regioselective isomerization of the 4,5-epoxyesters to γ-ketoesters is contrary to the result of Landini *et al.* In fact, when we first observed the formation of the ketoester **3d** from the reaction of **1d**, dismayed by the unexpected result we repeated the experiments of Landini *et al.*[2] Their results were reproduced. These are first examples which demonstrate that the reagent of Landini does not necessarily transform oxiranes to the corresponding fluorohydrins, but to cause isomerization of the oxiranes to the ketoesters in cases of 4,5-epoxyesters. Although the reason for the alternate reaction path in case of epoxyesters is not apparent presently to us and remains to be clarified, the present observation is important in view of the fact that the method of Landini has been known as an unique route to fluorohydrins which are valuable intermediates for the preparation of compounds having pharmacological interests. An additional work to this end and for finding the limitation of the regioselective isomerization is in progress.

Most of ring opening as well as isomerization reactions of monosubstituted epoxides are known to suffer from a lack of regioselectivity.[6] In this regard, the present protocol for the conversion of the epoxide in the epoxyesters to the corresponding methyl ketones may itself have a synthetic value

for the preparation of γ-ketoesters as an alternative to the method of Wacker oxidation,[7] since this new isomerization reaction of epoxides to methyl ketones is highly regioselective[4] and simple in experimental procedure.[8]

Acknowledgment. We thank the Korea Science and Engineering Foundations for the financial support of this work.

References

1. (a) Rossiter, B. E. In *Asymmetric Synthesis*; Morrision, J. D. Ed.; Academic Press: New York, 1985, vol. 5, chapter 7. (b) Hanson, R. M. *Chem. Rev.* **1991**, *91*, 437. (c) Rama Rao, A. V.; Chakraborty, T. K.; Purandara, A. V. *Tetrahedron Lett.* **1990**, *31*, 1443. (d) Skrydstrup, T.; Benechie, M.; Kuong-Huu, F. *Tetrahedron Lett.* **1990**, *31*, 7145. (e) Mitsunobu, O. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991, vol. 6, p 4-9. (f) Bonini, C.; Righi, G. *Synthesis* **1994**, 225.
2. (a) Landini, D.; Penso, M. *Tetrahedron Lett.* **1990**, *31*, 7209. (b) Landini, D.; Albanese, D.; Penso, M. *Tetrahedron* **1992**, *48*, 4163. (c) Lundt, I.; Albanese, D.; Landini, D.; Penso, M. *Tetrahedron* **1993**, *49*, 7295.
3. Landini, D.; Molinari, H.; Penso, M.; Rampoldi, A. Synthesis, **1988**, 953.
4. No aldehydes isomeric to the isolated methyl ketones was detected in the crude reaction products by ^{1}H NMR spectroscopy.
5. Transformations of epoxides catalyzed by transition metal and palladium complexes are known; Kulasegaram, S.; Kulawiec, R. J. *J. Org. Chem.* **1994**, *59*, 7195 and references cited therein.
6. Lewars, E. G. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R.; Rees, C. W., Ed.; Pergamon: Oxford, 1984, vol. 7, chapter 5.05.
7. Tsuji, J. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, 1991, vol. 7, chapter 3.4, p 449-468.
8. The presence of potassium hydrogen difluoride (KHF_2) is essential for the isomerization. When the reaction was carried out in the absence of KHF_2, no reaction occured.

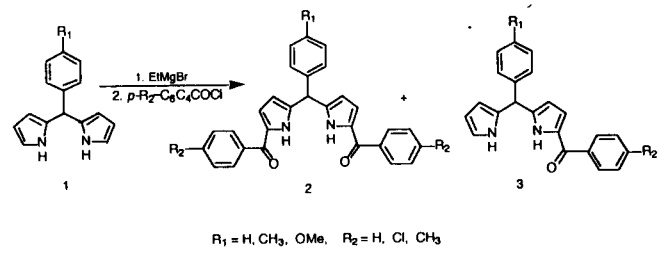
Synthesis of Partially Deuterated Porphyrins

Chang-Hee Lee* and Jin-Young Kim

**Department of Chemistry, Kangwon National University, Chun-Cheon 200-701, Korea*

Received October 30, 1995

The convenience of functionalization and the wealth of available meso-substituents make the meso-porphyrins ideally suited for use in various model systems.[1,2] Although porphyrin is easily obtainable in a facile manner from pyrroles and aldehydes, generic methods are still limited to symmetric porphyrins because of the isomeric porphyrin formation and consequent difficulties in separation and identification. A major limitation in the synthesis of isotopically labeled porphyrins is the construction of building subunits affording porphyrins by condensation. Thus methods for the synthesis of those subunit still leave much to be desired at least in creating sophisticated models of porphyrin-based enzymes. The existing synthetic routes are mainly the condensation of an aldehyde with pyrrole or pyrromethanes.[3,4] In the case of the porphyrins bearing two different types of meso-substituents, the synthesis can be achieved by a binary mixed aldehyde condensation and separation of mixture resulting from the condensation.[6]



Scheme 1.

A synthesis of porphyrins bearing deuterium specifically at β-pyrrolic position has not investigated well. Major difficulties in the synthesis are the problems associated with construction of the dipyrromethane components with partial deuteration. The great potentials of deuterated porphyrins in various model system led us to pursue an efficient synthesis of partially deuterated porphyrins.[7] Spectroscopic studies of porphyrins usually require deuterated porphyrins.[8] Simple meso-tetraarylporphyrins with β-pyrrolic deuteration are readily available from the condensation of aldehydes and pyrrole-d_5. But this method is not applicable to porphyrins with partial deuteration at β-pyrrolic position. Our current studies, we report an efficient synthesis of partially deuterated porphyrins by 2+2 condensation.

As shown in Scheme 1, the success of the synthesis solely relys on the facile construction of dipyrromethanes **1** and their acylation to 1,9-substituted dipyrromethanes **2**. Pyrrole generally undergoes electrophilic aromatic substitution easily, but α,α′-functionalization with acyl units cannot be achieved in a direct manner. But an α-substituted pyrrole can be acylated at the α′-position as long as the α-substituent is not electron-withdrawing. We recently reported one-flask synthesis of 1,9-unsubstituted, meso-substituted dipyrromethanes. The BF_3 or trifluoroacetic acid-catalyzed condensation of an aldehyde dissolved in 40 times excess pyrrole affords the meso-substituted dipyrromethanes in high yields depending on the nature of aldehydes. The selective introduction of acyl group at 1,9-position of dipyrromethanes was possible by utilizing ethyl magnesium bromide and acid chlorides.[9,10] Meso-aryldipyrromethanes **2** were treated with 2.2 equivalent of ethyl magnesium bromide in THF at room temperature and resulting dipyrromethane-Grignard reagent was treated with 1.4 equivalent of appropriate acyl chlorides. The reaction gave a mixture of the mono-acylated **3** in 21-34% and bis-acylated **2** in 18-48% after chromatographic separation. Another key step in this synthesis is the regioselective pro-