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Communication

An Efficient Conversion of Carboxylic Acids to One-Carbon Degraded Aldehydes *via* 2-Hydroperoxy Acids

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After the formation of dianions of a carboxylic acid with lithium diisopropylamide, oxygen was bubbled into the solution to produce 2-hydroperoxy acid. Then the reaction mixture was acidified with a 2 N HCl solution and subsequently elevated to 50 °C to afford the aldehyde with the loss of one carbon atom. Even saturated (C_{10}–C_{20}) and unsaturated ($C_{18:1}$) carboxylic acids were converted into the odd aldehydes (C_9–C_{19}, $C_{17:1}$) in high yields. This conversion was found to be an efficient method for the preparation of carboxylic acids (Cn) to one-carbon degraded aldehydes (Cn-1) *via* 2-hydroperoxy acids.

Key words: carboxylic acid; aldehyde; 2-hydroperoxy acid; decarboxylation

A variety of aldehydes occur in nature, and have physiological functions. The aldehyde species have also been used as valuable intermediates to synthesize target compounds. For these reasons, various transformation methods for aldehydes have been developed. The conversion of alcohols to aldehydes by means of oxidants is one of the most popular functional transformations in organic synthesis. For example, aldehydes are prepared from alcohols with PCC, Swern, Dess-Martin periodinane, or TEMPO as oxidants.[1–4] Carboxylic acid esters are also converted to aldehydes by means of DIBAH. In spite of the availability of many reagents for these transformations, there still exists a need for efficient and convenient methods.

In organisms, long-chain aldehydes (C_{15}, C_{17}) are generated enzymatically from the corresponding fatty acids (C_{16}, C_{18}) by α-oxygenase.[5,6] In this process, fatty acids (Cn) are converted into the corresponding 2-hydroperoxy acids, followed by decarboxylation, to afford aldehydes (Cn-1) with the loss of one carbon atom. Hence we became interested in this enzymatic process of even carboxylic acids to such odd aldehydes *via* 2-hydroperoxy acids. Herein, we report an efficient conversion of carboxylic acids to one-degraded aldehydes *via* 2-hydroperoxy acids.

The process is illustrated in Scheme 1. In our initial attempt, tetradecanoic acid (C_{14}) was used as an even carboxylic acid. Tetradecanoic acid was treated with lithium diisopropylamide at −20 °C to afford the dianion formation. Then oxygen was bubbled into the dianion solution at −78 °C to produce 2-hydroperoxytetradecanoic acid.[7] The reaction was monitored as 9-anthryldiazomethane derivatives by HPLC.[5] After purification by medium-pressure column chromatography, 2-hydroperoxy acid was assigned by NMR. In order to investigate the condition of decarboxylation, the 2-hydroperoxy acid was treated with 2 N HCl aqueous solution. When the temperature was raised to 50 °C, the reaction was complete within 60 min. After standard treatment and silica gel chromatography, tridecanal was obtained quantitatively.

According to essentially the same procedure, tridecanal was prepared by one-pot reaction. Thus, after the formation of 2-hydroperoxytetradecanoic acid at −78 °C, the reaction mixture was acidified with 2 N HCl solution and subsequently elevated to 50 °C for 1 h to afford tridecanal in high yield (85%).

In order to investigate the applicability of this method, we selected a variety of even saturated carboxylic acids (C_{10}–C_{20}). A series of carboxylic acids was converted under the same reaction condition into odd aldehydes (C_9–C_{19}) with the loss of one carbon atom in high yields (83–88%). On the other hand, unsaturated carboxylic acids ($C_{18:1}$, $n = 9$ (*Z*)- or (*E*)- form) were tested by this procedure. The corresponding aldehydes ($C_{17:1}$, $n = 9$) were obtained under the same condition at 70–76% yield, and the stereochemistry of double bond did not change in this reaction (no isomerization).

In summary, this conversion was found to be an efficient method for the preparation of carboxylic acids (Cn) to aldehydes (Cn-1) *via* the corresponding 2-hydroperoxy acids. This new procedure is very simple and cleanly affords the desired aldehydes at high yields.

Experimental

Representative experimental procedure. A solution

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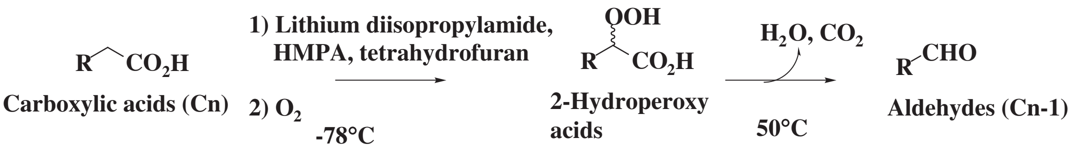

Scheme 1. Conversion of Carboxylic Acids (Cn) to Aldehydes (Cn-1) *via* 2-Hydroperoxy Acids.

of diisopropylamine (1.4 ml, 11 mmol) in tetrahydrofuran (20 ml) was treated with butyllithium (6.1 ml, 9.7 mmol), and then HMPA (0.8 ml, 4.4 mmol) was added at −20 °C. The mixture was stirred at −20 °C for 30 min. After formation of lithium diisopropylamide, tetradecanoic acid (1,000 mg, 4.4 mmol) in tetrahydrofuran (5 ml) was added dropwise to the mixture, and dianions formation was performed at −78 °C for 120 min.7) Then oxygen was bubbled into the dianion solution at −78 °C for 90 min. After removal of the cooling bath, the reaction mixture was quenched and acidified with 2 N HCl at −10–0 °C, and then the mixture was heated at 50 °C for 60 min. The reaction mixture was cooled to room temperature and then extracted with ether. The combined organic layer was washed with saturated $NaHCO_3$ and brine. After it was dried over Na_2SO_4, the extract was concentrated and purified by silica gel chromatography to yield tridecanal (590 mg, 85% yield).

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