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OXIDATIVE DECARBOXYLATION OF ACIDS *via* DIANION OXYGENATION

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The oxygenation of anions[1] or dianions[2] of carboxylate derivatives generated by lithium diisopropylamide (LDA) provides a useful route to α-hydroxy derivatives We now report that the α-hydroperoxides formed by the reactions of the dianions of carboxylic acids with molecular oxygen undergo ready decarboxylative elimination to yield the degraded ketones in good yields

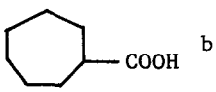
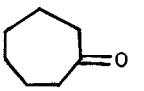
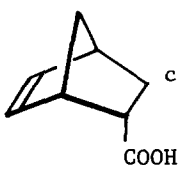
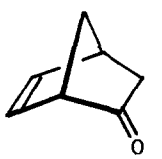
The oxidative decarboxylation may be accomplished very easily by refluxing a THF solution of the intermediate hydroperoxide (1) with p-toluenesulfonic acid Alternatively, one can avoid the acidic treatment by the use of N,N-dimethylformamide dimethylacetal (DMF acetal) Under either of these conditions, the reaction provides an efficient method of oxidative decarboxylation, which compares very favorably with the sulfenylation-chlorination procedure recently described by Trost and Tamaru [3]

Table I lists the acids investigated in the present work and illustrates the diversity in the choice of substrates These may include α,α-diaryl, arylalkyl, or dialkyl substituted acids Monosubstituted acids also undergo oxidative decarboxylation, although yields were significantly lower (*ca* 25%) except for special cases such as phenylacetic acid It is noteworthy that the reaction can be carried out in the presence of the double bond of norbornene carboxylic acid (Table I) In these oxidations, it was not necessary to isolate the intermediates, assumed to be hydroperoxides After solvent exchange, solutions of these peroxides in methylene chloride were sufficiently pure for direct treatment with either acid or acetal in the final fragmentation step [4]

In a typical experiment, a THF solution[5] of LDA (12 5 mmol) at 0° was added dropwise with stirring to a THF solution of 2-phenylbutyric acid (5 mmol) After 3 hr, the dianion was cooled to -78° and added *via* syringe to a reaction well[6] containing Et_2O at -78° into which dry oxygen was continuously circulated [7] Uptake of oxygen was quantitative and essentially instantaneous The reaction mixture was decanted, concentrated *in vacuo* to *ca* 5 ml, diluted with Et_2O and poured into cold aqueous 10% HCl Extraction with Et_2O followed by drying (Na_2SO_4) and exchange of solvent[8] afforded a practically colorless solution of

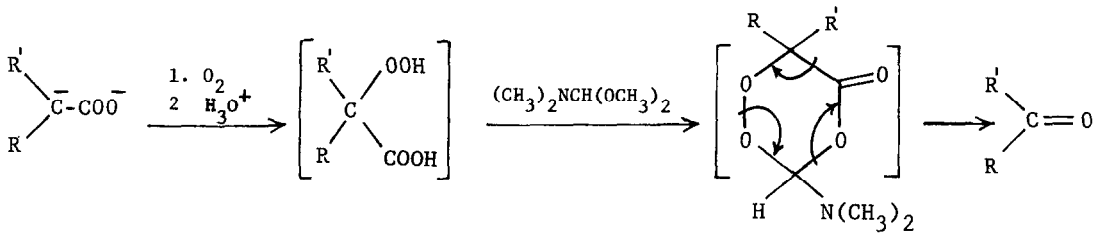
the α-hydroperoxy acid in CH_2Cl_2 To this solution at -78° under N_2, the DMF acetal (ca 4 equiv in CH_2Cl_2) was added dropwise, and the solution then allowed to warm up slowly to room temperature Stirring was continued until the starch-iodide test for peroxides was negative Removal of solvent followed by workup with ether and bulb-to-bulb distillation yielded propiophenone (72%)

TABLE I

Acid [a]	Decarboxylation [d] Conditions	Product [e]	Yield,% [f]
 [b]	DMF acetal in refluxing $CHCl_3$, 1 hr		75[g]
$Ph_2CHCOOH$ [b]	DMF acetal in CH_2Cl_2, 25°, 24 hr	$Ph_2C{=}O$	80[g]
 [c]	DMF acetal in CH_2Cl_2 25°, 12 hr		60[g] 67[h]
PhCHCOOH [b] CH_2CH_3	DMF acetal in CH_2Cl_2, 25°, 6 hr	Ph-C=O CH_2CH_3	72[i]
$PhCH_2COOH$ [c]	DMF acetal in CH_2Cl_2, 25°, 21 hr	PhCHO	65[i]
$(PhCH_2)_2CHCOOH$ [c]	TsOH in refluxing THF, 48 hr	$(PhCH_2)_2C{=}O$	70[j]

[a] The dianion was formed using 2 5 equiv of LDA at 0-5° for 3 hr. [b] Solvent THF. [c] Solvent THF/HMPA. [d] Chlorinated solvents were dried over and distilled from P_2O_5 prior to use. [e] The structures of all products were confirmed by comparison (IR, NMR) with authentic samples. [f] No attempt was made to optimize yields, overall yields were based on starting acid [g] Isolated as the 2,4-DNP. [h] By GLPC [i] Pure distilled product. [j] By NMR analysis.

While we have made no attempt to isolate intermediates in the reactions involving the acetal, we suggest that a six-membered peroxy lactone (2) may be formed by reaction of the hydroperoxide with DMF acetal The second-stage breakdown of 2 would thus be analogous to the elimination of β-hydroxy acids recently described by Yamamoto, et al [9]



1 2

Alternatively, the decarboxylation could take place by a fragmentation process similar to the breakdown of α-t-butylperoxy carboxylic acids [10,11]

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References and Notes

1 H H Wasserman and B H Lipshutz, Tetrahedron Lett , 1731 (1975)

2 P E Pfeffer and L S Silbert, U S Patent 3,652, 612 (March 28, 1972), Chem Abstr 76, 1, 399, 382 (1972)

3 B M Trost and Y Tamaru, J Amer Chem Soc , 97, 3528 (1975)

4 For related oxygenations or degradation reactions leading to the formation of ketones, see A H Davidson and S Warren, Chem Comm , 148 (1975), S J Selikson and D S Watt, Tetrahedron Lett , 3029 (1974); D S Watt, J Org Chem , 39, 2799 (1974)

5 In some cases (see Table I) HMPA (1 ml) was added to increase the solubility of the dianion

6 C S Foote and R S Vickers, Boll Chim Farm , 109, 599 (1970)

7 Inverse addition is not mandatory in these oxidations Satisfactory results may be obtained by bubbling oxygen directly into the solution of the dianion, although a longer reaction time is required

8 As the Et_2O was removed *in vacuo*, CH_2Cl_2 was added to maintain a volume of *ca* 10 ml

9 S Hara, H Taguchi, H Yamamoto and H Nozaki, *Tetrahedron Lett* , 1545 (1975)

10 W H Richardson and R S Smith, *J Amer Chem Soc* , **89**, 2230 (1967)

11 We are investigating the use of this oxidative decarboxylation reaction in the conversion of α-amino acids to amides In work to be published, we will report the conversion of azetidine carboxylic acids to β-lactams by this route