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NEW SELECTIVE OXIDATION OF ALCOHOLS CONTAINING ESTER GROUP WITH AN OXOAMINIUM SALT.

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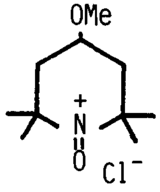
Abstract: While 1-oxo-4-methoxy-2,2,6,6-tetramethylpiperidinium chloride 1 does not oxidize the hydroxy group of 2-hydroxyethyl benzoate and 3-hydroxypropyl benzoate, it oxidizes those of 4-hydroxybutyl benzoate, 5-hydroxypentyl benzoate and 6-hydroxyhexyl benzoate. Oxidation of 2-hydroxyethyl 4-hydroxybutyl phthalate with 1 selectively gives 2-hydroxyethyl 4-oxobutyl phthalate.

Nitroxyl radical forms reversible redox system, and the redox system has been applied to organic syntheses.[1] Recently we have reported that the oxoaminium salt 1, the oxidized form of the nitroxyl radical, can selectively oxidize primary and secondary alcohols to the corresponding aldehydes and ketones, respectively.[2]



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In the process of our study on the application of this reversible redox system to organic syntheses, an unexpected result was obtained. That is, no oxidation product was obtained in the reaction of 2-hydroxyethyl methacrylate (HEMA) with 1, although most of primary or secondary alcohols are oxidized quantitatively under the same conditions.[2] The attempt to obtain the oxidized HEMA was failed even using excess amount of 1. As for the reason for this unexpected result, the effect of the ester or the double bond groups of HEMA was pointed out. Then, some control experiments were carried out as follows. 2-Hexanol was oxidized with 1 in the presence of hexyl acetate to give 2-hexanone quantitatively, and hexyl acetate was completely recovered. This result showed no possibility that the ester group prevents the oxidation reaction. Furthermore, the participation of double bond was also ruled out by the result that allyl alcohol was quantitatively oxidized to acrolein by 1.

From these results it was suggested that the ester group present in the same molecule does prevent the oxidation reaction intramolecularly. Then, the oxidation of ω-hydroxyalkyl benzoates by 1 was planned on the basis of the presumption that the change of the chain length between hydroxyl and ester groups would vary the strength of the interaction between them. Results are summarized in Table.

As expected, the oxidation profile depends on the chain length between hydroxyl and ester groups. When the number of the methylene group was less than four ($n<4$), the oxidation was suppressed. On the other hand, the number was more than or equal to four ($n=>4$), the oxidation proceeded to yield the corresponding aldehydes. The difference of the oxidation profile between $n=3$ and $n=4$ is dramatic. In the Table, the material balance can be fair when the amount of benzoic acid formed during the reaction was taken into account.[3]

Table Oxidation of ester-alcohols with 1[a)]

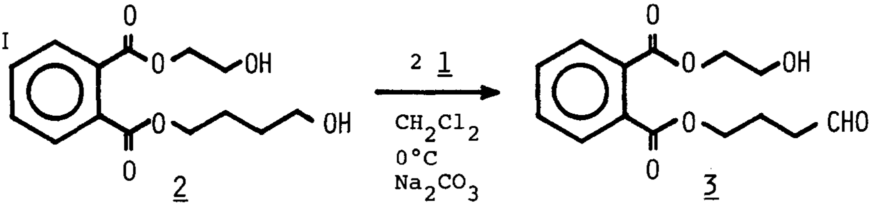
Substrate	Oxidant (equiv)	time (min)	Yield of CHO[b)] (%)	Recovered[b)] Alcohol (%)
$PhCOO(CH_2)_2OH$	1.0	60	0	78
$PhCOO(CH_2)_3OH$	1.0	60	trace	37
$PhCOO(CH_2)_4OH$	1.0	60	58	0
$PhCOO(CH_2)_5OH$	1.0	60	42	0
$PhCOO(CH_2)_6OH$	1.0	60	58	0

a) Oxidation was carried out in dichloromethane at room temperature.
b) Estimated by GC using internal standard.

A simple steric hindrance cannot explain this selectivity, for sterically more hindered secondary alcohols are oxidized in good yields under the same conditions.[2] It may be attributed to the effect of an intramolecular hydrogen bonding between hydroxyl and ester groups. Though it is not exactly clear that what kind of interaction gives this selectivity, the data in the Table suggest the possibility of regioselective oxidation of dihydroxy compounds. For example, it is expected that the oxidation of 2-hydroxyethyl 4-hydroxybutyl phthalate (2) by 1 will give only 2-hydroxyethyl 4-oxobutyl phthalate (3). The oxidation of 2 was carried out with two equivalent of 1 in dichloromethane at 0°C in the presence of sodium carbonate as an acid scavenger. The product obtained by the usual work-up was 2-hydroxyethyl 4-oxobutyl phthalate 3 whose structure was determined by IR and ^{1}H-NMR spectral data[4]. The yield of 3 was 81% by GC (46% isolated yield by column chromatography)(Scheme I). As expected, no other products such as 2-oxoethyl 4-hydroxybutyl phthalate or 2-oxoethyl 4-oxobutyl phthalate were detected even with the use of excess 1.

The studies on the other applications and on the origin of this selectivity are now in progress.

Scheme I



References and Footnotes

1)(a) Golubev,V.A.; Rozantsev,E.G.; Neiman,M.B. Bull. Acad. Sci. USSR **1965**, 1898. (b) Rozantsev,E.G.; Sholle,V.D.; Synthesis **1971**, 401. (c) Semmelhack, M.F.; Chou,C.S.; Cortes, D.A. J. Am. Chem. Soc. **1983**, 105, 4492. (d) Hunter, D.H.; Racok,J.S.; Rey,A.W.; Ponce,Y.Z. J. Org. Chem. **1988**, 53, 1278.

2) (a) Miyazawa,T.; Endo,T.; Shiihashi,S.; Okawara,M. J. Org. Chem. **1985**, 50, 1332. (b) Miyazawa,T.; Endo,T, ibid. **1985**, 50, 3930. (c) idem J. Mol. Catal. **1985**, 32, 357.

3) Presumably benzoic acid was formed by the hydrolysis of the ester catalyzed by hydrochloric acid, which was generated during the oxidation along with the reduced form of 1, 1-hydroxy-4-methoxy-2,2,6,6-tetramethylpiperidine.

4) IR spectral data (cm^{-1}); 3437(OH), 3070(Ph), 2962,2899,2829(CH_2), 2731(CHO), 1732,1720(C=O), 1600,1597,1489(Ph), 1448,1384(CH_2), 1280(COO), 1130,1076(COH), 744,705(Ph). ^{1}H-NMR spectral data; δ(ppm)=9.88 (s, 1H), 7.9-7.6 (m, 4H), 4.58 (t, J=6.0Hz, 2H), 4.37 (t, J=6.0Hz, 2H), 3.77 (t, J=6.0Hz, 2H), 2.60 (t, J=6.0Hz, 2H), 2.15 (tt, J=6.0Hz, 6.0Hz, 2H), 1.80 (br. 1H).

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