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A New Catalytic System for the Selective Aerobic Oxidation of Large Ring Cycloalkanes to Ketones

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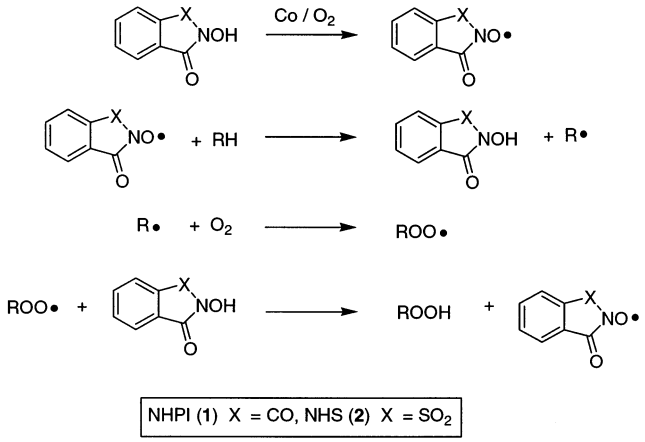
Abstract:

The combination of cobalt with *N*-hydroxysaccharin proved to be an effective catalyst for the aerobic oxidation of large ring cycloalkanes to the corresponding ketones.

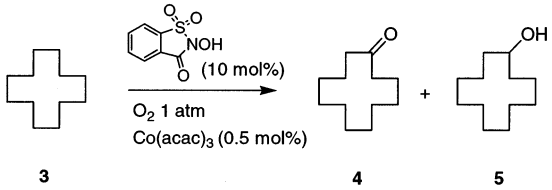
Introduction

The oxidation of saturated hydrocarbons with molecular oxygen is a reaction of considerable industrial importance.[1] The selective transformation of large-ring cycloalkanes (e.g., cyclododecane **3**) to the corresponding ketones is a particularly important reaction since the oxidation products are intermediates for the fragrances industry and for the production of dicarboxylic acid precursors for polyamides and polyesters.[2] However, aerobic oxidations of (cyclic)alkanes usually proceed in low selectivities, owing to overoxidation of the ketone to complex mixtures of products. To obtain reasonable selectivities the reaction is usually performed according to the Bashkirov method.[2,3] This involves aerobic oxidation in the presence of stoichiometric amounts of B_2O_3 to give the borate ester of cyclododecanol as the major product (80%) along with 10% of cyclododecanone at 30% conversion. The borate ester is subsequently hydrolysed to the alcohol and boric acid. A shortcoming of this method is that it is circuitous, involving three steps—oxidation, hydrolysis, and subsequent dehydrogenation of the alcohol to the ketone—and recycling of large quantities of boric acid. Ishii and co-workers[4] discovered that *N*-hydroxyphthalimide (NHPI) **1** in combination with cobalt catalyses the autoxidation of hydrocarbons under mild conditions (25−100 °C, O_2 1 atm). The promoting effect of NHPI was explained on the basis of the mechanism shown in Scheme 1. NHPI is converted into its corresponding phthalimide *N*-oxyl (PINO) radical which is able to abstract a hydrogen atom from the organic substrate, thus propagating the autoxidation chain. In this way PINO is the actual chain carrier, which leads to longer propagation chains and, hence, to higher rates and selectivities compared to those from standard autoxidation.

Scheme 1



The introduction of electron-withdrawing groups in the aryl ring of NHPI was shown to have a beneficial effect on the catalyst performance for the aerobic oxidation of alkylbenzenes[5] and the electrocatalytic oxidation of alcohols.[6] We reasoned that the use of *N*-hydroxysaccharin[7] (NHS) **2**, in which one carbonyl group (CO) is replaced by the more electron-withdrawing sulfonyl (SO_2) group, could provide an even more effective promoter. This proved to be the case, and we report herein our results on the aerobic oxidation of large-ring cycloalkanes with metal catalysts in combination with NHS (reaction 1).



(1)

Results and Discussion

Under the standard conditions described by Ishii et al.[4] (10 mol % NHPI, 0.5 mol % $Co(acac)_2$ in acetic acid at 100

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Table 1. **Oxidation of cyclododecane 3 in AcOH[a]**

run	catalyst	*T* (°C)	time (h)	conv. (%)	sel. (%)[b] 4	5	6	total
1	$Co(acac)_2$	100	24	<4	0	0	0	0
2	$Co(acac)_2$/NHS	100	6	64	31	8	16	55
3	$Co(acac)_2$/NHPI	100	6	58	29	5	30	64
4	$Co(acac)_2$/NHS	75	8	47	41	10	12	63
5	$Co(acac)_2$/NHPI	75	8	36	42	8	23	73
6[c]	$Co(acac)_2$/NHS	50	24	42	47	14	20	81
7[c]	$Co(acac)_2$/NHPI	50	24	0	−	−	−	0

[a] Cyclododecane **3** (3 mmol), NHS or NHPI (0.3 mmol), cocatalyst (0.015 mmol), AcOH (7.5 cm^3), O_2 1 atm. [b] Based on cyclododecane **3** reacted. [c] 5 cm^3 AcOH.

°C and 1 bar O_2) cyclododecane **3** afforded a mixture of cyclododecanone **4** (29%), cyclododecanol **5** (5%), and 1,12-dodecanedioic acid **6** (30%) at 58% conversion (Table 1, entry 3). In addition to **6**, other major byproducts were identified by GC−MS analysis, as two isomeric hydroxycyclododecanones and two isomeric cyclododecadienones. The formation of these byproducts is attributed to competing transannular hydrogen abstraction by an intermediate cyclododecylperoxy radical, analogous to that observed in the autoxidation of cyclohexylbenzene.[8] The products reported in the tables plus the isomeric hydroxycyclododecanones and cyclododecadienones accounted for more than 90% of the substrate converted. Identification of the remaining (<10%) byproducts is part of ongoing optimization studies and will be reported in due course.

Substitution of NHPI by NHS (entry 2) afforded a slightly higher conversion (64%) and a slightly higher selectivity to ketone and alcohol (31 and 8%, respectively). Higher selectivities were obtained by decreasing the reaction temperature to 75 °C (runs 4 and 5) whereby the higher activity of NHS became more pronounced. When the reaction temperature was decreased further to 50 °C, no reaction was observed with NHPI/$Co(acac)_2$. In contrast NHS/$Co(acac)_2$ gave 42% cyclododecane conversion and a selectivity to ketone and alcohol of 47% and 14%.

We next turned our attention to the use of α,α,α-trifluorotoluene as solvent. $PhCF_3$ was used by Ishii[9] as a solvent for the metal-free autoxidation of adamantane catalysed by NHPI in the presence of tetrabutylammonium bromide. Oxidation of cyclododecane under similar conditions in the presence of NHS (Table 2) led to a low conversion (9%) with good overall selectivity (entry 1). Replacement of the tetrabutylammonium salt by $Co(acac)_2$ led to an increase in rate and, with NHS, an increase in selectivity to ketone + alcohol (74% at 32% conversion, entry 2).

The reaction rate and selectivity were further increased by replacing $Co(acac)_2$ with $Co(acac)_3$ (35% conversion and 81% selectivity after 4 h, entry 4). The highest selectivity (90% to a 4:1 mixture of ketone/alcohol at 24% conversion) was observed with a combination of NHS and $Co(acac)_3$ at

Table 2. **Oxidation of cyclododecane 3 in $PhCF_3$[a]**

run	catalyst	*T* (°C)	time (h)	conv. (%)	sel. (%)[b] 4	5	6	total
1	Bu_4NBr/NHS	80	24	9	41	33	n.d.	74
2	$Co(acac)_2$/NHS	100	24	32	54	20	0	74
3	$Co(acac)_2$/NHPI	100	24	43	48	8	6	62
4	$Co(acac)_3$/NHS	100	4	35	64	17	5	86
5	$Co(acac)_3$/NHPI	100	8	23	63	21	5	89
6	$Co(acac)_3$/NHS	80	10	24	72	18	0	90
7	$Co(acac)_3$/NHPI	80	24	23	42	16	5	63

[a] Cyclododecane (3 mmol), NHS or NHPI (0.3 mmol), cocatalyst (0.015 mmol), $PhCF_3$ (9 cm^3), O_2 1 atm. [b] Based on cyclododecane **3** reacted.

Table 3. **Oxidation of different cycloalkanes in $PhCF_3$ catalysed by NHS[a]**

run	substrate	time (h)	conv (%)	sel. (%)[b] ketone	alcohol	diacid
1	cyclododecane	10	24	72	18	0
2	cyclodecane	5	31	61	24	2
3	cyclooctane	1.5	30	55	22	20

[a] Cycloalkanes (3 mmol), $Co(acac)_3$ (0.015 mmol), NHS (0.3 mmol), $PhCF_3$ (9 cm^3), 80 °C, O_2 1 atm. [b] Based on substrate reacted.

80 °C in $PhCF_3$. Under these conditions no formation of 1,12-dodecanedioic acid was observed.

In all these experiments, the selectivity (for alcohol + ketone) decreases with increasing conversion. At higher conversions further oxidation of the ketone product starts to become important, and we have demonstrated this in competition experiments.[10] The conditions developed for the oxidation of cyclododecane in α,α,α-trifluorotoluene were applied to the oxidation of different large-ring cycloalkanes, and the results are presented in Table 3.

As a result of ring strain caused by transannular interaction, cyclodecane and cyclooctane are more reactive under autoxidation conditions than cyclododecane. In the oxidation of cyclodecane, for example, 31% conversion was obtained in 5 h to give cyclodecanone in 61% selectivity along with 24% cyclodecanol and only 2% 1,10-decanedioic acid. The oxidation of cycloctane was even faster (30% conversion in 1.5 h) Cyclooctanone, cyclooctanol, and 1,8-octanedioic acid were formed in 55, 22, and 20% selectivity, respectively.

Conclusions

Summarising, we have shown that the combination of *N*-hydroxysaccharin with $Co(acac)_3$ is an efficient catalyst for the aerobic oxidation of large-ring cycloalkanes, displaying a higher activity than the previously described NHPI-based catalyst. The selectivity toward ketone + alcohol (90% of a 4:1 ketone alcohol mixture at 24% conversion) is as

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(10) We have performed competition experiments where we added cyclopentadecanone (0.42 mmol) after 1 h to a typical reaction of cyclododecane in $PhCF_3$ at 100 °C with NHS (as in run 4, Table 2). In this case 12% of the added ketone was decomposed after 6 h into a variety of products. A similar procedure was used to test the alcohol stability under these conditions using a mixture of cyclopentadecanol and cyclododecane. It was demonstrated that the alcohol is converted for almost 85% to the ketone and 9% to the diacid.

good as or better than that observed with the Bashkirov method,[2] and the procedure is considerably less circuitous.

Experimental Section

N-Hydroxysaccharin (NHS) was synthesised according to a seven-step synthesis starting from 2-sulfobenzoic anhydride, published by Nagasawa et al.[7] in 1995. The overall yield was 17%. Numerous attempts to synthesise NHS via a different route failed. Direct reaction of the 2-sulfobenzoic anhydride with hydroxylamine in the presence of base, analogous to the synthesis of *N*-hydroxyphthalimide derivatives,[5] gave no NHS. Also direct oxidation of saccharin with electrophilic oxidants such as H_2O_2 (basic conditions), H_2O_2/WO_4^{2-}, $KHSO_5$ (oxone), dimethyloxirane, or methyl(trifuoromethyl)dioxirane failed.

In a typical experiment, the catalytic run was carried out in a two-necked 25-cm^3 round-bottom flask containing a magnetic stirrer, equipped with a condenser and connected to a gas buret filled with molecular oxygen. In a typical experiment 504 mg (3 mmol) of cyclododecane, 60 mg (0.3 mmol) of *N*-hydroxysaccharin, 5.3 mg (0.015 mmol) of $Co(acac)_3$, and 200 mg of 1,2,4-trichlorobenzene were weighed in the flask before addition of 7.5 or 9 mL of acetic acid. A series of vacuum/molecular oxygen were applied before the reaction was started. The reaction was monitored by gas chromatography using a CP-WAX 52 CB column (50 m $\times$ 0.53 mm). A typical temperature program starts at 50 °C (5 min) with a ramp of 8°/min up to 220 °C. The reported yields are thus GC yields, and are determined using 1,2,4-trichlorobenzene as the internal standard. 1,12-Dodecanedioic acid, 1,10-decanedioic acid, and 1,8-octanedioic acid were analysed by HPLC (Waters Symmetry C18 reversed phase column; eluent, water/methanol 50:50, 0.1% TFA) using octanoic acid as an internal standard.

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