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NOVEL ALLYLIC OXIDATION REAGENTS

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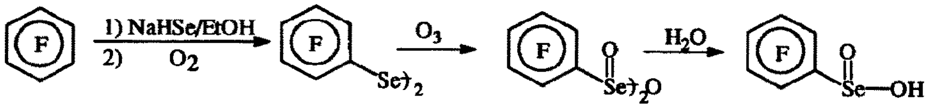
Abstract: Pentafluorobenzeneseleninic acid and 2-(N-oxido)pyridineseleninic anhydride were prepared and used efficiently in the oxidation of alcohols and in the allylic oxidation of alkenes.

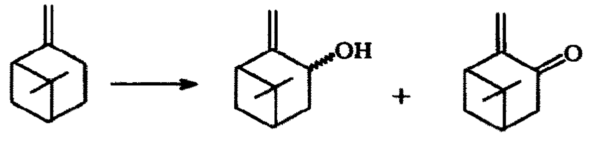
The oxidation of activated methyl or methylene groups and of allylic systems using selenium reagents is an important method for introducing a hydroxyl or carbonyl groups into various organic structures.[1] The classical reagent, selenium dioxide, is frequently used for this purpose, but residue selenium is always a problem particularly in industry. The commercially available benzeneseleninic anhydride avoids the residue problem but allylic or benzylic oxidation is sluggish. We found that the oxidation reactions of 2-pyridineseleninic anhydride are more efficient than those of bezeneseleninic anhydride (BSA).[2] This may be attributed to the greater electron-withdrawing effect of the pyridine nucleus which renders the Se=O bond a better eneophile.[2] We herein wish to report the preparation and application of 2-(N-oxido)pyridineseleninic anhydride and pentafluorobenzeneseleninic acid. The introduction of stronger electron-withdrawing groups was made to increase further the eneophilicity of the reagent so that the reactions might be performed at lower temperatures.

Hexafluorobenzene **1** reacted with NaHSe in ethanol to afford the selenol, which could be oxidized by dioxygen in the air to diselenide **2**.[3] Pentafluorobenzeneseleninic anhydride **3** was prepared by the ozonolysis of the corresponding diselenide **2** in anhydrous dichloromethane. Anhydride **3** absorbed water very easily and the corresponding acid **4** was obtained eventually in 90% overall yield from diselenide **2**. Its ^{77}Se NMR spectrum (a singlet at 1227 ppm referred to diphenyldiselenide at 475 ppm in $CDCl_3$) and microanalysis are consistent with the acidic structure.[1] The latter is stable at room temperature in the solid state. However its solutions in dichloromethane or acetone slowly became yellow.



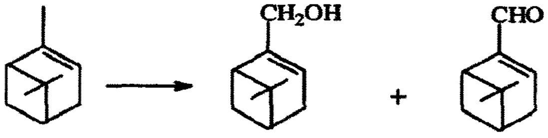
1 **2** **3** **4**

At room temperature in benzene, **4** oxidized 1 equiv. of β-pinene **5** to give a mixture of alcohol **6** (35%) and ketone **7** (36%) during 14 h (Table, Entry 1). Under the same conditions, BSA did not react with β-pinene **5**. When 2 equiv. of **4** were used, a mixture of **6** (20%) and **7** (75%) was obtained after 14 h at 20 °C (Entry 2); When heated to reflux in benzene for 2 h, **7** was isolated in 90% yield (Entry 3).



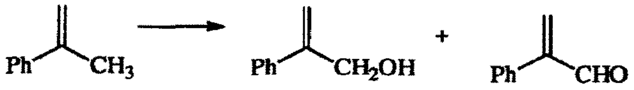
5 **6** **7**

The oxidation of α-pinene **8** is slower; **8** was oxidized by 1 equiv. of **4** to give a mixture of myrtenol **9** (45%) and myrtenal **10** (20%) when heated to reflux for 2 h (Entry 4). With 2 equiv. of **4**, **8** was oxidized to myrtenal **10** in 85% yield in benzene under reflux for 2 h (Entry 5).



8 **9** **10**

With 1 Equiv. of **4**, α-methyl styrene gave the corresponding aldehyde **13** in 45% yield at 20 ^{0} after 14 h (Entry 6). With 1.5 equiv. of **4**, a mixture of **12** (45%) and **13** (44%) was obtained in 2 h under reflux in benzene (Entry 7). With 2 equiv of **4**, **13** was obtained in 90% yield in 2 h under reflux in benzene (Entry 8).

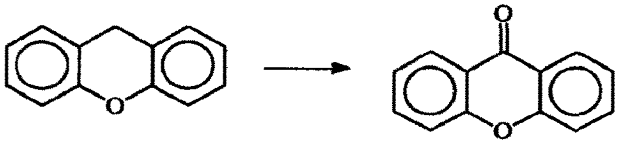


11 **12** **13**

The oxidation of an alcohol is facile. 1-Octanol **14** was oxidized to 1-octanal **15** in 90% yield with 1 equiv. of **4** at 20 °C during 2 h (Entry 9).

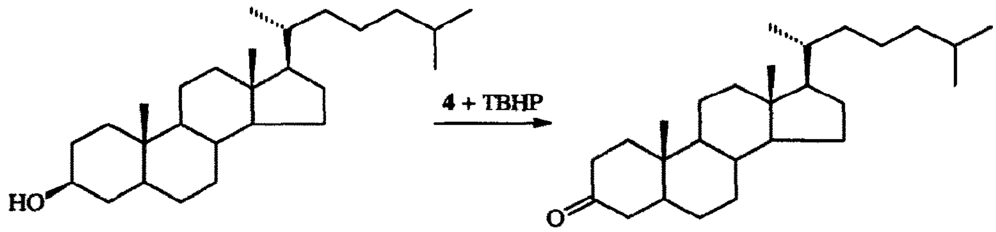
14 **15**

The reaction of pentafluorobenzeneseleninic acid **4** could be made catalytic using tert-butyl hydroperoxide (TBHP) as a reoxidant. When 10% **4** was added, TBHP can oxidize 0.5 equiv. of β-pinene to the corresponding ketone **7** in 90% yield under reflux in benzene for 2 h (Entry 10). Under the same conditions, xanthene **16** was oxidized to xanthone **17** in quantitative yield in 2 h (Entry 11).



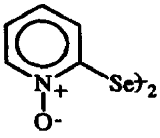
16 **17**

Under the same conditions, dihydrocholesterol **18** was oxidized to the corresponding ketone **19** in 90% yield (Entry 12).



18 **19**

2-(N-oxido)pyridineseleninic anhydride **21** was prepared by the ozonolysis of the corresponding diselenide **20**[4] in anhydrous CH_2Cl_2 at 0 °C in almost quantitative yield. A singlet appeared at 1347 ppm in its ^{77}Se NMR spectrum. When it was allowed to stand in air for some time, this peak shifted to 1191 ppm. The first one is in accordance to its anhydride form and the latter was assigned to its acidic form after the absorption of water. This compound was not stable and would explode mildly even at room temperature. However it is stable in the suspension in anhydrous CH_2Cl_2. Thus it should be prepared *in situ* before the oxidation reaction.



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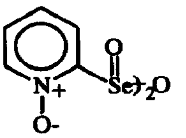

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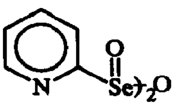
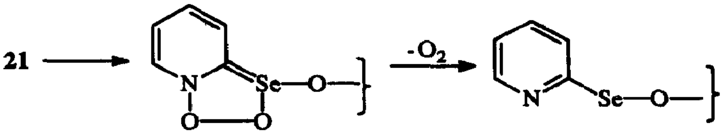


22

Using the diselenide **20** as a catalyst and TBHP as oxidant might make a useful oxidation system. Presumably the explosion was caused by rearrangement of **21** to **23** followed by loss of oxygen. This reaction deserves further study.



23 **24**

When 0.5 molar equiv. of β-(-)-pinene **5** was added to a newly prepared suspension of **21** in CH_2Cl_2 and the mixture was stirred for 6 h, alcohol **6** was obtained in 90% yield (Entry 13). The half life time of the reaction is about 60 minutes. The reaction of 2-pyridineseleninic anhydride **22** at 20 ° with β-pinene **5** to give the alcohol **6** in 74% yield took 24 h (Entry 14). The half life time was 9 h. These results showed that the oxygen bonding to the nitrogen increased the electron-withdrawing effect and made the reagent a better eneophile. When 1 equiv of β-pinene **5** was added to the suspension of **21** in benzene, ketone **7** was obtained in 92% yield after reflux for 2 h (Entry 15). With 0.6 equiv. of **4**, α-pinene **8** was oxidized to give a mixture of alcohol **9** (57%) and aldehyde **10** (28%) at room temperature overnight (Entry 16).

$PhI(OAc)_2$ could be used as the re-oxidant of the diselenide **20**. A mixture of 0.1 equiv of **21** and 2 equiv of $PhI(OAc)_2$ can oxidize β-pinene **5** to give a mixture of **6** (13%) and **7** (79%) after reflux in benzene for 6 h (Entry 17). Under the same condition, xanthene **16** and diphenylmethane **25** were oxidized to xanthone **17** (Entry 18) and benzophenone **26** (Entry 19) in 95% and 71% yields respectively.

$$\underset{\mathbf{25}}{Ph_2CH_2} \longrightarrow \underset{\mathbf{26}}{Ph_2C{=}O}$$

A typical procedure for ozonolysis: Ozone was bubbled into a solution of diselenide in anhydrous CH_2Cl_2 at 0 °C until the yellow color of the diselenide disappeared and a large amount of white solid came out (about 30 min). Ozone was then purged by nitrogen for 10 min. 2-(N-oxido)pyridineseleninic anhydride was used immediately. Pentafluorobenzeneseleninic acid was filtered and further purified by recrystallization from acetone-dichloromethane, m.p. 108-9 °; Microanalysis: Theory: C, 25.83%, H 0.36%; Found C 25.61%, H 0.53%.

A typical procedure for the oxidation reaction: A mixture of an alkene or an alcohol and the selenium reagent in benzene was stirred at 20 ° or refluxed for some time. After cooling, the solvent was removed by vacuum to give a residue, which was purified by column chromatography on silica gel eluting with CH_2Cl_2 to give the product.

Table

Entry	Substrate[1]	Oxidant (Equiv)	Time (h)	Temp (°C)	Products (%)[2]		
1	**5**	**4** (1)	14	20	**5** (35)	**6** (36)	**7** (20)
2	**5**	**4** (2)	14	20		**6** (20)	**7** (75)
3	**5**	**4** (2)	2	reflux			**7** (90)
4	**8**	**4** (1)	2	reflux	**8** (25)	**9** (45)	**10** (20)
5	**8**	**4** (2)	2	reflux			**10** (85)
6	**11**	**4** (1)	14	20	**11** (47)		**13** (45)
7	**11**	**4** (1.5)	2	reflux		**12** (48)	**13** (44)
8	**11**	**4** (2)	2	reflux			**13** (91)
9	**14**	**4** (1)	2	20	**15** (90)		
10	**5**	**4**+TBHP[3]	4	reflux			**7** (90)
11	**16**	**4**+TBHP[3]	4	reflux			**17** (100)
12	**18**	**4**+TBHP[3]	4	reflux			**19** (90)
13	**5**	**21** (0.5)	6	20		**6** (90)	
14	**5**	**22** (0.5)	24	20		**6** (74)	
15	**5**	**21** (1)	2	reflux			**7** (92)
16	**8**	**21** (0.6)	18	20		**9** (57)	**10** (28)
17	**5**	**21**+PhI(OAc)$_2$[4]	4	reflux		**6** (13)	**7** (79)
18	**16**	**21**+PhI(OAc)$_2$[4]	4	reflux			**17** (95)
19	**25**	**21**+PhI(OAc)$_2$[4]	4	reflux	**25** (25)		**26** (70)

1) All substrates are 1 Equiv.; 2) All reactions were performed in benzene except Entries 13 and 16.
3) **4**, 0.1 Equiv.; TBHP), 2 Equiv.; 4) **21**, 0.05 equiv.; PhI(OAc)$_2$, 2 Equiv..

In conclusion, allylic methyl and methylene groups were performed under mild conditions by using selenium (IV) reagents. Electron-withdrawing groups increased the eneophilicity of the reagent.

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