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OXIDATION OF OLEFINS WITH 2-PYRIDINESELENINIC ANHYDRIDE

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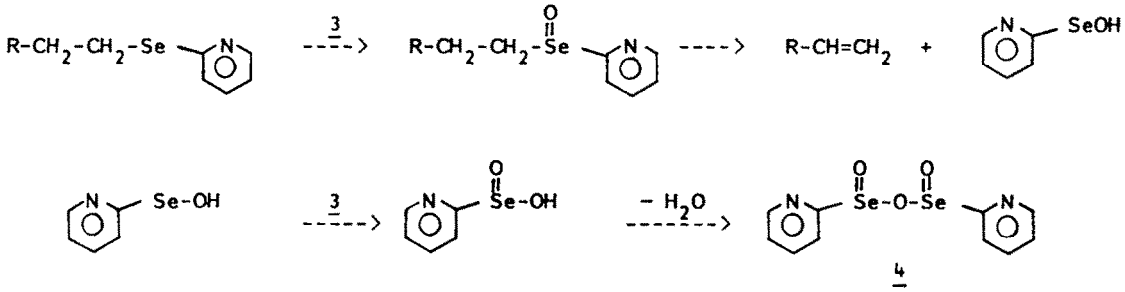
Abstract - 2-Pyridineseleninic anhydride, prepared in situ by oxidation of the corresponding diselenide with iodoxybenzene, is an efficient reagent for the conversion of olefins to unsaturated ketones with retention of the original position of the double bond. This reagent is, therefore, much more reactive towards olefins than benzeneseleninic anhydride. An explanation has been offered.

In our recent synthesis of (L)-vinylglycine we were led to study the reaction of the model alkyl-2'-pyridylselenide 1 with various oxidants.[1] Treatment of 1 with excess iodoxybenzene 3 in toluene at reflux led surprisingly, not to the expected olefin 2a, but instead to the allylic alcohol 2b as the only isolated product. We concluded that the first formed product 2a was undergoing rapid allylic oxidation by some species present in the reaction mixture. We were subsequently able to isolate 2a in reasonable yield when the reaction was carried out in the presence of 1-hexene as a sacrifical olefin.[1] Given that the allylic oxidation of olefins is classically affected with selenium dioxide in stoichiometric amounts[2] or more recently as a catalyst with t-butylhydroperoxide as oxidant[3] we considered that the over oxidation of 2a to 2b was brought about by 2-pyridineseleninic anhydride 4 generated in situ by the iodoxybenzene oxidation of 2-pyridineselenenic acid (Scheme 1). We therefore determined to test this hypothesis by the treatment of simple model olefins with a mixture of dipyridyldiselenide 5 and iodoxybenzene 3 and report here the results of these studies which culminated in the elaboration of a new allylic oxidation system based upon an organoselenium catalyst.



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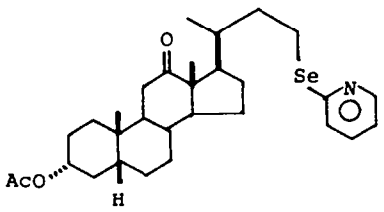
Scheme 1



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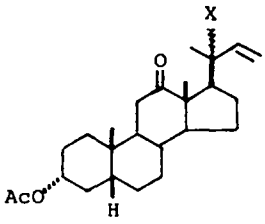
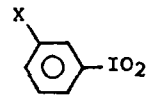
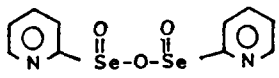


2a X = H (20 R)
2b X = OH

Benzene seleninic anhydride, used in catalytic quantities with either iodoxybenzene or m-iodoxybenzoic acid is a very useful reagent for the formation of certain enones from ketones.[4] It is known to be an allylic oxidant for olefins only in exceptional cases. It has been used for the oxidation of benzylic hydrocarbons.[5] Hori and Sharpless[6] have acheived the allylic oxidation of olefins with migration of the double bond by the addition of benzeneselenenic acid to the olefin and subsequent oxidative elimination. Reich et al[7] studied the fate of benzeneselenenic acid formed in syn eliminations of selenoxides, and its reactions with olefins, but observed no allylic oxidation. Alkyl-2-pyridylselenoxides have been reported[8] to undergo syn elimination much more readily than the corresponding alkylphenylselenoxides, however the use of 2-pyridineseleninic anhydride as a reagent for allylic oxidation of olefins has not been reported before.



3 X = H
8 X = CO_2H



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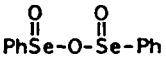


6

PhSeSePh

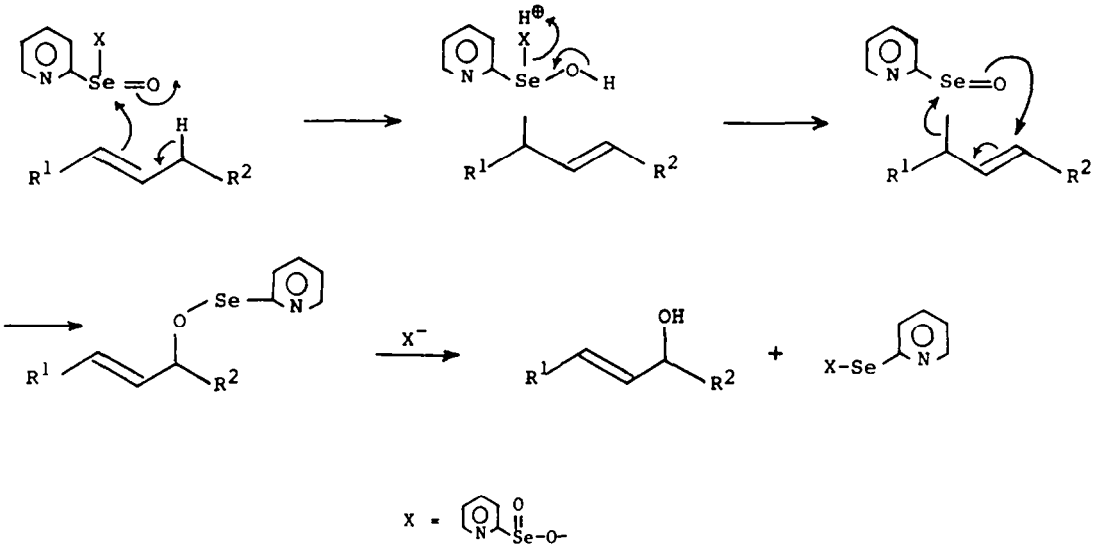
7

PhIO

9

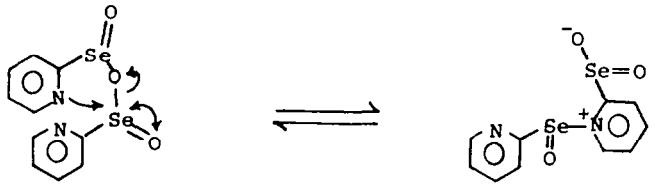
We first sought confirmation that the allylic oxidation reaction was indeed due to an organoselenium species and not to the excess of iodoxybenzene employed. Thus treatment of β-pinene 10 in benzene at reflux with excess iodoxybenzene for 1 hr led to the quantitative recovery of starting material (Table, Entry 1). The reaction was repeated but in the presence of a catalytic quantity of 2-pyridylseleninic anhydride, conveniently introduced as 2,2'-dipyridyldiselenide[8] 5. After 1.5 hr at reflux the substrate 10 had been consumed. The reaction medium was filtered, evaporated to dryness and chromatographed on silica to give the allylic ketone (+)-pinocarvone 11 in 95% yield (Table, Entry 2). The use of benzene seleninic anhydride introduced as diphenyl diselenide 7, in place of 2-pyridine seleninic anhydride, under the same conditions gave only 50% of 11 and 50% recovered 10 after 24 hrs at reflux (Table, Entry 3). This clearly demonstrates the difference in reactivity between 2-pyridine and benzeneseleninic anhydrides. The use of an excess of pyridine in the oxidation of β-pinene with iodoxybenzene and benzeneseleninic anhydride however led to an increase in reaction rate and we were able to obtain 11 in 45% yield after 4 hrs at reflux (Table, Entry 4). Although we did not attempt the isolation of allylic alcohols from the reaction mixture,

these were observed by t.l.c. during the course of the reactions. It is evident therefore that the reaction gives first the allylic alcohol which is rapidly oxidised in situ to the allylic ketone. On the basis of the above observations we considered this new allylic oxidation reaction to take place via the mechanism outlined in Scheme 2.



Scheme 2

The difference in reactivity between 2-pyridineseleninic anhydride and benzeneseleninic anhydride towards olefins could possibly be attributed to the greater electron-withdrawing properties of the pyridine nucleus which renders the Se=O bond a better eneophile. A second possibility is that 2-pyridineseleninic anhydride exists in equilibrium with a pyridinium salt as shown in Scheme 3 and that it is in fact this latter which affects allylic oxidations. Hence



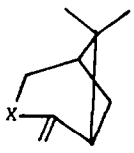
Scheme 3

the addition of pyridine to benzeneseleninic anhydride generates a similar pyridinium salt which is capable of undergoing the ene reaction.

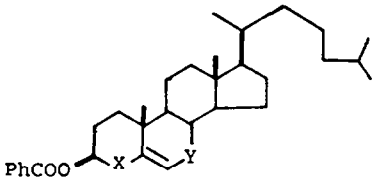
Having demonstrated that 2-pyridineseleninic anhydride is superior to benzeneseleninic anhydride in our system we attempted to replace iodoxybenzene 3 with m-iodoxybenzoic acid 8 in the hope of eliminating the chromatographic work-up as previously demonstrated in the formation of dienones from ketones.[4] In the event (Table, Entry 5) β-pinene was not oxidised by m-iodoxybenzoic acid and a catalytic quantity of 2,2'-dipyridyldiselenide. We assume this to be the result of the formation of a salt of the diselenide (which was not oxidised to the anhydride), or that the pyridine salt of Scheme 3 could not be formed. Thus addition of an excess of pyridine (Table, Entry 6) to the reaction restored the oxidising power and 11 was obtained in almost quantitative yield after 3.5 hrs at reflux. We also attempted the use

of m-iodoxybenzoic acid with the diphenyldiselenide/pyridine system (Table, Entry 7), however neither the diphenyldiselenide nor the β-pinene were oxidised. This last result was not totally unexpected as the t-butyl-tetramethylguanidinium salt of m-iodoxybenzoic acid is reported[9] to be a milder oxidising agent than the free acid and does not affect oxygen transfer to diphenyldiselenide. We also demonstrated the effectiveness of iodosobenzene 9 as overall oxidant in this system (Table, Entry 8).

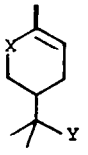
Dipyridyl diselenide / iodoxybenzene is clearly the most efficient of the various systems tested above and we therefore proceeded to apply this system to the oxidation of various other olefins. Selenium dioxide oxidation of cholesteryl benzoate 12 is not a clean reaction and the yield of 4β-hydroxycholesteryl benzoate 13 is of the order of 30%.[10] The reaction of cholesteryl benzoate 12, with iodoxybenzene and a catalylic quantity of 2,2'-dipyridyldiselenide gave a 62% yield of the corresponding 4-ketone 13 after 10 hrs at reflux in benzene. The 7-ketone 14 was the only other product formed in this very clean reaction (Table, Entry 9). The oxidation of α-terpineol 15 under the standard conditions failed completely (Table, Entry 10). We reasoned that this was due to the formation of an ester between 15 and pyridineseleninic acid which results in catalyst deactivation. This hypothesis was confirmed when α-terpineol acetate 16 underwent facile oxidation to the ketone 17 in 4 hrs under standard conditions (Table, Entry 11). It would seem therefore that this system is not suitable for the oxidation of olefins leading to tertiary allylic alcohols, this minor draw-back could easily be circumvented by the use of 5 in half stoichiometric quantities as demonstrated by our original observation of the oxidation of 2a to 2b. We note also that in the oxidation of 16 no products resulting from the oxidation of the 1-methyl substituent were observed.



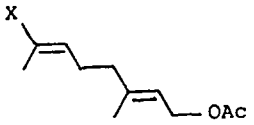
10 X = CH_2
11 X = CO



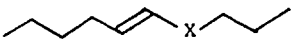
12 X = Y = CH_2
13 X = CO, Y = CH_2
14 X = CH_2, Y = CO



15 X = CH_2, Y = OH
16 X = CH_2, Y = OAc
17 X = CO, Y = OAc



18 X = CH_3
19 X = CHO



20 X = CH_2
21 X = CO

We next turned our attention to the oxidation of geraniol acetate 18. Selenium dioxide oxidation of 18 by the Sharpless catalytic method leads mainly to the aldehyde 19 in 55% yield.[13] Under our standard conditions 18 was oxidised in 20 hrs to the aldehyde 19 in 55% yield (Table, Entry 12). Attempts to increase the reaction rate by conducting the reaction in chlorobenzene at reflux led to lower yields (Table, Entry 13). It was not possible to allow the reaction to go to completion in this latter case as over oxidation of 19 was a competing reaction. Finally we were able to oxidise trans-5-decene 20 to trans-5-decene-4-one 21 in excellent yield (Table, Entry 14).

Table

Entry	Substrate	Catalyst (mmol)	Oxidant (mmol)	Temp. (°C)	Time (hrs)	Products (% Yields)
1	10	-	3 (3)	80	1	-
2	10	5 (0.1)	3 (3)	80	1.5	11 (95)
3	10	7 (0.1)	3 (3)	80	24	11 (50) + 10 (50)
4	10	7 (0.1) + Py (10)	3 (3)	80	4	11 (45)
5	10	5 (0.1)	8 (3)	80	24	-
6	10	5 (0.1) + Py (10)	8 (3)	80	3.5	11 (95)
7	10	7 (0.1) + Py (10)	8 (3)	80	10	-
8	10	5 (0.1)	9 (3)	80	3	11 (95)
9	12	5 (0.1)	3 (3)	80	10	12 (15) + 13 (67) + 14 (18)
10	15	5 (0.1)	3 (3)	80	24	-
11	16	5 (0.1)	3 (3)	80	4	17 (55)
12	18	5 (0.1)	3 (3)	80	20	19 (55)
13	18	5 (0.1)	3 (3)	133[a]	7	18 (38) + 19 (39)
14	20	5 (0.1)	3 (3)	80	8	21 (81)

a) Chlorobenzene as solvent.

The regioselectivity observed in these allylic oxidation reactions closely resembles that found[2a,11] in classical selenium dioxide oxidations and is in accord with the proposed mechanism. Thus the attack of the catalyst on the olefin takes place whenever possible with the bulky selenium atom oriented towards the least substituted end of the double bond.

We have thus been able to develop a new system for the allylic oxidation of olefins, which only uses a catalytic amount of an organoselenium reagent, proceeds without migration of the double bond and which requires no aqueous work-up.

Experimental

General

Melting points are uncorrected and were determined with a Reichart hot-stage apparatus. 60 MHz NMR spectra were measured with a Varian EM 360L Spectrometer for solutions in deuterochloroform. Chemical shifts (δ) are given in ppm downfield from tetramethylsilane as internal standard. Optical rotations were recorded with a Perkin-Elmer 141 MC polarimeter, infra red spectra with a Perkin Elmer 297 Spectrophotometer and 70 eV E.I. mass spectra with an AEI MS-9 apparatus.

All solvents were dried and distilled by standard techniques.

2,2-Dipyridyldiselenide (7), iodoxybenzene (3), m-iodoxybenzoic acid (8) and iodosobenzene (9) were prepared according to literature procedures.

General Method for the Allylic Oxidation of Olefins

The oxidant (3 mmol) (see Table), and then the catalyst (0.1 mmol) (see Table) were added to a solution of the substrate (1 mmol) in the appropriate solvent (10 ml) (see Table) and the solution heated to reflux with stirring under nitrogen. At the end of the reaction (t.l.c.) the mixture was cooled to room temperature, filtered on celite and evaporated to dryness. The products, described below, were then isolated by flash chromatography on silica gel.

(+)-6,6-Dimethyl-4-methylenebicyclo[3,1,1]heptan-3-one (11) [(+)-pinocarvone] -This pale yellow oil was eluted with dichloromethane. It had b.p. 130°C/15 mm (Kugelrohr); $[\alpha]_D^{20}$ + 62° (c = 1.2 in $CHCl_3$) lit.[12] $[\alpha]_D$ + 63°; δ0.9 (3H, s, 10 CH_3), 1.45 (3H, s, 9 CH_3), 2.30 (1H, d, J = 5 Hz), 6.10 (1H, d, J = 5Hz), 6.10 (1H, d, J = 5 Hz). A sample was converted by standard techniques into the dinitrophenylhydrazone which had m.p. 170-172°C (EtOH). Lit.[13] m.p. 172-174°C.

Oxidation of 3β-Benzoyloxycholest-5-ene - Oxidation and subsequent chromatography on silica gel (eluant: dichloromethane-pentane 3:1) gave first recovered substrate 12 (15%), then 3β-benzoyloxylcholest-5-ene-4-one (13) (67%) which had m.p. 160-160.5°C (acetone); $[\alpha]_D^{20}$ -40° (c = 1.3 in $CHCl_3$); lit.[10] m.p. 158-160°; $[\alpha]_D$ -39°, and finally 3β-benzoyloxycholest-5-en-7-one (14) (18%) which was characterised as having m.p. 158-161°C, $[\alpha]_D^{20}$ -53° (c = 0.2 in $CHCl_3$), lit.[14], m.p. 159.5 -161°C, $[\alpha]_D$ -54°.

(±)4(1'-Acetoxymethylethyl)-1-methylcyclohex-1-en-6-one (8-Acetoxycarvotanacetone) (17) - Oxidation of (±) α-terpineol acetate (16) gave (±)-8-acetoxycarvotanacetone (17) in 55% yield after chromatography (eluant: dichloromethane) which had b.p. 150°C/2 mm (Kugelrohr); δ 1.50 (6H, s), 1.80 (3H, broad s, vinylic CH_3), 2.00 (3H, s, CH_3CO), 2.40 (5H, m), 6.90 (1H, m); ν(film) 1720, 1670, 1370, 1260, 1135, 1020cm^{-1} (Found: C, 68.37; H, 8.53. Calc. for $C_{12}H_{18}O_3$:C, 68.55; H, 8.63%).

8-Acetoxy-2,6-dimethyldeca-2E,6E-dien-1-al (19) - Geraniolacetate provided the aldehyde 19 which was eluted with dichloromethane. This product was an oil with b.p. 160°/15 mm (Kugelrohr); δ 1.66 (6H, 9 + 10 CH_3), 2.00 (3H, s, CH_3CO), 2.16 (2H, t, J = 7 Hz), 2.40 (2H,m), 4.50 (2H, d, J = d, J = 7 Hz), 5.33 (1H, t, J = 7 Hz), 6.42 (1H, t, J = 7 Hz), 9.37 (1H, s, CHO); ν(film) 1725, 1675, 1230, 1025 cm^{-1}; m/z 150 ($M-CH_3CO_2H^+$). Lit.[3] for NMR of similar compounds.

5-Decen-4-one (21) - Oxidation of trans-5-decene followed by chromatography (eluant: dichloromethane) gave the enone 21 as a colourless oil with δ 6.1 (1H, d, J = 17.5 Hz, 6.8 (1H, d t, J_1 = 17.5 Hz, J_2 = 7 Hz 6H). Lit.[15] δ (CCl_4) 6.1 (1H, d, J = 16 Hz), 6.8 (1H, d t, J_1 = 16 Hz, J_2 = 7 Hz).

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