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TRANSITION METAL(II) SCHIFF'S BASE COMPLEXES CATALYZED OXIDATION OF trans-2-(1-PROPENYL)-4,5-METHYLENEDIOXYPHENOL TO CARPANONE BY MOLECULAR OXYGEN

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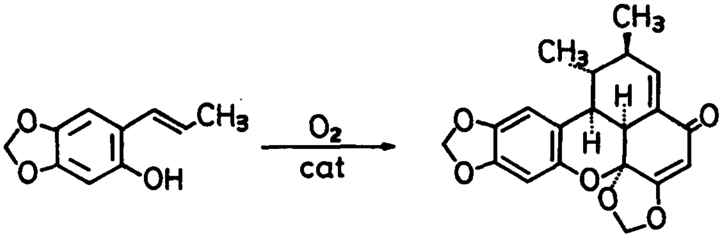
Summary: Carpanone was synthesized in an excellent yield by the oxidation of trans-2-(1-propenyl)-4,5-methylenedioxyphenol with molecular oxygen in the presence of transition metal complexes such as Co(II)salen, Co(II)salpr, Fe(II)salen, and Mn(II)salen.

The oxidation of phenols has received much attention and the oxidative phenolic coupling has become one of the most important synthons in organic synthesis.[1] Although molecular oxygen is known to oxidize phenolic compounds in the presence of a catalyst, there have been few examples where it is used as an oxidant in the synthesis of natural products, such as lignans and isoquinoline alkaloids, by the oxidative phenolic coupling. We applied metal catalyzed oxidation by molecular oxygen to the synthesis of carpanone (1), a lignan obtained from the bark of the carpano tree.[2,3]

We used Co(II)salpr (2a) as a catalyst, which is known to bind molecular oxygen reversibly and to be active in the oxidation of substituted phenols by



3 1

molecular oxygen.[4] A solution of *trans*-2-(1-propenyl)-4,5-methylenedioxyphenol (3) (300mg) and the complex 2a (15mg) in dichloromethane (5ml) was stirred under an oxygen atmosphere (1 atm) at room temperature for 1.5 h. The reaction mixture was concentrated and chromatographed on Al_2O_3 (Woelm Neutral, activity grade IV). Elution with hexane - dichloromethane (1:1) gave the desired carpanone (1)[5] as colorless crystals in a 90% yield.[6] When similar oxidation of 3 was made by the use of such catalyst as Co(II)salen (2b), Fe(II)salen (2c), and Mn(II)salen (2d), 1 was produced in high yield as shown in the Table.[7] It is worth pointing out that 2b and 2c were active in the present system, though they have been reported to be inactive in the autooxidation of phenols.[8] On the other hand, the stoichiometric oxidation of 3 with Fe(III) salts such as $FeCl_3$ and $K_3Fe(CN)_6$ gave scarcely fruitful results, although they are often used in the synthesis of isoquinoline alkaloids.

In the reaction by metal(II) Shiff's base complexes, the initial step in the catalytic oxidation is reasonably considered to be hydrogen abstraction or one-electron transfer which takes place *via* M(II)-O_2 complexes (M = Co, Fe, Mn), as has been mentioned in the cases of Co(II)salpr and Co(II)salen-py by Nishinaga.[4] In the present catalytic reaction, M(II)-O_2 may oxidize one

Table Synthesis of Carpanone (1) by the Oxidation of Phenol 3

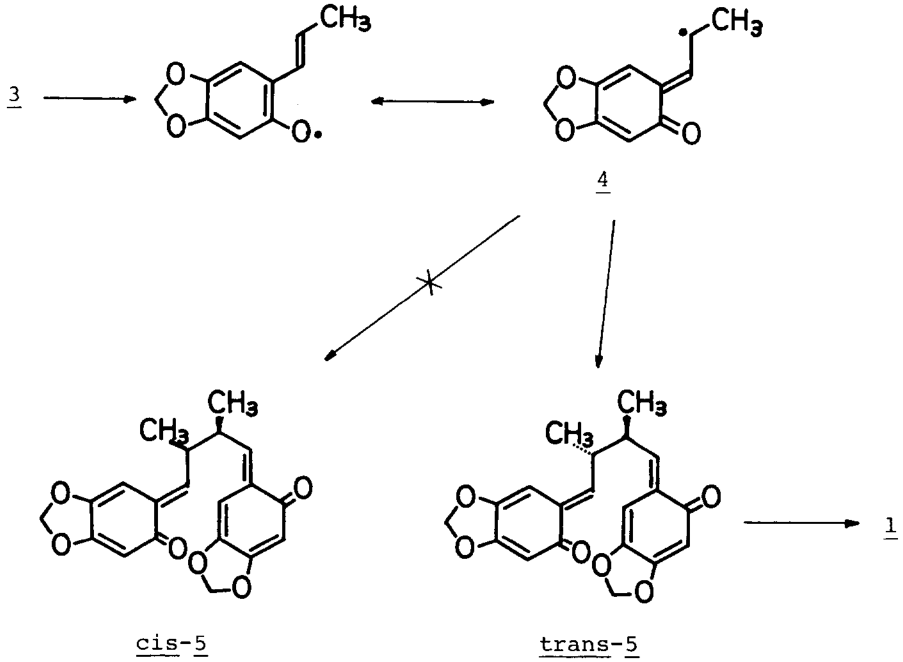
Oxidant	Catalyst	Yield (%)
O_2	Co(II)salpr (2a)	90
O_2	Co(II)salen (2b)[7]	94
O_2	Fe(II)salen (2c)[7]	78
O_2	Mn(II)salen (2d)[7]	80
$PdCl_2$ - NaOAc[3]	-----	46(62)
O_2 / hν / TPP[9]		29
BPO[10]	-----	40
ABIN[10]	-----	14

salpr:
bis(3-salicylideneaminopropyl)amine

salen:
bis(salicylidene)-ethylenediamine

molecule of 3 to a radical 4 and resulting reduced species such as $M(II)-O_2^-$ may produce another 4. Thus, the results described here show that there is no necessity for produce two molecules of 4 at the same time by two-electron oxidant such as Pd(II).

To form carpanone (1), which has five contiguous asymmetric centers, two intermediary radicals 4 must couple together and give the bis-o-quinonemethide trans-5 not but cis-5 with required stereochemistry, as has been shown by Chapman.[3] This demand may be satisfied merely by the intrinsic steric and electronic characters of the radical 4 with no aid of the metal complexation. The suggestion was confirmed by the facts that both the sensitized photo-oxidation[9] and the radical hydrogen abstraction[10] of 3 gave carpanone in the moderate yields. The quinonemethide trans-5 may undergo suprafacial 4π + 2π intramolecular cycloaddition to afford carpanone with correct stereochemistry. In these oxidation systems, intermediary quinonemethide 5 was not detected even at the early stage of the reaction, so that the intramolecular cyclization probably is a rapid reaction. In the biochemical system, carpanone may also arise from simple coupling of 4 formed by the oxidation of carpacin[2] or its demethylated compound 3.



We described here a successful application of autooxidation of phenols by transition metal catalyst to a lignan sysnthesis. Further applications will be expected in the field of organic synthesis by the use of oxidative phenolic coupling.

References and Notes

1. For a review, see T. Kametani and K. Fukumoto, Synthesis, **1972**, 657.
2. G. C. Brophy, J. Mohandas, M. Slaytor, S. Sternhell, T. R. Watson, and L. A. Wilson, Tetrahedron Lett., **1969**, 5159.
3. Carpanone has been systhesized by Pd(II) oxidation of **3** in a yield of 46 (62)%; O. L. Chapman, M. R. Engel, J. P. Springer, and J. C. Clardy, J. Amer. Chem. Soc., **93**, 6696 (1971).
4. A. Nishinaga, K. Watanabe, and T. Matsuura, Tetrahedron Lett., **1974**, 1291. and references cited therein.
5. Mp. 210°C (Lit.[2] mp 210 - 212°C): NMR, IR, and Mass spectral data of synthetic **1** were compared with those[2] of natural **1** and their identity was established.
6. Together with **1**, a slight amount of another product, which may be a configurational isomer of **1**, was obtained.
7. Pyridine (15mg) was added to the reaction system.
8. L. H. Vogt, Jr., J. G. Wirth, and H. L. Finkbeiner, J. Org. Chem., **34**, 273 (1969).
9. A solution of **1** (300mg) and tetraphenylporphine (5mg) in dichloromethane (15ml) was irradiated with Na vapor lamps (60W x 8) under an oxygen atmosphere at 5°C.
10. The phenol **3** was heated with an equimolar amount of a radical initiator such as azobisisobutyronitrile (ABIN) and dibenzoyl peroxide (BPO) in benzene or CCl_4.

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