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LIGAND EFFECT IN EPOXIDATIONS BY HYDROPEROXIDES USING MOLYBDENUM CATALYST: EPOXIDATION OF 3-CARENE+

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Abstract — Epoxidation of (+)-3-carene with pinane hydroperoxide in presence of various transition metal catalysts, has been evaluated as a preparative method for (+)-3α,4α-epoxycarane. Catalysts based on Mo(VI) were found to be most suitable. A distinct ligand effect was noted for this oxidation and a plausible rationale is put forward.

Epoxidation of olefins by organic hydroperoxides in presence of certain transition metal catalysts, a reaction first described by Hawkins[1] in 1950, has in recent years, attracted considerable attention,[2] essentially because of industrial interest, such as in the production of propylene oxide.[3] In general, catalysts based on V(v), Mo(VI), W(VI) and Ti(IV) have been found to be effective, though Mo(VI) catalysts have proved to be generally superior,[4,5] except when the substrate is an allylic alcohol for which V(III) showed outstanding performance.[6]

In connection with the development of a suitable technology for the manufacture of (+)-carene oxide (3), a valuable intermediate for certain pyrethroids,[7] epoxidation of (+)-3-carene (1) by a suitable hydroperoxide appeared attractive. This route, using pinane hydroperoxide (2) as the oxidant, appeared all the more interesting since the co-product pinanol (4) is a valuable intermediate in the manufacture of linalool.[8] Preliminary experiments aimed at evaluating different transition metal catalysts[5] (Table 1, entries 1-3) gave only poor results, the best selectivity (3; 32%) being obtained with molybdenum oxyacetylacetonate {$MoO_2(acac)_2$}. In an effort to improve the yields of 3, a variety of molybdenum catalysts[4] were investigated and during the course of this investigation a distinct ligand effect for homogeneous catalysts was noted. These results, as well as, evaluation of the ligand effect in other hydroperoxide-olefin systems forms the subject matter

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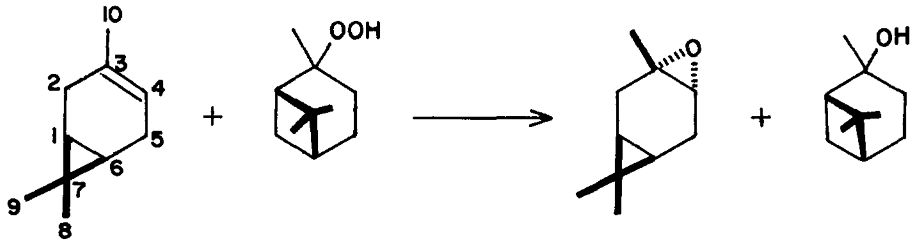


(1) (2) (3) (4)

of the present communication. At this stage it may be mentioned that in catalysts based on Mo(VI), the nature of the coordinating ligands is considered to be unimportant,[9] though evidence to the contrary has been obtained by another group.[10]

RESULTS AND DISCUSSION

From the results summarised for the system pinane hydroperoxide/carene in Table 1, it is clear that best yields were obtained with molybdenum stearate. A comparison of entries 3,8,9 (Table 1), representing essentially homogeneous

Table 1. Epoxidation with pinane hydroperoxide[a]

No.	Catalyst	Olefin			
		3-carene		2-Menthene[b]	
		Conversion[d] (%)	Selectivity[e] (%)	Conversion (%)	Selectivity (%)
1	TiO_2-on-SiO_2[c]	0	0		-
2	$VO(acac)_2$	93	15		-
3	$MoO_2(acac)_2$	91	32	77	23
4	MoO_3	60	63		-
5	Na_2MoO_4	0	0		-
6	MoS_2	54	67		-
7	$Na_4\{Mo_2O_6(EDTA)\}.8H_2O$[c]	0	0	0	0
8	Molybdenum stearate	85	60	76	23
9	$MoO_2(oxine)_2$	81	53	73	28

[a] The reaction was carried out without solvent, at 80$\pm$0.1° for 4 hr; pinane hydroperoxide (cis/trans: 4/1)

[b] cis/trans : 3/1

[c] These catalysts appeared to be practically insoluble in the reaction mixture, while others were completely soluble except for $MoO_2(oxine)_2$ which was only partly soluble.

[d] $$\text{Conversion (\%)} = \frac{\text{Moles of hydroperoxide consumed}}{\text{Moles of hydroperoxide taken}} \times 100$$

[e] $$\text{Selectivity (\%)} = \frac{\text{Moles of epoxide formed}}{\text{Moles of hydroperoxide consumed}} \times 100$$

reaction mixtures, reveals a distinct ligand effect. To see if such an effect is also valid for other systems, three more hydroperoxide-olefin systems were investigated and the results are summarised in Table 1 and Table 2. From these results it is clear that with 2-menthene, selectivity does not change significantly both for pinane hydroperoxide and tert-butyl hydroperoxide. On the other hand, when 3-carene is the substrate, a ligand effect is again observed, now using tert-butyl hydroperoxide as the oxidant, best selectivity (100%) being given by $MoO_2(oxine)_2$ (Table 2).

Mechanism of transition metal-catalyzed epoxidation of olefins by hydroperoxides has been quite extensively investigated and certain aspects of the mechanism are now fairly well-understood.[2,11-13] Epoxidation reaction is not a free radical reaction, and the epoxidation selectivity is determined by the rate of this reaction in competition with the homolytic decomposition of the hydroperoxide. It is generally agreed that a catalyst-hydroperoxide reversible complex is first formed, which is the active oxidant. Using ^{18}O-labelling it has been recently confirmed[11] that the epoxide oxygen arises from metal-alkylperoxide containing the intact alkyl peroxidic group. In the case of homogeneous catalysis based on metals containing an oxometal group (e.g., V, Mo), the active species may be represented by (5)[5,10a] or (6).[11-13] (Fig. 1). It may be noted that coordination of metal with peroxide oxygen remote from the alkyl group is preferred[11]. Two types of transition states for the epoxidation step have been proposed: (7),[5,11] which is reminiscent of epoxidation by organic peracids and , (8),[13] which places this reaction inside the scope of other metal-catalyzed transformations of olefins (Fig.2). Metal-alcohol complex (9) reacts further with the alkyl hydroperoxide to regenerate the oxidant (6/5) and produce the

Table 2. Epoxidation with tert-butyl hydroperoxide[a]

No.	Catalyst	Olefin			
		3-Carene		2-Menthene	
		Conversion (%)	Selectivity (%)	Conversion (%)	Selectivity (%)
1	$MoO_2(acac)_2$	87	73	66	46
2	Molybdenum stearate	80	68	59	44
3	$MoO_2(oxine)_2$	47	100	34	48
4	$Na_4\{MoO_6(EDTA)\}.8H_2O$	10	29	0	0

[a] See footnotes to Table 1.

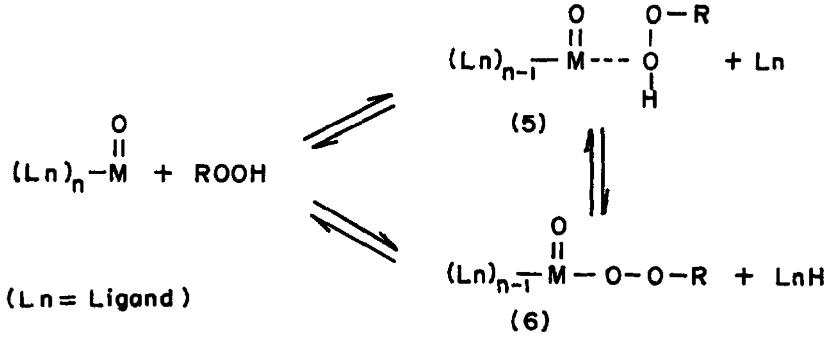


Fig. I

co-product of the reaction, the alcohol corresponding to the hydroperoxide.

The rôle of coordinating ligands in the epoxidation reaction has been discussed.[2] Since ligands should affect the Lewis acidity of the metal, one might expect a ligand effect. However, in practice, this has been found[5,2b,14] to be unimportant, (except for the initial stages of the reaction), due to rapid displacement of the original ligands by 1,2-diol derived from the epoxide, resulting in the formation of a new complex, such as (10), which takes over as the catalyst, irrespective of which compound was initially added as the catalyst. *This situation, however, need not prevail in every case.* Conceivably, in the case of certain cyclic olefins, the structure of the resulting 1,2-diol could be such as to inhibit the formation of a complex such as 10, due to geometrical constraints inherent in the 1,2-diol structure. We believe this is one of the factors responsible for the ligand effect we observe in the epoxidation of 3-carene. The epoxide

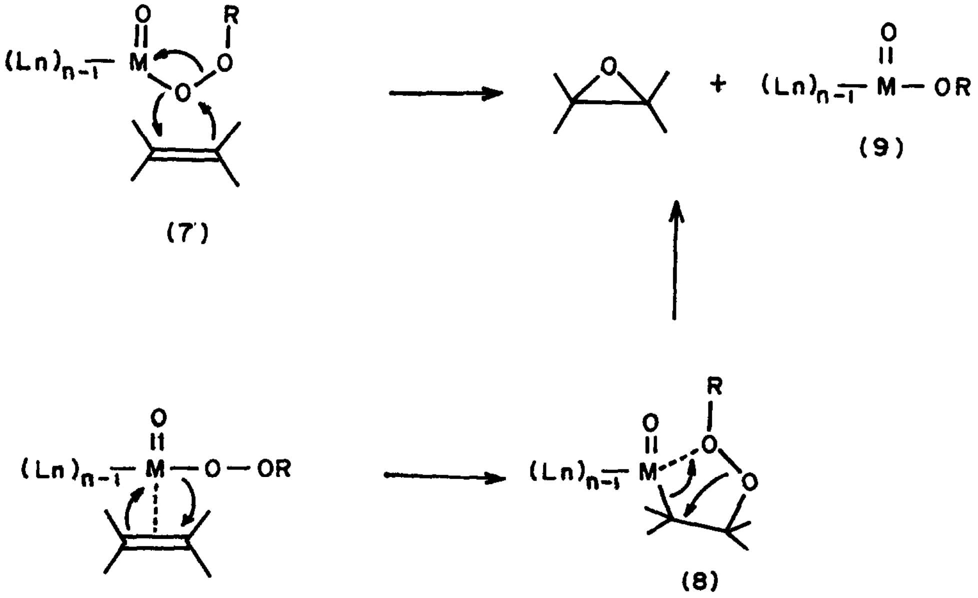


Fig.2

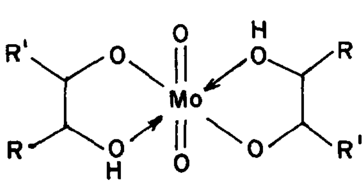
obtained in this oxidation was shown to have the expected α-epoxide structure (3).[15,16] From the known[15] chemistry of this oxide, it is clear that the diol involved in the generation of a complex of type 10 would be the *trans*-diol (11), geometrically ill-suited[17] for involvement in a 5-membered pseudocycle of the type envisaged in 10.

Another factor which would inhibit the formation of a diol-complex (10) relates to the mechanism of its formation. There is experimental evidence[5] to show that diol complexes of type 10 arise from reaction of Mo(VI) catalyst with the epoxide in presence of the hydroperoxide. If this is conceded, then attack of the Mo(VI) catalyst on the oxirane function in carene oxide (3), which should occur from the back-side (*cf.* 12), would be inhibited as the 8-Me group and the two axial-type hydrogens at C-2 and C-5 would tend to block the approach of the bulky nucleophile.

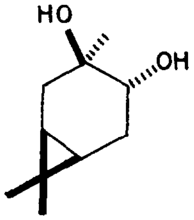
Thus, both these factors would operate so as to preserve the identity of the original ligands in the 3-carene/alkylhydroperoxide system, leading to a ligand effect. It may be noted that both of these factors are unimportant in the case of 2-menthene, where practically no such effect was encountered. It may thus be concluded that a ligand effect may be expected, when stereochemical factors inhibit the loss of identity of the original ligands.

EXPERIMENTAL

B.ps are uncorrected. GLC were carried out on Hewlett-Packard 5712A and 7624A gas chromatographs (Al columns, 360 cm x 0.6 cm; support, 60-80 mesh Chromosorb W; carrier gas, H_2).



(10)



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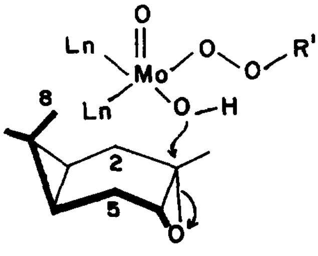

(12)

Materials

(a) *Olefins*. 3-Carene was freshly distilled (b.p. 110°/100 mm, n_D^{25} 1.4718) and was at least 95% pure by GLC (10% Carbowax 20M, 100°, 60 ml H_2/min). 2-Menthene (b.p. 104°/100 mm, n_D^{25} 1.4502) was 92-94% pure by GLC (same conditions) and was a mixture of *cis/trans* isomers (3/1).

(b) *Hydroperoxides*. *tert*-Butyl hydroperoxide was prepared by a known procedure[19] and purified further[20] to get a product of 90% purity. Air oxidation of pinane, according to a known[21] procedure, led to a material containing 17-20% hydroperoxide. This was concentrated in a falling-film evaporator at 95°/1 mm to get a 70% concentrate. Further concentration was achieved as follows: To the cooled (~0°) and stirred 70% pinane hydroperoxide (72 g), was slowly added 50% NaOH aq (25 g) so that the temp did not exceed 10°(~2 hr). After stirring for an additional 15 min, light petroleum (b.p. 60-80°; 100 ml) was added to remove, by decantation, soluble material. This operation was repeated eight times with 25 ml of light petroleum every time. To the residue, light petroleum (75 ml) was added, followed by 50 ml of H_2O and CO_2 gas was bubbled till pH of aq. phase became 8. Work up of the organic phase and removal of solvent at ~80 mm in a current of N_2 furnished pinane hydroperoxide (20 g) of 88% purity.

(c) *Catalysts*. Molybdenum oxide (B.D.H) and sodium molybdate (SD's Lab-Chem) were of analytical grade, while molybdenum sulphide (Riedel De Haen) was of laboratory reagent grade. Molybdenum dioxyacetylacetonate,[22] molybdenum oxinate[23], molybdenum-EDTA[24], and molybdenum stearate[25] were all prepared as per directions given in the cited references, and the products had the reported characteristics (physical appearance/m.p., IR).

Epoxidation procedure

The catalyst (amount equiv. to 0.002 g atom of Mo), olefin (0.025 mole) and the alkyl hydroperoxide (0.01 mole, 100% hydroperoxide content) were introduced into a 50 ml RB flask in that order. The flask was fitted with a reflux condenser and the reaction mixture heated in a thermostat at 80 ± 0.1° under magnetic stirring for 4 hr. After this period, the reaction mixture was cooled by tap water and a sample analysed iodometrically for peroxide content.

A weighed amount (4.0 g) of the above reaction product was taken in a 50 ml Erlenmeyer flask, rectified spirit (4 ml) was added followed by $NaBH_4$ (0.2 g). The reaction mixture was kept aside for 1/2 hr at room temp. (25°) with occasional swirling, when the peroxide test (ferrous thiocyanate) became negative. The material was transferred with the aid of ether (30 ml + 10 ml x 3) to a separating funnel and washed with water (5 ml x 3) and brine (2 ml). The washings were combined and extracted with one 10 ml portion of ether and washed with water (5 ml x 1) and brine (2 ml). This was mixed with the original ether extract and dried ($MgSO_4$, 500 mg). The desiccant was filtered off and washed with ether (3 ml x 2). The combined ether soln was freed (Vigreux column) of solvent and the residue distilled at 2 mm upto 140^{o} (bath temp.). The wt. of the product was taken and the material analysed by GLC (10% Carbowax 20M, 170^{o}, 60 ml/min; RRT: carene/carene epoxide/*trans*-pinanol/*cis*-pinanol = 1.00/3.57/4.57/5.43).

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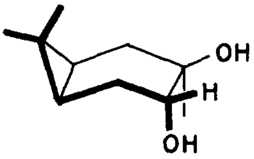
[16] The term α (or β) is used with respect to the way the structures have been drawn in this paper.

[17] An examination of molecular models (Dreiding) shows that the diol should have the preferred conformation (i); in all other possible alternatives, there is a severe interaction of the

8-Me group either with the O of hydroxyl at C-3 or with H at C-4. This diol is also known to be resistant to cleavage by lead tetraacetate,[18] a reaction requiring intermediacy of a 5-membered ring.



(i)

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