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COBALT MEDIATED CYCLISATIONS OF EPOXY OLEFINS

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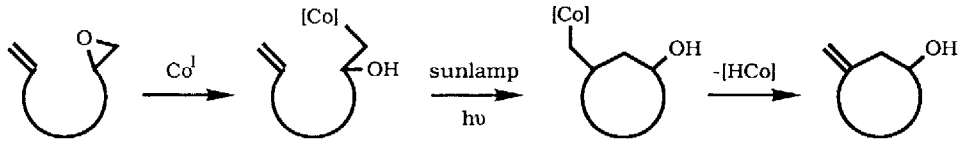
Summary: Irradiation of solutions of β-hydroxycobaloximes *e.g.* (2), (5), (9) and (13) derived from epoxy olefins [*e.g.* (1), (8) and (12)] and cobalt(I) dimethylglyoxime, using a *sunlamp* at room temperature, leads to facile cyclisation producing cycloalkanols *e.g.* (4), (6), (10) and (14). By contrast, only the products *viz* (3), (7) and (11) of dehydrocobaltation are produced when the same β-hydroxycobaloximes are *heated* under reflux in benzene.

Epoxides are central intermediates in a wide range of useful synthetic transformations. Their status in synthesis has been enhanced enormously in recent years with the discovery by Sharpless that chiral epoxides can be obtained in a convenient manner by the reaction that now bears his name - arguably the most significant development in synthesis methodology in the past decade.[1] Illustrations of the importance and use of chiral epoxide precursors in all aspects of synthesis abound in the contemporary literature. In recent extensive studies we have developed the scope and applications of a wide range of cobalt mediated radical reactions for effecting carbon-to-carbon and carbon-to-hetero atom bond forming reactions, together with the synthesis of carbo- and heterocyclic ring forming processes.[2] In these investigations the required organocobalt reagents, *e.g.* alkyl, vinyl, acyl, carbamyl, have been produced either from alkyl (acyl) halide precursors following nucleophilic substitution with cobalt(I) reagents, or *via* hydrocobaltation reactions of alkene and acetylene intermediates. We have now examined the reactivity of epoxides towards nucleophilic cobalt(I) and the use of the resulting β-hydroxycobalt reagents in synthesis.[3] In this *Letter* we summarise our preliminary results with ω-epoxy olefins and cobalt(I) dimethylglyoxime, and show that a variety of cycloalkanols can be obtained conveniently and in high yield following cyclisations of the intermediate β-hydroxycobaloximes (Scheme).

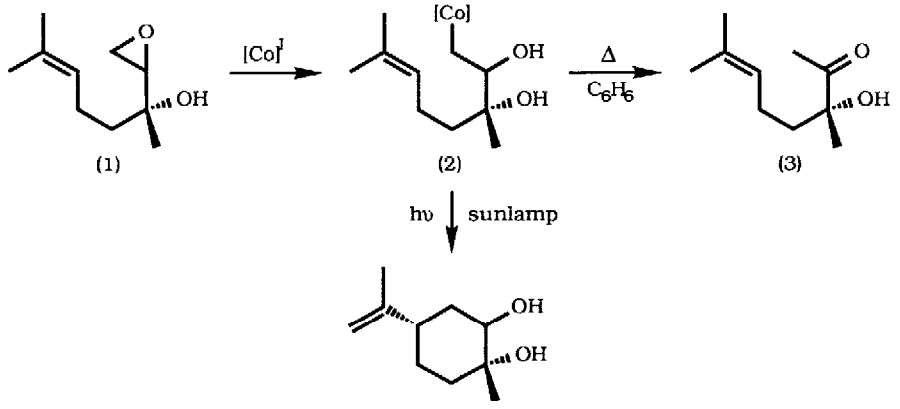


Scheme

We first examined the cobalt mediated cyclisation of the epoxy-alcohol (1) obtained from linalool. Thus, treatment of (±)-(1) with cobalt dimethylglyoxime (from $CoCl_2$, dimethylglyoxime, in MeOH-NaOH-C_5H_5N, under H_2) was found to be regioselective and led to the corresponding β-hydroxy-cobaloxime (2) resulting from ring opening at the sterically more accessible carbon centre in the epoxide (1); the β-hydroxycobaloxime was secured as a stable yellow powder m.p. 165°C (dec.) in 80% yield.[4] When a solution of (2) in benzene was heated under reflux, work-up led to a high (85%) yield of the

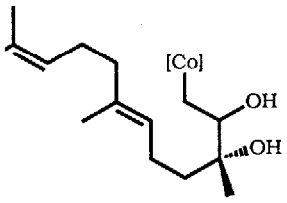
methyl ketone (3) resulting from dehydrocobaltation-tautomerism. However, when the β-hydroxycobaloxime (2) was irradiated with a 300 watt sunlamp *at room temperature*, only trace amounts (~2%) of (3) were observed and the major product was the anticipated cyclohexane-1,2-diol (4) (94%)[5].

In similar manner, the β-hydroxycobaloxime (5) derived from nerolidol produced the cyclohexanediols (6) (87%) on irradiation of benzene solutions at room temperature, whereas heating the solutions at reflux gave rise to only the corresponding ketone (7) (80%). Likewise the β-hydroxycobaloxime (9) produced from the epoxide (8)[5] led to the cyclohexanol (10) (51%) on irradiation at room temperature, and the ketone (11) (86%) on heating in benzene. The dramatic effect that temperature has in determining the products of the aforementioned reactions, no doubt reflects the relative ease of dehydrocobaltation over radical cyclisation from the β-hydroxycobaloximes at the elevated temperatures. Studies of the mechanism of dehydrocobaltation (β-elimination)[6] from organocobalt compounds have demonstrated that this is largely a *syn* process. We believe that in the cases studied here, an increase in temperature increases the population of those rotamers in the starting β-hydroxycobaloximes in which the cobalt and β-hydrogen atoms adopt a *syn*-periplanar relationship for facile dehydrocobaltation. At room temperature however, homolysis of the carbon-to-cobalt bond in the β-hydroxycobaloxime occurs upon irradiation leading to an intermediate carbon radical. Rapid 6-*exo*-trigonal cyclisation followed by dehydrocobaltation from the product radical centre then leads to the cyclic product. The unique dichotomous reaction pathway followed by the β-hydroxycobaloximes (2), (5) and (9), *i.e.* heat leading to dehydrocobaltation and light producing products of cyclisation is, to our knowledge, unprecedented.[7]



We have also examined the cyclisations of the organocobalt reagents (13) and (17) produced from cobalt(I) mediated ring opening of the corresponding epoxides (12) and (16) respectively. Thus, irradiation of (13) at room temperature in benzene led to a 63% yield of the volatile cyclopentanol (14) resulting from the anticipated 5-*exo*-trigonal mode of cyclisation. Interestingly, irradiation of the β-hydroxycobaloxime (13) in the presence of tetramethylpiperidine oxide[8] under high dilution allowed us to produce the product (15) resulting from cyclisation and simultaneous trapping of the product radical centre.

Treatment of the epoxide (16) with cobalt dimethylglyoxime under the usual conditions but with the



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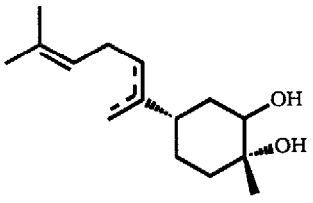

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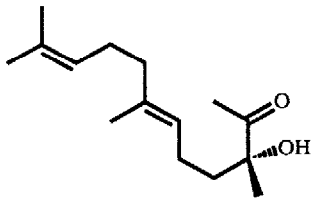

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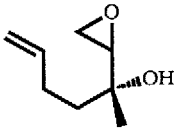

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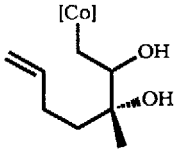

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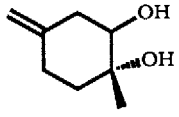

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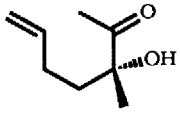

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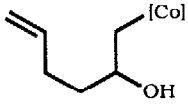

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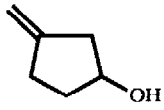

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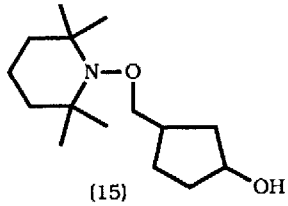

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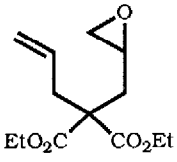

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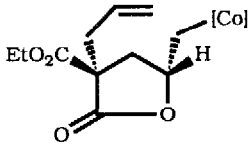

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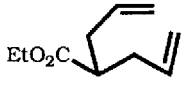

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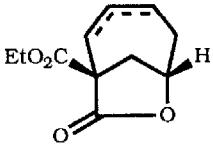

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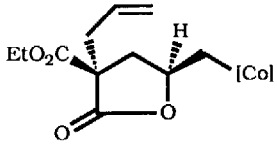

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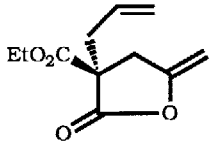

(21)

[Co] = $Co(dmgH)_2py$

addition of pyridine after 2h, led to a 5:4 mixture of diastereoisomers of the lactone cobaloxime (17) which results from transesterification in the first-formed β-hydroxycobaloxime product. When solutions of the mixtures of diastereoisomers of (17) in either benzene or toluene were heated under reflux for 24h the starting materials were recovered unchanged. However in pyridine under reflux for 14h decobaltation-decarboxylation resulted leading to the diene ester (18). Finally, irradiation of solutions of the mixtures of diastereoisomers in methanol at room temperature produced the product (19) of 7-*endo*-cyclisation (35-40%) together with the 'resolved' diasteroisomer (20) of the starting material (30-40%), while in benzene the cyclised material (19) was accompanied by the product (21) of dehydrocobaltation (20%)

Further studies are now in progress to (i) delineate the principles governing the dichotomous pathway followed by the β-hydroxycobaloximes mentioned here under thermal and irradiation conditions, and (ii) extend the scope of epoxy olefin cyclisation reactions in target synthesis.

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1. See (a) K.B. Sharpless and T.R. Verhoeven, *Aldrichimica Acta*, **1979**, *12*, 63; (b) A. Pfenninger, *Synthesis*, **1986**, 89.
2. See G. Pattenden, *Chem. Soc. Rev.*, **1988**, *17*, 361, and references cited therein. See also (a) G.B. Gill, G. Pattenden and S.J. Reynolds, *Tetrahedron Lett.*, **1989**, *30*, 3229; (b) A.R. Howell and G. Pattenden, *J. Chem. Soc., Chem. Commun.*, **1990**, 103.
3. For some earlier studies of the reaction between epoxides and cobalt(I) species, including mechanistic aspects see (a) H. Su, L. Walder, Z.-d. Zhang and R. Scheffold, *Helv. Chim. Acta*, **1988**, *71*, 1073; (b) G.N. Schrauzer and R.J. Windgassen, *J. Am. Chem. Soc.*, **1966**, *89*, 143; (c) F.R. Jensen and R.C. Kiskis, *J. Am. Chem. Soc.*, **1975**, *97*, 5825.
4. All new compounds showed satisfactory spectroscopic data together with microanalytical or mass spectrometry data.
5. The cobaloximes (2), (5), and (9) were obtained as 3:2 mixtures of diastereoisomers, reflecting the ratio of epimers of the epoxide precursors *e.g.* (1) and (8) used in their synthesis (see D.J. Morgans, Jr., K.B. Sharpless and S.G. Traynor, *J. Am. Chem. Soc.*, **1981**, *103*, 462). Furthermore, the cyclisations of the cobaloximes to the corresponding cyclohexane-1,2-diols *e.g.* (4) and (6) proceeded with almost complete stereocontrol at the C-4 centre, but the diols were obtained as ca 3:2 isomeric mixtures at their C-1, C-2 centres. These conclusions followed from inspection of n.m.r. spectroscopic data and comparison with reported literature data; see (a) P. Crews and E. Kho-Wiseman,*Tetrahedron Lett.*, **1978**, 2483; (b) E. Murayama and T. Sato, *Bull. Chem. Soc. Jpn.*, **1978**, *51*, 3022; *e.g.* the cyclohexandiol (4; major isomer) had δ_H 4.7 (2H), 3.41 (dd, *J* 11.4 and 4Hz, CHOH), 2.25 (OH), 1.95 (m, 1H), 1.9-1.7 (3H), 1.5 (m, CMe), 1.27 (CMe); δ_C 149.0, 108.9 (t), 75.2 (d), 70.9, 43.7 (d), 37.3 (t), 35.6 (t), 27.2 (q), 26.2 (t), 20.8 (q), p.p.m.
6. (a) K.N.V. Duong, A. Ahond, C. Merienne and A. Gaudemer, *J. Organomet. Chem.*, **1973**, *55*, 375; (b) P.J. Toscano and L.G. Marzilli, *Prog. Inorg. Chem.*, **1984**, *31*, 105.
7. For an interesting complementary study of the cyclisations of 6,7-epoxy-1-heptenes in the presence of titanium (III) species leading to *cyclopentane* derivatives see W.A. Nugent and T.V. RajanBabu, *J. Am. Chem. Soc.*, **1988**, *110*, 8561.
8. See reference 2 and also E.G. Samsel and J.K. Kochi, *J. Am. Chem. Soc.*, **1986**, *108*, 4790.

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