Regioselective Hydroxylations of 1,3-Dienes *via* Hydrocobaltation Reactions. Facile Conversion of Myrcene to Geraniol and to (±)-Linalool

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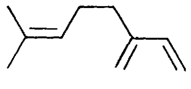
Regioselective (1,4-) hydrocobaltation of myrcene (**1**) leads to a 2 : 1 mixture of (*E*)- and (*Z*)-allylcobaloximes (**2**) which can be converted *via* the corresponding hydroxylamines (**5**) to geraniol (**6a**) and nerol (**6b**); by contrast, in the presence of molecular oxygen, (**2**) is converted into the peroxyallylcobalt complex (**7**), a precursor to linalool (**8**) and to linalool oxide (**10**).

In previous studies we have demonstrated the enormous scope for alkyl, acyl, and carbamyl cobalt complexes, based on vitamin B_{12}, in the synthesis of a range of functionalised carbo- and hetero-cyclic ring systems *via* inter- and intra-molecular oxidative free-radical carbon-to-carbon bond forming reactions.[1,2] In related work, we have also shown that cross-coupling reactions between two alkenes can be smoothly accomplished by 'hydrocobaltation' of one of the alkenes followed by homolysis of the resulting organocobalt reagent in the presence of the second alkene substrate.[3] We have now embarked on a program to examine the selectivity of hydrocobaltation reactions of 1,3-dienes and the uses of the resulting allylcobalt complexes in synthesis. In this communication we show how this chemistry can be combined to provide useful and interesting conversions of myrcene (**1**) to geraniol (**6**), to (±)-linalool (**8**) and to linalool oxide (**10**).

Thus, hydrocobaltation of myrcene (**1**), using cobalt dimethylglyoxime (from $CoCl_2$ and dimethylglyoxime in MeOH containing pyridine and NaOH) in the presence of hydrogen, proceeded in a regioselective (1,4-addition) fashion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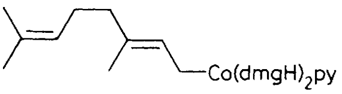

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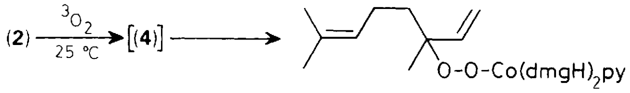

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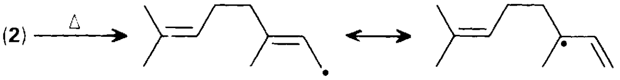

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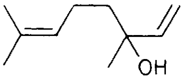

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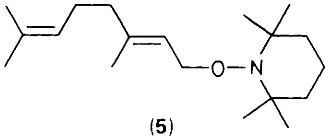

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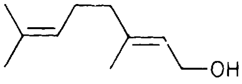

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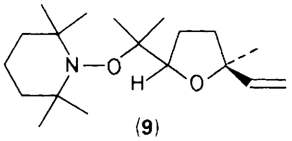

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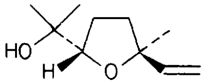

(10)

a; (*E*)-isomer; b; (*Z*)-isomer
(dmg = dimethylglyoximato,
py = pyridine)

and gave rise to a 2 : 1 mixture of geranyl [(**2a**); δ 1.25 (:CMe), 2.42 (d, *J* 9.5, CH_2Co)] and neryl cobaloximes [(**2b**); δ 1.16 (:CMe), 2.45 (d, *J* 9.5, CH_2Co)], which was isolated as a stable, orange solid, m.p. 85 °C (decomp.) in 60—70% yield.[4,5] When a solution of this orange solid in toluene was heated under reflux for 0.25 h in the presence of tetramethylpiperidine oxide (TEMPO), work-up and chromatography led to a 2 : 1 mixture of the corresponding (*E*)-(**5a**) and (*Z*)-hydroxylamines (**5b**) in a combined yield of 55%.[6] The hydroxylamines (**5**) result from selective trapping by TEMPO at the primary radical centre (**3a** and **3b**) in the intermediate allyl radical produced on thermal homolysis of (**2**). Reduction of the mixture of hydroxylamines (**5**), using zinc dust in 50% aqueous acetic acid at 100 °C, finally gave geraniol (**6a**) and nerol (**6b**) in a combined yield of 60%.[7]

In contrast to the outcome of the reaction between the cobaloxime (**2**) and TEMPO, when a solution of (**2**) in dichloromethane containing dissolved oxygen was left to stand at 25 °C for 48 h, chromatography separated the corresponding linalool peroxycobaloxime [(**7**), green powder, m.p. 185 °C (decomp.); 35%] resulting from 'insertion' of triplet oxygen between the cobalt centre and the tertiary allyl carbon centre in (**2**) [possibly *via* (**4**)].[8] This dichotomy in reactivity no doubt reflects the relative steric demands of TEMPO and O_2, with the larger TEMPO reagent precluding attack at the tertiary radical centre in (**4**). When the linalool peroxycobalt complex (**7**) was reduced with sodium borohydride in methanolic sodium hydroxide, (±)-linalool (**8**) was produced (40%).

When a solution of (**7**) in toluene was heated at 100 °C in the presence of TEMPO for 0.25 h, chromatography separated the diastereoisomers of the 1 : 1 mixture of tetrahydrofuran-methanol–TEMPO adducts [(**9**) 46%] as colourless oils.[9] Reduction of each of the adducts (Zn dust, aq. HOAc) then produced (±)-linalool oxide [(**10**), 60%] and the corresponding *syn*-diastereoisomer.

Further work is now in progress to evaluate the use of hydrocobaltation reactions in the selective functionalisations of other 1,3-dienes, and also to exploit the uses of alternative allyl radicals in general synthesis.[10]

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References

1 See G. Pattenden, *Chem. Soc. Rev.*, 1988, **17**, 361, and references cited therein.
2 G. B. Gill, G. Pattenden, and S. J. Reynolds, *Tetrahedron Lett.*, 1989, **30**, 3229.
3 V. F. Patel and G. Pattenden, *J. Chem. Soc., Chem. Commun.*, 1987, 871; H. Bhandal and G. Pattenden, *ibid.*, 1988, 1110.
4 *Cf.* A. E. Crease, B. D. Gupta, M. D. Johnson, E. Bialkowska, K. N. V. Duong, and A. Gaudemer, *J. Chem. Soc., Perkin Trans. 1*, 1979, 2611.
5 For recent studies of selective hydrogenations of 1,3-dienes in the presence of cobalt complexes see: T. Nakayama and H. Kanai, *Bull. Chem. Soc. Jpn.*, 1985, **58**, 16, and references cited therein.
6 For other studies of allylcobaloximes see ref. 4 and: D. Dodd and M. D. Johnson, *J. Am. Chem. Soc.*, 1974, **96**, 2279; A. Bury, C. J. Cooksey, T. Funabiki, B. D. Gupta, and M. D. Johnson, *J. Chem. Soc., Perkin Trans. 2*, 1979, 1050; C. J. Cooksey, D. Dodd, M. D. Johnson, and B. L. Lockman, *J. Chem. Soc., Dalton Trans.*, 1978, 1814; M. Veber, K. N. V. Duong, F. Gaudemar, and A. Gaudemar, *J. Organomet. Chem.*, 1979, **177**, 231; M. R. Ashcroft, B. D. Gupta, and M. D. Johnson, *J. Chem. Soc., Perkin Trans. 1*, 1980, 2021; M. D. Johnson, *Acc. Chem. Res.*, 1983, **16**, 343, and references cited therein.
7 For an example of the use of π-allylpalladium complexes of myrcene in the synthesis of nerol and citral see: M. Takahashi, H. Urata, H. Suzuki, Y. Moro-oka, and T. Ikawa, *J. Organomet. Chem.*, 1984, **266**, 327.
8 The formation of (**7**) from (**2**) could also occur through a six-centred transition state *via* a radical equivalent of a cobalt-ene reaction, or alternatively through rearrangement of an initially formed geranyl/neryl peroxycobalt complex.
9 For recent studies of allyloxy radicals in tetrahydrofuran synthesis see: A. Johns and J. A. Murphy, *Tetrahedron Lett.*, 1988, **29**, 837, and references cited therein.
10 *E.g.* N. J. G. Cox, G. Pattenden, and S. D. Mills, *Tetrahedron Lett.*, 1989, **30**, 621.