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RADICAL REACTIONS IN SYNTHESIS. HOMOLYSIS OF ALKYL COBALT SALOPHENS IN THE PRESENCE OF RADICAL TRAPPING AGENTS.

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Summary: Photolytic homolysis of the alkyl cobalt 'salophens' (10), (20a) and (20b) in the presence of radical trapping agents e.g. O_2, TEMPO, NO, SO_2, PhSSPh, PhSeSePh, $MeSO_2Cl$, $BrCCl_3$ and I_2, leading to oxygen, nitrogen, sulphur, selenium and halogen functionalised products, is used to demonstrate the versatility of cobalt-mediated radical reactions in synthesis.

Free radical carbon-to-carbon bond forming reactions have now become part of the day to day armoury of the synthetic chemist. The use of carbon radicals in the elaboration of carbo- and hetero-cyclic molecules is particularly illustrative, and has provided a new dimension in this important area.[1] The versatility of radical initiated carbon-to-carbon bond forming reactions would be enhanced still further if practical procedures could be developed to introduce functionality in concert with C- C bond formation, using appropriate radical trapping agents.[2]

In earlier work we have highlighted the importance and use of intra-molecular oxidative free radical cyclisations, using cobalt reagents, in the synthesis of butyrolactones and reduced heterocycles.[3,4] These reactions proceed via Co(I)-mediated radical cyclisations, followed by in situ trapping of the product radical centre(2) with Co(I), and 1,2-elimination of Co-H(Scheme); in some circumstances the intermediate organo-cobalt complexes, viz (5), can be isolated and characterised. In this Letter, we demonstrate further scope for these reactions in synthesis, and show how the intermediate organo-cobalt complexes (5 ; Scheme) can be employed to synthesise oxygen, nitrogen, sulphur, selenium and halogen substituted adducts of the type (3).[5]

Treatment of the iodoaryl-allyl ether (7) with the cobalt 'salophen' reagent (8) (1% NaHg, THF, 25°C, dark)[6] resulted in smooth 5-exo trig aryl radical cyclisation followed by in situ trapping of the product radical centre (9) leading to the cobalt complex (10; 70%) which crystallised from pyridine-water as a black crystalline solid mp>350°C.[7] Irradiation of a refluxing solution of (10) in methylene chloride under nitrogen, using a 300W sunlamp, led to (11) *via* 1,2-elimination of H-Co, whereas irradiation of the solution of (10) in the presence of air, followed by reduction of the intermediate peroxy-cobalt complex produced the carbinol (12*a*, 25% overall).[4] A more practical procedure for inserting oxygenation at the product radical centre(9) was by irradiation of the organo-cobalt intermediate in the presence of tetramethylpiperidino oxide (TEMPO)[8] followed by reduction of the resulting adduct (13) using zinc in acetic acid; in this manner overall yields of 75% were realised for the conversion of (10) to the carbinol acetate (12*b*).

The incorporation of nitrogen at the product radical centre (9) resulting from cyclisation of (7) was readily accomplished when a solution of the corresponding 'trapped' organo-cobalt intermediate (10) in dimethylformamide containing triethylamine was irradiated in the presence of nitrogen monooxide. This procedure led to a 1:1 mixture of *Z*- and *E*-isomers of the oxime (14; 78%) which could then be reduced to the corresponding amine (15) using sodium in *iso*-propanol.

In a similar manner, irradiation of solutions of (10) in the presence of diphenyldisulphide or diphenyldiselenide produced the corresponding substituted sulphide (16*a*; 85%) and selenide (16*b*; 75%) respectively, and halogen could be introduced at the product radical centre (9) by treatment of the organo-cobalt intermediate (10) with either methanesulphonyl chloride (to 17*a*; 78%), bromotrichloromethane (to 17*b*; 79%), or iodine (to 17*c*; 42%). A less practical way to introduce sulphur at the product radical centre in (9) was by irradiation of (10) in the presence of sulphur dioxide,[9] followed by acid work-up of the intermediate cobalt sulphone (18); only low yields (20% overall) of the sulphinic acid (19) were realised by this method.

As a corollary to these studies with the cobalt salophen reagent (10), we also examined briefly the chemistry of the corresponding cobalt compounds (20*a*) and (20*b*) obtained from (8) and 2-iodopropane and 1-iodo-2-phenylethane respectively. This chemistry was unexceptional, and by similar methodologies to those described above we were able to access the corresponding carbinol acetates, oximes and amines from these two reagents.

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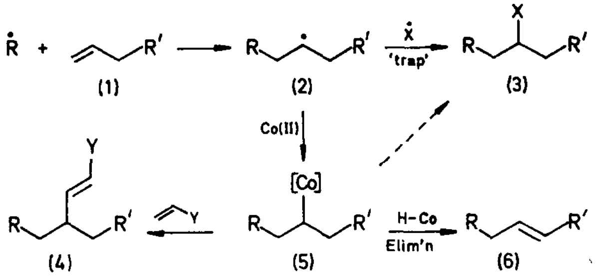
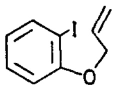


Scheme



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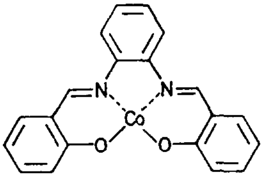

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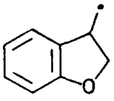

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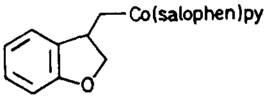

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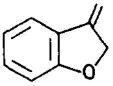

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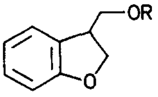
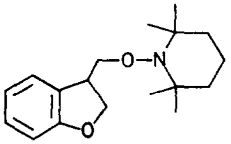


(12)

a, R = H;
b, R = Ac



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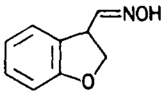

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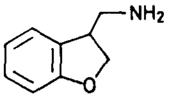

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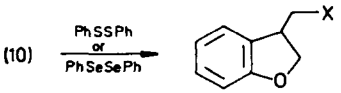
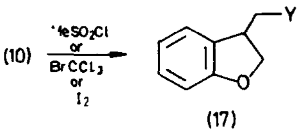


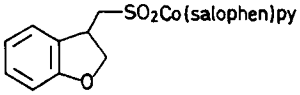
(16)

a, X = SPh
b, X = SePh



(17)

a, Y = Cl; *b*, Y = Br
c, Y = I



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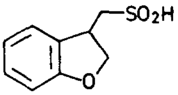
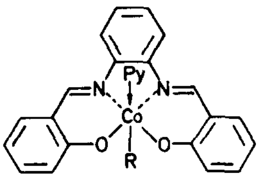


(19)



(20)

a, R = Me$_2$CH—
b, R = Ph—CH$_2$CH$_2$—

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