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COBALT(II)CHLORIDE CATALYSED ACYLATION OF ANISOLE

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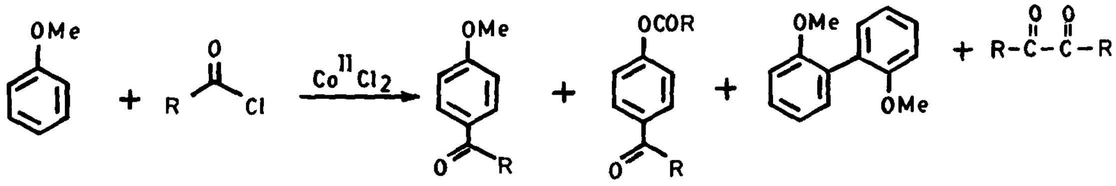
Abstract : Cobalt(II)chloride catalysed acylation of anisole with variety of acid chlorides proceeds via an acyl radical to give p-acylated anisoles in good yields.

The acylation of aromatic ring with acid halides in presence of aluminium trichloride (The Friedel-Crafts reaction) is an extremely useful organic transformation in the domain of electrophilic aromatic substitution reactions. These acylations can be promoted by other Lewis acids, however, the scope of this reaction is severely limited owing to the requirement of the Lewis acid in stoichiometric amounts. The acylation of activated arenes like anisole may be promoted[2] by Bronsted acid in moderate yields. In contrast, copper(I) promoted acylation[3] of anisole with selenol esters may be achieved in good yields. However, the use of selenium compounds in these acylations severely limits the scope of these reactions. In view of the above limitations, the use of a catalyst during these acylations seemed an attractive alternative and therefore, we now show that cobalt(II)chloride is an efficient catalyst for the acylation of anisole with various acyl chlorides.

Typically, acid chloride (16 mmol) and aromatic compound (8 mmol) is added to a solution of anhydrous cobalt(II)chloride (5 mol %) in dry acetonitrile (30 ml) and the resulting mixture is heated at 80°C for 10-15 hours. The acetonitrile is removed under vacuum and the residue taken into ether (80 ml) and washed successively with saturated solution of sodium bicarbonate and water. Drying ($MgSO_4$) and evaporation of the organic layer yielded a liquid which on flash column chromatography gave the acylated products 2 and 3 in good yields (Scheme1). These reactions work well with electron rich aromatic compounds like anisole. The acylation of anisole gave mainly the para acylated compounds (2a-d) which are accompanied by a very small amount (~ 5%) of the corresponding ortho isomers. Benzene, toluene and thioanisole do not give a good yield of the acylated products under these conditions. These acylations are always accompanied by 5-10% of the biacyl derived from the corresponding acid chloride. Small amounts of ester 3 and the coupled product 4 were obtained in all the reactions.

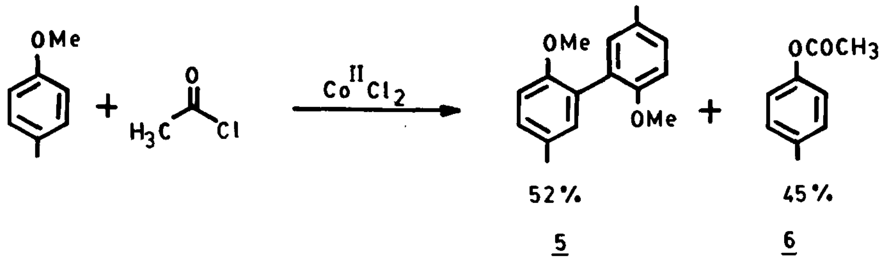


	2	3	4	7
(a) R = Me	68 %	10 %	10 %	5 - 10 %
(b) R = C_6H_5	72 %	-	10 %	-
(c) R = $C_3^nH_7$	78 %	-	12 %	-
(d) R = $CH_3-CH=CH-$	71 %	-	15 %	-

(Scheme 1)

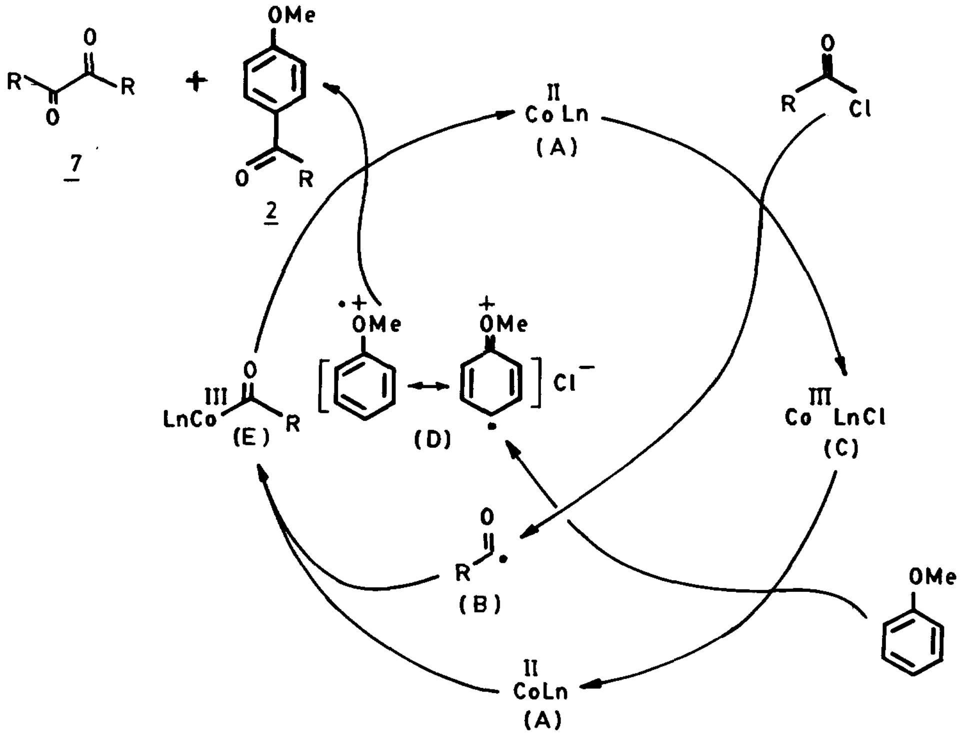
The reaction of anisole with acetyl chloride is critically dependent upon the quantity of the latter during the acylations. The use of 2 equivalents of acetyl chloride always results in the formation of the coupled product 4a in high yields. However, the use of 5 equivalents of acetyl chloride leads to the formation of 2a in good yields. The acylation of p-methyl anisole with acetyl chloride mainly gives rise to the coupled product and the corresponding ester as the major product (Scheme 2). Any attempt to encourage the acylation of p-methylanisole met with very little success.

Mechanistically, these reactions seem to be very interesting as we observe the formation of biacyl, esters 3 and the coupled products 4. The formation of these products can be explained only if we assume the formation of the radical species during these reactions. The formation of the radical species in presence of a paramagnetic cobalt(II) complex is not surprising as we have already shown earlier that the biacyls are obtained[4] as byproducts during cobalt(II)chloride catalysed acylative cleavage of ethers with acid chlorides. Thus, the mechanism of these reactions can be understood if we invoke an initial transfer of electron from cobalt(II) complex (A) to an acyl halide to give an acyl radical (B) and cobalt(III) species (C) (Scheme 3). The cobalt(III) complex (C) will oxidize the anisole to give the corresponding radical cation (D) and cobalt(II) complex (A). The acyl radical (B) will react with complex (A) to yield an acyl cobalt complex (E). The radical cation (D) may react with the acyl cobalt complex (E) in an S_H2 manner to



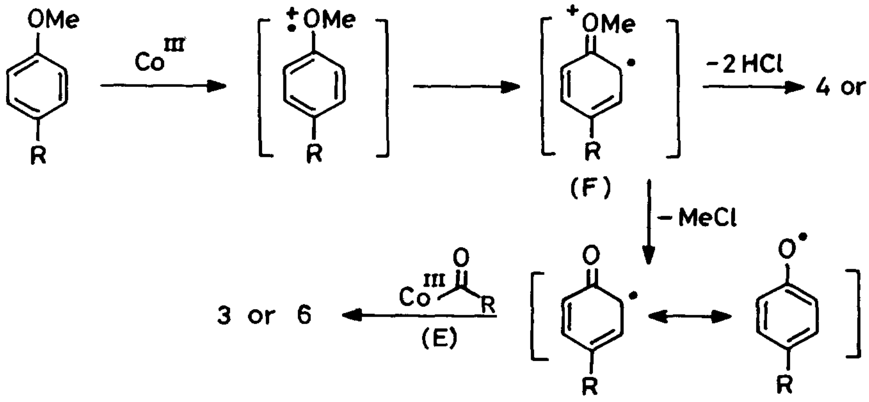
(Scheme 2)

yield the para acylated products 2 and the complex (A) will be regenerated to complete the cycle. The oxidation of ethers by cobalt(III) complex have already been proposed in our earlier studies[4]. The oxidation of anisole by cobalt(III) complex will be very facile as it leads to the formation of a radical cation which can be stabilised by the aromatic ring. The high para selectivity in these reactions indicates that these acylations are taking place via an acyl cobalt complex (E)[5] which may not react with the ortho position due to its bulkiness. This



Scheme 3)

observation is supported by the fact that p-methylanisole does not give any ortho acylated product under these conditions (Scheme 2). The formation of esters 3 and 6 can be explained by demethylation of radical cation (F) followed by an O-acylation of the resulting phenoxy radical. On the other hand the coupling of (F) will yield products 4 or 5 (Scheme 4). These reactions are remarkably suppressed by addition of 2, 6-di-t-butyl-4-methylphenol (BHT)[6], and this observation further supports the presence of radical species during these acylations.



(Scheme 4)

In conclusion the present study indicate that the acylation of anisole with acyl chloride can be catalysed by cobalt(II)chloride via a non-ionic process.

REFERENCES AND NOTES

1. G.A. Olah: Friedel-Crafts and related reactions. Interscience, New York, 1964, vol. 3, p.3.
2. (a) Unger, F., Liebigs Ann. Chem. 1933, 504, 267 (b) Dorofeenko, G.N., Zh. Obshch. Khim. 1961, 31, 994 (c) Effenberger, F., Epple, G., Angew, Chem. Internat. Edit., 1972, 11, 300.
3. Kozikowski, A.P.; Ames, A.; J. Am. Chem. So., 1980, 102, 860.
4. Iqbal, J.; Srivastava, R.R.; Tetrahedron, 1991, 47, 3155.
5. For acylcobalt complex see : Francalance, F.; Garduo, A.; Abis, L.; Fiorani, T.; Foa, M., J. Organomet. Chem. 1983, 243, 87.
6. Murata, S.; Tamatani, A.; Suzuki, K.; Miure, M.; Nomura, M., Chem. Lett., 1990, 757.

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