

Cobalt(II)-Catalyzed Reaction of Aldehydes with Acetic Anhydride under an Oxygen Atmosphere: Scope and Mechanism

Beena Bhatia, T. Punniyamurthy, and Javed Iqbal*

Department of Chemistry, Indian Institute of Technology, Kanpur 208016, India

Received March 9, 1993*

The reaction of aldehydes with acetic anhydride in the presence of catalytic cobalt(II) chloride under an oxygen atmosphere at ambient temperature is dependent upon the reaction medium. Aliphatic aldehydes react in acetonitrile to give 1,2-diones whereas the aromatic aldehydes are acylated to yield the corresponding acylals. On the other hand, carboxylic acids are obtained from aliphatic and aromatic aldehydes by conducting the reaction in dichloroethane or benzene. Cobalt(II) chloride in acetonitrile catalyzes the conversion of aliphatic aldehydes to the corresponding anhydrides in the absence of acetic anhydride whereas aromatic aldehydes remain largely unaffected under these conditions. A preliminary mechanistic study in three different solvents (i.e. acetonitrile, dichloroethane, and DMF) has revealed that in acetonitrile and in the presence of acetic anhydride, aliphatic aldehydes behave differently than aromatic aldehydes. Some trapping experiments using methyl acrylate and stilbene have been conducted to demonstrate the occurrence of an acyl cobalt and peroxyacyl cobalt intermediate during these reactions.

In a previous communication, we reported¹ that aliphatic and aromatic aldehydes can be converted to the corresponding 1,2-diones in acetonitrile in the presence of acetic anhydride and a catalytic amount of cobalt(II) chloride. A reinvestigation of this reaction has revealed that the aromatic aldehydes are largely converted to the diacetoxy compounds (acylals) instead of the 1,2-diones as was reported. On the other hand, the aliphatic aldehydes are efficiently transformed to 1,2-diones, in agreement with our earlier findings. This dichotomous behavior has led us to investigate this reaction in detail. Following are our results, which correct our earlier reported structure for the products derived from the reactions of aromatic aldehydes.

Results and Discussion

The cobalt(II) chloride-catalyzed reactions of aromatic aldehydes with 3 equiv of acetic anhydride in acetonitrile lead to the formation of acylals 1-10a in excellent yields (Table I). These transformations can be performed at ambient temperature over a period of 10-12 h. The reaction with phenolic aldehydes results in the acetylation² of the hydroxyl group as well as the formation of the corresponding acylals. When 4-nitrobenzaldehyde was subjected to this treatment, only unreacted aldehyde was recovered from the reaction mixture, even after 24 h. However, the reaction with benzaldehyde yielded acylal (entry 1, Table I) in good yield, an observation that is in contrast with the findings³ of Fry and co-workers. The formation of an acylal is also quite facile with enals such as cinnamaldehyde. The acylals derived from aromatic aldehydes are crystalline solids, most with sharp melting points. The structural assignments of the acylals were confirmed by ¹H NMR and combustion analysis. A small

amount (5-10%) of biacetyl was found to be produced in most of these reactions although its formation can be diminished by reducing the quantity of acetic anhydride. No attempt was made to optimize the formation of biacetyl in these reactions.

A dramatic change in the reactivity of the aldehyde group was observed upon changing the reaction medium to dimethylformamide (DMF). Thus, no acylals were observed when DMF was used as a solvent instead of acetonitrile, and starting aldehydes were recovered unchanged (entries 2-6, Table I). However, the hydroxyl groups of the phenolic aldehydes underwent smooth acetylation to provide the corresponding acetylated aldehydes in quantitative yields. Interestingly, changing the reaction medium to a less polar solvent like dichloroethane or benzene resulted in the oxidation of aldehydes to the corresponding⁵ carboxylic acids in very good yields (Table I). A variety of aromatic aldehydes and enals can be oxidized to the carboxylic acids under the extremely mild conditions. The phenolic aldehydes also undergo acetylation of the hydroxyl group to give the corresponding acetylated carboxylic acids. The acylative oxidation of phenolic aldehydes has been used to convert salicylaldehyde to aspirin in a single step, in excellent yield. It is noteworthy that 4-nitrobenzaldehyde and 4-(dimethylamino)benzaldehyde remained unaffected under these conditions even with prolonged reaction time.

On the other hand, the cobalt(II) chloride-catalyzed reactions of aliphatic aldehydes and acetic anhydride in acetonitrile under aerobic conditions furnished 1,2-diones 18 and 19 in good yields (eq 1). A mixture of symmetrical and unsymmetrical diones were obtained with a variety of aliphatic aldehydes. A careful analysis of the reaction mixtures revealed that no acylal formation had taken place under these conditions. However, we observed the formation of the corresponding carboxylic acids in small

* Abstract published in *Advance ACS Abstracts*, August 15, 1993.

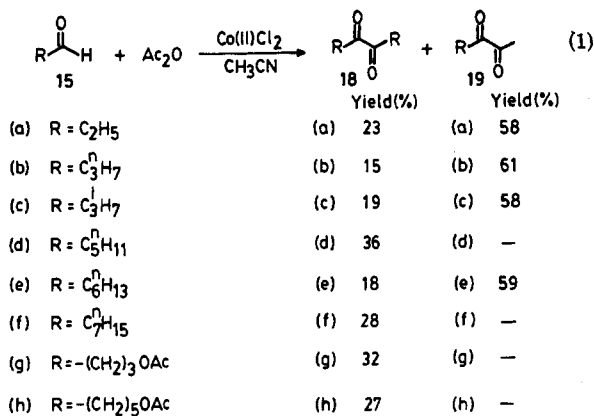
(1) Ahmad, S.; Iqbal, J. *J. Chem. Soc., Chem. Commun.* 1987, 692.

(2) For CoCl₂-catalyzed acylation of the hydroxyl group with acetic anhydride see: (a) Ahmad, S.; Iqbal, J. *J. Chem. Soc., Chem. Commun.* 1987, 114. (b) Iqbal, J.; Srivastava, R. R. *J. Org. Chem.* 1992, 57, 2001.

(3) We had assigned incorrect structures¹ for the products derived from aromatic aldehydes and acetic anhydride catalyzed by CoCl₂. This fact was previously pointed out by Fry, A. J.; Rho, A. K.; Sherman, L. R.; Sherwin, C. S. *J. Org. Chem.* 1991, 56, 3283.

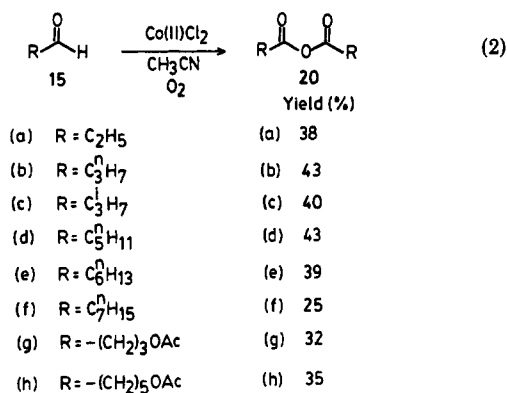
(4) Fry et al. have reported³ that benzaldehyde does not react under our conditions; on the contrary, we always obtain a very high yield (71%) of (diacetoxyethyl)benzene under the experimental condition described in ref 1.

(5) For nickel-catalyzed oxidation of aldehydes to carboxylic acid see: Yamada, T.; Rhode, O.; Takai, T.; Mukaiyama, T. *Chem. Lett.* 1991, 1, 5.



amounts, in addition to the 1,2-diones. The yields of carboxylic acid were quite erratic and controlled experiments have indicated that this product arises from the oxidation of the aldehyde.

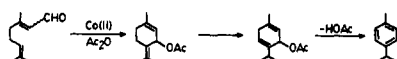
The aliphatic aldehydes 15 are also quite sensitive to changes in the reaction medium. Thus, in DMF, the reactions of aliphatic aldehydes with acetic anhydride in the presence of cobalt(II) chloride and an oxygen atmosphere, lead to the formation of carboxylic acids (Table I). These results are in contrast with similar reactions of aromatic aldehydes where the aldehyde group remained unaffected under these conditions. However, when the reaction medium is changed to 1,2-dichloroethane, the aromatic aldehydes are oxidized to the corresponding carboxylic acids in moderate to good yields. The α,β -unsaturated aldehydes, such as crotonaldehyde or citral, follow a different reaction course and do not yield carboxylic acids. Citral yielded *p*-cymene,⁶ whereas crotonaldehyde gave a mixture of unidentified products. Interestingly, the aliphatic aldehydes 15 can be converted to the corresponding anhydrides 20 in the absence of acetic anhydride under aerobic conditions (eq 2). However, no



reaction was observed in the absence of acetic anhydride and aerial oxygen, and the starting aldehydes were recovered unchanged. The anhydrides were also accompanied by small amounts of carboxylic acid whose presence can be diminished by increasing the reaction time.

Mechanism. The mechanism of these reactions is not understood, however, some preliminary observations can justify some speculation about the reaction pathway. The

(6) *p*-Cymene may be obtained by a CoCl₂-catalyzed acylative cyclization-aromatization of citral in presence of acetic anhydride. Bhatia, B.; Iqbal, J. *Tetrahedron Lett.* 1992, 33, 7961.



syntheses of acylals 1-10a and 13a from aromatic aldehydes and enals may be explained by the formation of a complex between the aldehyde and the metal ion,^{7,8} which undergoes a nucleophilic attack by acetic acid followed by the acylation of the intermediate hemiacetal. Thus, cobalt(II) chloride may be acting as a weak Lewis acid, as suggested by Fry and co-workers³ for a similar reaction using large excess of the catalyst. The unreactivity of aromatic aldehydes in DMF may be due to the reduced Lewis acidity of cobalt(II), which is expected if a more nucleophilic solvent than acetonitrile (i.e. DMF) is acting as a ligand to the metal.

The oxidation of aromatic aldehydes to carboxylic acids in 1,2-dichloroethane is occurring via an entirely different pathway and the mechanism of this reaction may have some similarity with that proposed⁹ by Bawn et al. for the metal-catalyzed autoxidation of benzaldehyde. According to their proposal, the acyl radicals are likely to be the intermediates and the corresponding peracids may be formed subsequent to dioxygen incorporation. However, an alternative ionic pathway cannot be ruled out for such transformations. The failure of 4-(dimethylamino)benzaldehyde and 4-nitrobenzaldehyde to react under these conditions¹⁰ suggests that a redox process may be involved in these oxidations. The role of acetic anhydride in these oxidations is not clear; however, it is conceivable that the peracid formed may be oxidizing it to acetyl methyl carbonate or acetyl peroxide which may then undergo decomposition in the presence of cobalt(II) complex.

The formation¹¹ of 1,2-diones 18 and 19 from the aliphatic aldehydes in acetonitrile can be explained by the catalytic cycle shown in Scheme I. An electron transfer^{1,10} from cobalt(II) complex (a) to acetic anhydride will give rise to an acetyl radical and cobalt(III) complex (b). The oxidation of aldehyde by complex b will afford the corresponding acylcobalt species (c) which upon homolytic cleavage may provide the acyl radical (d), and cobalt(II) complex (a) will be regenerated to complete the cycle. Subsequently, the coupling of radical d will yield a 1,2-dione. Similarly, the cross coupling between acyl radical (d) and acetyl radical will yield the unsymmetrical 1,2-dione. Alternatively, the acylcobalt species (c) may react with acetic anhydride to give unsymmetrical 1,2-dione and complex b via the intermediate e. The oxidation of aldehyde with b will regenerate the acylcobalt complex (c). The presence of a small amount of carboxylic acid in this reaction may be explained by the incorporation¹² of dioxygen in acylcobalt species (c) to give peroxyacyl cobalt complex (f) (Scheme II). The reaction of complex f with aldehyde will provide a labile intermediate (g) which may

(7) Mann, F. H.; Sanderson, J. J.; Hauser, C. R. *J. Am. Chem. Soc.* 1950, 72, 847.

(8) (a) Kanwarpal, K. S.; Balkrishna, B. S.; Deshpande, R. P.; Rajadhyaksha, S. N.; Pinnick, H. W. *J. Org. Chem.* 1983, 48, 1765. (b) Michie, J. K.; Miller, J. A. *Synthesis* 1981, 824.

(9) (a) Bawn, C. E. H.; Jolley, J. E. *Proc. R. Soc. Ser. A* 1956, 237, 313. (b) Bawn, C. E. H. *Discuss. Faraday Soc.* 1953, 14, 181. (c) Kochi, J. K. In *Organometallic Mechanisms and Catalysis*; Academic Press: New York, 1978; Chapter 5.

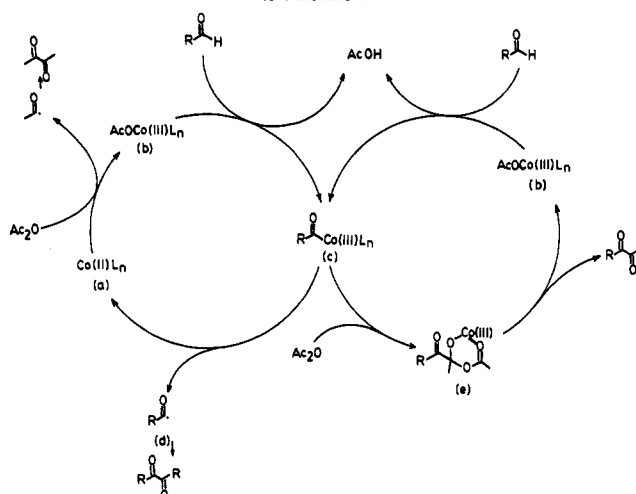
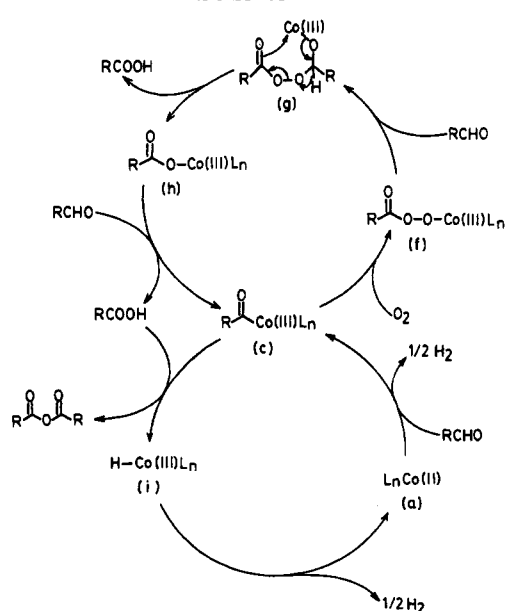
(10) For electron transfer-induced formation of acyl radical from aldehydes see: (a) Wiberg, K. B.; Richardson, W. H. *J. Am. Chem. Soc.* 1962, 84, 2800. (b) Wiberg, K. B.; Ford, P. C. *J. Am. Chem. Soc.* 1969, 91, 124. (c) Nikishin, G. I.; Vinogradov, M. G.; Verenchikov, S. P. *Bull. Acad. Sci. USSR* 1969, 1698. (d) Nikishin, G. I.; Vinogradov, M. G.; Kereselidze, R. V. *Bull. Acad. Sci. USSR* 1967, 1570.

(11) For the synthesis of 1,2-diones from acetaldehyde and manganese(III) acetate see ref 10c.

(12) For the incorporation of dioxygen in a carbon-cobalt bond see: (a) Patel, V. F.; Pattenden, G. *Tetrahedron Lett.* 1987, 28, 1451. (b) Inoki, S.; Mukaiyama, T. *Chem. Lett.* 1990, 67.

Table I. Cobalt(II) Chloride Catalyzed Reaction of Aldehydes with Acetic Anhydride under Aerobic Conditions in Different Solvents

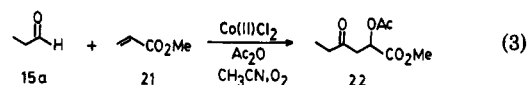
entry	aldehyde	product (% yield)		
		CH ₃ CN	DMF	1,2-DCE
1	benzaldehyde (1)	(diacetoxyethyl)benzene (1a) (71)	—	benzoic acid (1c) (41)
2	4-hydroxybenzaldehyde (2)	4-acetoxy-1-(diacetoxyethyl)benzene (2a) (91)	4-acetoxybenzaldehyde (2b) (86)	4-acetoxybenzoic acid (2c) (93)
3	3-hydroxybenzaldehyde (3)	3-acetoxy-1-(diacetoxyethyl)benzene (3a) (75)	3-acetoxybenzaldehyde (3b) (77)	3-acetoxybenzoic acid (3c) (79)
4	2-hydroxybenzaldehyde (4)	2-acetoxy-1-(diacetoxyethyl)benzene (4a) (57)	2-acetoxybenzaldehyde (4b) (59)	2-acetoxybenzoic acid (4c) (71)
5	3-hydroxy-4-methoxybenzaldehyde (5)	3-acetoxy-4-methoxy-1-(diacetoxyethyl)benzene (5a) (70)	3-acetoxy-4-methoxybenzaldehyde (5b) (69)	3-acetoxy-4-methoxybenzoic acid (5c) (73)
6	2,4-dihydroxybenzaldehyde (6)	2,4-diacetoxy-1-(diacetoxyethyl)benzene (6a) (59)	2,4-diacetoxybenzaldehyde (6b) (64)	2,4-diacetoxybenzoic acid (6c) (68)
7	4-methylbenzaldehyde (7)	1-(diacetoxyethyl)-4-methylbenzene (7a) (78)	—	4-methylbenzoic acid (7c) (62)
8	4-methoxybenzaldehyde (8)	4-methoxy-1-(diacetoxyethyl)benzene (8a) (73)	—	4-methoxybenzoic acid (8c) (68)
9	4-chlorobenzaldehyde (9)	4-chloro-1-(diacetoxyethyl)benzene (9a) (79)	—	—
10	3-aminobenzaldehyde (10)	3-(acetylamino)-1-(diacetoxyethyl)benzene (10a) (79)	—	—
11	cinnamaldehyde (11)	—	—	cinnamic acid (11c) (72)
12	indolecarboxaldehyde (12)	—	—	indolecarboxylic acid (12c) (77)
13	phthalaldehyde (13)	3-acetoxy-1-(3 <i>H</i>)-isobenzofuranone (13a) (83)	—	—
14	citral (14)	—	—	<i>p</i> -cymene (14a) (61)
15	isobutyraldehyde (15c)	—	isobutyric acid (16) (18)	isobutyric acid (16) (22)
16	<i>n</i> -heptanol (15e)	—	heptanoic acid (17) (34)	heptanoic acid (17) (35)

Scheme I**Scheme II**

fragment readily to afford the corresponding carboxylic acid and the carboxylate cobalt complex (h). The interaction of aldehyde with complex h via a redox process may lead to the corresponding carboxylic acid and the

acyl cobalt species (c). A similar process may be involved during the oxidation of aldehydes in the presence of acetic anhydride in 1,2-dichloroethane, as described in Table I. The formation of an acyl radical by oxidation of an aldehyde by cobalt(II) complexes is known from previous studies.^{10c}

The intermediacy of an acyl radical can be demonstrated by trapping experiments. Thus, the cobalt(II)-catalyzed reactions of aliphatic aldehydes with acetic anhydride in the presence of excess methyl acrylate led to the formation of adduct 2-acetoxy-4-oxo esters 22 and the corresponding carboxylic acids, the yields being nearly equal (eq 3). The

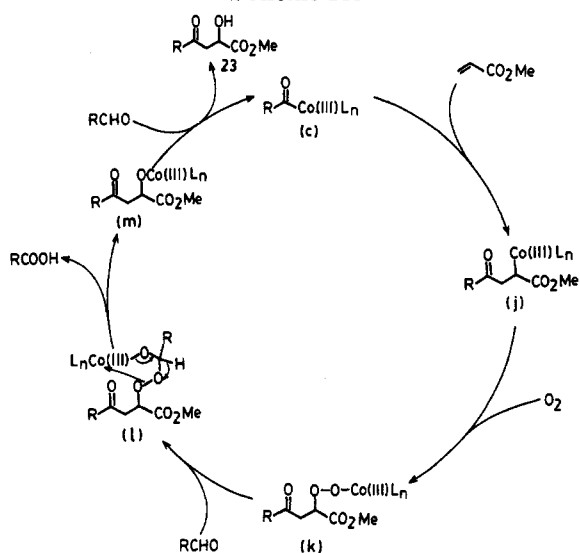


formation of 1,2-diones 18 and 19 was reduced substantially under these conditions indicating¹³ that the addition of the acylcobalt species to the acrylate is the major¹⁴ pathway. The formation of adduct 22 clearly indicates the presence of an acyl radical during these reactions. The acyl cobalt(III) species (c), generated by the oxidation of aldehyde with cobalt(III) complex (b) adds to the electron-deficient olefin to give a new cobalt(III)-stabilized radical (j), which incorporates dioxygen to give the peroxy intermediate (k) (Scheme III). The reaction of the peroxycobalt complex (k) with a molecule of aldehyde may produce a labile species (l) which will readily fragment to the corresponding carboxylic acid and a cobalt alkoxide (m). A redox reaction involving m and another molecule of aldehyde may afford the adduct 23, and the acylcobalt complex (c) will be regenerated to complete the cycle. The oxidation of aldehydes with a cobalt(III) complex is well documented in the literature. Pattenden and co-workers¹³ have already established the facile addition of acyl cobalt(III) complexes to electron-deficient olefins under thermal or photochemical conditions.

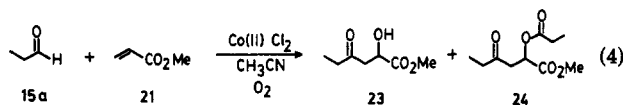
(13) For addition of an acylcobalt complex to ethyl acrylate see: Coveney, D. J.; Patel, V. F.; Pattenden, G. *Tetrahedron Lett.* 1987, 28, 1949.

(14) The acylcobalt complex is quite prone to insertion of dioxygen; however, in the presence of an excess of methyl acrylate the addition of acyl radical to acrylate is favored and adduct 22 is formed in preference to 1,2-diones. We have already shown that cobalt-stabilized carbon-centered radicals preferentially react with methyl acrylate in the presence of dioxygen. See: Iqbal, J.; Bhatia, B.; Nayyar, N. K. *Tetrahedron* 1991, 47, 6457.

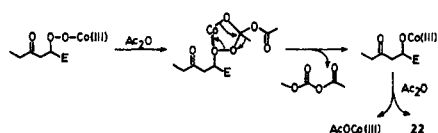
Scheme III



The formation of anhydrides from aliphatic aldehydes in the absence of acetic anhydride may be explained by assuming the intermediacy of an acylcobalt complex (Scheme II). Such a complex can result from the interaction of aldehyde with the cobalt(II) complex (a) via a redox process. Incorporation of dioxygen in complex c will yield peroxyacyl cobalt complex (f) which may react with another molecule of aldehyde to give a labile intermediate (g). The latter, upon fragmentation, affords the carboxylic acid and a carboxylate cobalt complex (h) which oxidizes another molecule of aldehyde to generate carboxylic acid and the cobalt complex (c). The reaction of carboxylic acid with complex c may provide¹⁶ the anhydride and a cobalt(III) hydride intermediate (i) which readily loses hydrogen gas and regenerates the cobalt(II) complex (a). These experiments clearly indicate that acetic anhydride results in the formation of 1,2-diones from aldehydes, whereas its absence permits anhydride formation. However, these two products are obtained from a common acylcobalt intermediate (c) whose presence can be proven by a trapping experiment. Accordingly, the cobalt(II)-catalyzed reaction of propionaldehyde in the presence of excess methyl acrylate under aerobic condition leads to the formation of 2-hydroxy-4-oxo ester adduct 23 and the corresponding 2-propionoxy-4-oxo ester 24 in good yields (eq 4). The latter experiment clearly reveals¹⁷ that



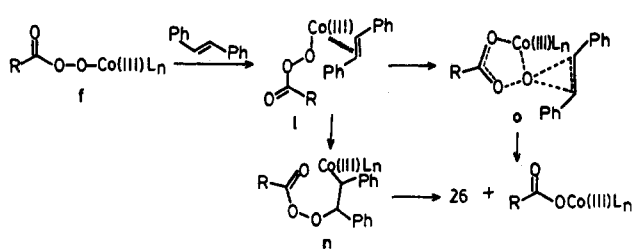
(15) Alternatively, acetic anhydride may be acting as a reductant during conversion of peroxyacyl cobalt complex (k) to the adduct 22 via the following pathway.



(16) For cobalt acetate-mediated synthesis of anhydride from aldehydes see: Twigg, G. H. *Chem. Ind. (London)* 1966, 476.

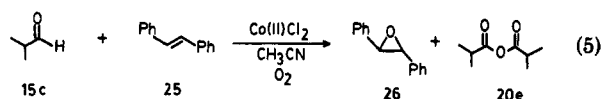
(17) The formation of propionate ester 24 clearly establishes the role of aldehyde as reductant to the peroxy intermediate (k). The propionate ester 24 can be derived from the acylation of the initially formed 23 with propionic anhydride which may arise from the propionic acid produced during this reaction as described in Scheme II.

Scheme IV



the formation of 1,2-dione and anhydride proceed via a common acyl radical species.

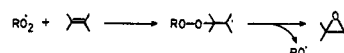
Strong evidence for the mechanism described in Scheme II can be further gathered by proving the intermediacy of peroxyacyl cobalt complex (f). Thus, the cobalt(II)-catalyzed reaction of isobutyraldehyde in the presence of *trans*-stilbene and dioxygen results in the formation of stilbene oxide 26 and isobutyric anhydride in excellent yields (eq 5). Stilbene oxide may be derived from a



reaction¹⁸ between *trans*-stilbene and the peroxyacyl cobalt complex (f) via the intermediate n or o (Scheme IV). It is evident that such a process will yield carboxylic acid, which may eventually lead to the formation of the corresponding anhydride. Thus, the formation of adducts 22–24 and stilbene oxide 26 strongly support the intermediacy of an acylcobalt and (peroxyacyl)cobalt complex during the cobalt(II)-catalyzed reactions of aliphatic aldehydes under a dioxygen atmosphere.

In conclusion, the products of the cobalt(II)-catalyzed reaction of aromatic aldehydes with acetic anhydride under aerobic conditions are dependent upon the reaction medium. The less-polar solvents (i.e. benzene, 1,2-dichloroethane) favor oxidation to the carboxylic acid whereas a more-polar solvent (i.e. acetonitrile) encourages the formation of acylals. On the other hand, the aliphatic aldehydes undergo oxidation to the carboxylic acid in less-polar solvents (i.e. benzene, 1,2-dichloroethane) whereas 1,2-diones are obtained in acetonitrile medium under the above reaction conditions. The role of acetic anhydride is quite important in these reactions as its absence brings about a dramatic change in the reactivity profile of the aldehydes. When these reactions are conducted in the absence of acetic anhydride, aromatic aldehydes are unreactive whereas aliphatic aldehydes are transferred to the corresponding anhydrides. A brief mechanistic investigation involving trapping experiments with olefins has revealed that the reactions with aliphatic aldehydes are proceeding via acylcobalt and (peroxyacyl)cobalt complexes. These studies have also indicated that novel routes to compounds 22–24 and the epoxides can be developed from a common intermediate by appropriate choice of an olefin.

(18) Cobalt(II)-catalyzed epoxidation of olefins with dioxygen is proposed to proceed via a β -peroxyalkyl radical intermediate shown below. See: Budnik, R. A.; Kochi, J. K. *J. Org. Chem.* 1976, 41, 1384.



Experimental Section

Materials and Methods. Acetonitrile, dimethylformamide, 1,2-dichloroethane, and acetic anhydride were purified by the standard procedure. CoCl_2 was purchased from LOBA India Ltd., Bombay, and dried at 110 °C for 2–3 h before the reaction. Flash chromatography was performed by using ACME TLC silica gel. Aldehydes were purchased commercially and purified prior to use. ^1H NMR spectra were recorded at 60 and 80 MHz in CDCl_3 or CCl_4 . Elemental analysis was conducted using Coleman automatic C, H, and N analyzer. All the known compounds, were characterized by comparing the data from the literature.

General Procedure for the Synthesis of Acylals. Aldehyde (10 mmol) and acetic anhydride (30 mmol) were added to a stirred solution of CoCl_2 (5 mol%) in anhydrous acetonitrile (60 mL). The mixture was stirred at ambient temperature (20 °C) for 20–24 h. The solvent was evaporated in vacuo, and the residue was dissolved in ether. The ether layer was washed successively with saturated aqueous NH_4Cl (3 × 20 mL) and water (2 × 20 mL). Drying (MgSO_4) and evaporation of solvent gave the crude product which was purified by column chromatography or by Kugelrohr distillation. This reaction was also performed in dimethylformamide medium according to the procedure described above. DMF was removed by pouring the reaction mixture into diethyl ether (50 mL) and the resulting mixture was washed successively with saturated aqueous NH_4Cl (3 × 20 mL) and water (3 × 25 mL). The organic layer was dried (MgSO_4) and evaporated to give a crude mixture which was subjected to purification as described above.

General Procedure for the Synthesis of Carboxylic Acid. Aldehyde (10 mmol) and acetic anhydride (30 mmol) were added to a stirred mixture of CoCl_2 (5 mol%) in dry 1,2-dichloroethane (40 mL). The mixture was stirred under aerobic condition (oxygen balloon) at 25 °C for 15–20 h. Dichloromethane (20 mL) was added to this mixture and it was washed with saturated solution of NH_4Cl (2 × 20 mL) and water (2 × 20 mL). Drying (MgSO_4) and evaporation yielded the crude product which was purified by crystallization or distillation.

General Procedure for the Synthesis of 1,2-Diones. Aliphatic aldehydes (10 mmol) and acetic anhydride (30 mmol) were subjected to the reaction condition as described for acylals. The usual workup followed by Kugelrohr distillation afforded 1,2-diones.

General Procedure for the Synthesis of Anhydrides. Aliphatic aldehyde (10 mmol) was added to a solution of CoCl_2 (5 mol%) in dry acetonitrile (50 mL). The mixture was stirred at 25 °C under aerobic condition for 12–15 h. The workup was carried out as described above, and the anhydrides were purified by Kugelrohr distillation and evaporated to give the residue which was purified by column chromatography.

4-Acetoxy-1-(diacetoxyethyl)benzene (2a). 4-Hydroxybenzaldehyde (2) (0.61 g, 5 mmol) and acetic anhydride (1.5 g, 15 mmol) were stirred in presence of CoCl_2 (~30 mg) in dry acetonitrile for 15 h at 25 °C. The usual workup followed by flash chromatography (5% EtOAc/petroleum ether) afforded **2a** (1.21 g, 91%) as a solid: mp 58 °C; IR (KBr) ν_{max} 1755, 1735 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3) δ 7.5 (s, 1H), 7.4 (d, 2H, $J = 8$ Hz), 6.9 (d, 2H, $J = 8$ Hz), 2.2 (s, 3H) 2.0 (s, 6H). Anal. Calcd for $\text{C}_{13}\text{H}_{14}\text{O}_6$: C, 58.64; H, 5.2. Found: C, 58.90; H, 5.23.

3-Acetoxy-4-methoxy-1-(diacetoxyethyl)benzene (5a). 3-Hydroxy-4-methoxybenzaldehyde (5) (0.76 g, 5 mmol), acetic anhydride (1.53 g, 15 mmol), and CoCl_2 (30 mg) were subjected to the reaction condition described above. The usual workup followed by purification on column chromatography (5% EtOAc/petroleum ether) yielded **5a** (1.04 g, 70%) as a solid: mp 134 °C; IR (KBr) ν_{max} 1760–1725 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 7.45 (s, 1H), 7.4–6.9 (m, 4H), 2.3 (s, 3H), 2.15 (s, 6H). Anal. Calcd for $\text{C}_{14}\text{H}_{16}\text{O}_7$: C, 56.75; H, 5.40. Found: C, 56.81; H, 5.46.

2,4-Diacetoxy-1-(diacetoxyethyl)benzene (6a). 2,4-Dihydroxybenzaldehyde (6) (0.69 g, 5 mmol), acetic anhydride (1.53 g, 15 mmol), and CoCl_2 (~30 mg) were subjected to the reaction condition as described above. The usual workup followed by purification using flash chromatography (2% EtOAc/petroleum ether) afforded **6a** (1.62 g, 59%) as a solid: mp 148 °C; IR (KBr) ν_{max} 1750 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 7.5 (s, 1H), 7.45–6.9 (m, 3H),

2.2 (s, 6H), 2.1 (s, 6H). Anal. Calcd for $\text{C}_{15}\text{H}_{16}\text{O}_8$: C, 55.61; H, 4.9. Found: C, 55.61; H, 4.91.

1-(Diacetoxyethyl)-4-methylbenzene (7a). 4-Methylbenzaldehyde (7) (0.60 g, 5 mmol), acetic anhydride (1.53 g, 15 mmol), and CoCl_2 (~30 mg) were subjected to the reaction condition as described above. The usual workup followed by purification using flash chromatography (5% EtOAc/petroleum ether) afforded **7a** (0.86 g, 78%) as a solid: mp 69 °C (lit.¹⁹ mp 68–70 °C) IR (KBr) ν_{max} 1755 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 7.5 (s, 1H), 7.4–6.9 (m, 4H), 2.4 (s, 3H), 2.1 (s, 6H). Anal. Calcd for $\text{C}_{12}\text{H}_{14}\text{O}_4$: C, 64.8; H, 6.3. Found: C, 64.90; H, 6.33.

4-Methoxy-1-(diacetoxyethyl)benzene (8a). 4-Methoxybenzaldehyde (8) (0.68 g, 5 mmol), acetic anhydride (1.53 g, 15 mmol), and CoCl_2 (~30 mg) were subjected to the reaction condition as described above. The usual workup followed by flash chromatography (5% EtOAc/petroleum ether) yielded **8a** (0.87 g, 73%) as a solid: IR (KBr) ν_{max} 1760, 1680 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 7.5 (s, 1H), 7.45 (d, 2H, $J = 7.6$ Hz), 6.8 (d, 2H, $J = 7.8$ Hz), 3.75 (s, 3H), 2.25 (s, 3H), 2.05 (s, 6H). Anal. Calcd for $\text{C}_{12}\text{H}_{14}\text{O}_6$: C, 60.49; H, 5.90. Found: C, 60.52; H, 6.0.

4-Chloro-1-(diacetoxyethyl)benzene (9a). 4-Chlorobenzaldehyde (9) (0.70 g, 5 mmol), acetic anhydride (1.53 g, 15 mmol), and CoCl_2 (~30 mg) were subjected to the reaction condition as described above. The usual workup followed by chromatography (10% EtOAc/petroleum ether) afforded **9a** (0.96 g, 79%) as a solid: mp 81–82 °C (lit.¹⁹ mp 81–81.5 °C); IR (KBr) ν_{max} 1750 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 7.4 (s, 1H), 7.25 (s, 4H), 2.1 (s, 6H). Anal. Calcd for $\text{C}_{11}\text{H}_{11}\text{O}_4\text{Cl}$: C, 54.40; H, 4.50. Found: C, 54.44; H, 4.51.

3-(Acetylamino)-1-(diacetoxyethyl)benzene (10a). 3-Aminobenzaldehyde (10) (0.60 g, 5 mmol), acetic anhydride (1.53 g, 15 mmol), and CoCl_2 (30 mg) were subjected to the reaction condition as described above. The usual workup followed by chromatography (40% EtOAc/petroleum ether) afforded **10a** (0.91 g, 71%) as a solid: mp 110 °C; IR (KBr) ν_{max} 3305, 2260, 1760, 1730 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 8.2 (bs, 1H), 7.6–7 (m, 4H), 7.45 (s, 1H), 2.15 (s, 3H), 2.10 (s, 6H). Anal. Calcd for $\text{C}_{13}\text{H}_{15}\text{NO}_6$: C, 58.86; H, 5.6. Found: C, 58.80; H, 5.69.

2-Acetoxy-4-oxo-3,4-dibenzofuran (13a). Phthalaldehydic acid (13) (0.75 g, 5 mmol), acetic anhydride (1.53 g, 15 mmol), and CoCl_2 (~30 mg) were subjected to the reaction condition as described for the synthesis of acylals. The usual workup followed by crystallization (methanol–petroleum ether, 1:2) afforded **13a** (0.80 g, 83%) as a solid: mp 61–62 °C; IR (KBr) ν_{max} 1790, 1765 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 7.9–7.5 (m, 4H), 7.3 (s, 1H), 2.2 (s, 3H). Anal. Calcd for $\text{C}_{10}\text{H}_8\text{O}_4$: C, 62.50; H, 4.19. Found: C, 62.93; H, 4.20.

Hexadecane-8,9-dione (18f). Octanal (15f) (1.23 g, 10 mmol), acetic anhydride (3.06 g, 30 mmol), and CoCl_2 (~30 mg) were subjected to the reaction condition as described for the synthesis of the 1,2-dione. The usual workup followed by distillation on a Kugelrohr afforded **18f** (0.71 g, 28%) as an oil: IR (thin film) ν_{max} 1711, 1463 cm^{-1} ; $^1\text{H NMR}$ (CCl_4) δ 2.35 (t, 4H, $J = 7$ Hz), 1–1.7 (m, 20H), 0.85 (t, 6H, $J = 7$ Hz). Anal. Calcd for $\text{C}_{16}\text{H}_{30}\text{O}_2$: C, 76.13; H, 11.89. Found: C, 76.19; H, 11.92.

1,8-Diacetoxyoctane-4,5-dione (18g). 4-Acetoxybutanal (15g) (0.65 g, 5 mmol), acetic anhydride (1.53 g, 15 mmol), and CoCl_2 (~30 mg) were reacted under the general conditions as described for the 1,2-dione synthesis. The usual workup followed by distillation yielded **18g** (0.51 g, 32%) as an oil: IR (thin film) ν_{max} 1820, 1730, 1360 cm^{-1} ; $^1\text{H NMR}$ (CCl_4) δ 3.95 (t, 4H, $J = 6.8$ Hz), 2.35 (t, 4H, $J = 7$ Hz), 2.15 (s, 6H), 1.4–1.8 (m, 4H). Anal. Calcd for $\text{C}_{12}\text{H}_{18}\text{O}_6$: C, 55.83; H, 6.9. Found: C, 55.89; H, 7.0.

1,2-Diacetoxydodecane-6,7-dione (18h). 6-Acetoxyhexanal (15h) (0.79 g, 5 mmol), acetic anhydride (1.53 g, 15 mmol), and CoCl_2 (~30 mg) were subjected to the reaction condition as described for the general syntheses of the 1,2-dione. The usual workup followed by distillation afforded **18h** (0.42 g, 27%) as an oil: IR (thin film) ν_{max} 1819, 1741.8 cm^{-1} ; $^1\text{H NMR}$ (CCl_4) δ 3.95 (t, 4H, $J = 7$ Hz), 2.35 (t, 4H, $J = 6.8$ Hz), 2.15 (s, 6H), 1.4–1.85 (m, 8H). Anal. Calcd for $\text{C}_{16}\text{H}_{28}\text{O}_6$: C, 61.12; H, 8.3. Found: C, 61.17; H, 8.38.

Methyl 2-Acetoxy-4-oxohexanoate (22). Propionaldehyde (15a) (0.58 g, 10 mmol), acetic anhydride (3.06 g, 30 mmol), and methyl acrylate (21) (2.58 g, 30 mmol) were added to a stirred solution of CoCl₂ (5 mol%) in dry acetonitrile (80 mL). The reaction mixture was stirred at ambient temperature under aerobic condition for 12–15 h. Removal of acetonitrile yielded a residue which was taken into ether (50 mL), and the organic layer was washed successively with saturated sodium bicarbonate solution (3 × 20 mL) and water (3 × 25 mL). Drying (MgSO₄) and evaporation yielded a residue which was subjected to column chromatography (5% EtOAc/petroleum ether) to afford 22 (1.52 g, 75%) as a gum: ¹H NMR (CCl₄) δ 5.2 (t, 1H, *J* = 6.8 Hz), 3.6 (s, 3H), 2.8 (d, 2H, *J* = 7 Hz), 2.35 (q, 2H, *J* = 7.2 Hz), 2.0 (s, 3H), 1.1 (t, 3H). Anal. Calcd for C₉H₁₄O₅: C, 53.45; H, 6.90. Found: C, 53.55; H, 7.11.

Methyl 2-Hydroxy-4-oxohexanoate (23). Propionaldehyde (15a) (0.58 g, 10 mmol) and methyl acrylate (2.58 g, 30 mmol) and CoCl₂ (~30 mg) were subjected to the reaction condition as described for the preparation of compound 22. The usual workup followed by column chromatography (20% EtOAc/petroleum

ether) afforded 23 (0.23 g, 14%) as a gum: ¹H NMR (CCl₄) δ 4.3 (t, 1H, *J* = 6.5 Hz), 3.8 (s, 3H), 2.8 (d, 1H, *J* = 7.2 Hz), 2.4 (q, 2H, *J* = 6.9 Hz), 1.1 (t, 3H, *J* = 6.8 Hz). Anal. Calcd for C₇H₁₂O₄: C, 52.49; H, 7.5. Found: C, 52.90; H, 7.31.

Methyl 2-Propionyloxy-4-oxohexanoate (24). Propionaldehyde (15a) (0.58 g, 10 mmol), methyl acrylate 21 (2.58 g, 30 mmol), and CoCl₂ (~30 mg) were subjected to the reaction condition as described for the preparation of 22. The usual workup followed by column chromatography (5% EtOAc/petroleum ether) afforded 24 (0.50 g, 23%) as a liquid: ¹H NMR (CCl₄) δ 5.15 (t, 1H, *J* = 6.8 Hz), 3.6 (s, 3H), 2.75 (d, 2H, *J* = 8 Hz), 2.25 (q, 4H, *J* = 7.3 Hz), 1.05 (t, 6H, *J* = 7 Hz). Anal. Calcd for C₁₀H₁₆O₅: C, 55.57; H, 7.4. Found: C, 55.61; H, 7.8.

Stilbene Oxide (26). 2-Methylpropanal (15c) (1.44 g, 20 mmol) and *trans*-stilbene 25 (10 mmol) were added to a solution of CoCl₂ (~30 mg) in dry acetonitrile (60 mL). The reaction mixture was stirred at 25 °C under aerobic conditions for 12–15 h. The usual workup followed by column chromatography (5% EtOAc/petroleum ether) afforded *trans*-stilbene oxide (26) in quantitative yield, mp 69 °C (lit. mp 65–67 °C).