Tetrahedron Letters, Vol.31, No.22, pp 3171-3174, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

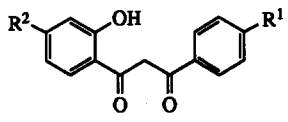
COBALT SCHIFF BASE COMPLEX PROMOTED RETRO-CLAISEN REACTION OF 1-(2-HYDROXYPHENYL)-3-PHENYL-1,3-PROPANEDIONES AND FLAVONE FORMATION

Akira NISHINAGA,* Kazushige MARUYAMA, Hiroyuki ANDO,
Ryoji SATO, and Takahiro MASHINO
Department of Applied Chemistry, Osaka Institute of Technology,
Ohmiya 5, Asahi-ku, Osaka 535, Japan
Akira INADA* and Tsutomu NAKANISHI
Faculty of Pharmaceutical Sciences, Setsunan University
45-1 Nagaotogecho, Hirakata, Osaka 573-01, Japan

Summary: Co(salpr) promotes the conversion of 1-(2-hydroxyphenyl)-3-phenyl-1,3-propanediones to retro-Claisen reaction products and flavones in methanol under oxygen. Base catalysis by Co(salpr)(OH) produced in situ is responsible for the reaction.

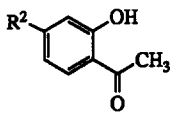
Cobalt Schiff base complexes [Co(SB)] are very interesting because of their characteristic behavior as artificial oxidoreductases: they catalyze dioxygenation in aprotic solvents, monooxygenation in protic solvents,[1-5] and dehydrogenation of alcohols,[4] hydrazones,[6] and amines.[7,8] The important key step in these model oxidoreductase reactions is the formation of oxygen sensitive substrate anion cobalt(III) complex intermediates resulting from an acid-base reaction of Co^{III}(SB)(OH) with the substrates.[9,10] Recently, we have shown the first direct evidence for the base catalysis of Co^{III}(SB)(OH) in the conversion of 2'-hydroxychalcones to the corresponding flavanones.[11] We now wish to report here that Co(salpr) [salpr = N^1,N^7-4-azaheptamethylenebis(salicylideneiminato)] promotes the conversion of 1-(2-hydroxyphenyl)-3-phenyl-1,3-propanediones to their retro-Claisen reaction products and the corresponding flavones in alcohols under oxygen. The base catalysis of Co^{III}(salpr)(OH) produced in situ is responsible for the present reaction.

A solution of 1-(2-hydroxyphenyl)-3-phenyl-1,3-propanedione (**1a**) (2 mmol) in methanol (50 ml) containing Co(salpr) (2 mmol) was stirred at 60 °C under an oxygen atmosphere until the reaction was completed. After evaporation of the solvent, the resulting reaction mixture was chromatographed on a silica gel plate being eluted with dichloromethane to give 2'-hydroxyacetophenone (**2a**) (20%), methyl benzoate (**3a**) (23%), methyl salicylate (**4a**) (6%), acetophenone (**5a**) (4%), flavone (**6a**) (42%), and chromanone (**7a**) (5%). Similar results are obtained with other substituted diketones **1** (Table 1). The structures **2** - **6** and **7a**[12] are identical with those of authentic samples (IR and ^{1}HNMR). The ^{1}HNMR signals around δ 2.8 and 4.5 ppm of compounds **7**[12] are characteristic for the chromanone ring protons. Further, the ^{13}CNMR data of **7b**[12] are identical with those reported.[13] Since the alcohol moiety of esters **3** and **4** comes from



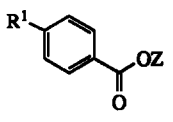
1

a; $R^1 = R^2 = H$
b; $R^1 = OMe, R^2 = H$
c; $R^1 = Me, R^2 = H$
d; $R^1 = Cl, R^2 = H$
e; $R^1 = NO_2, R^2 = H$
f; $R^1 = H, R^2 = OCH_2OCH_3$



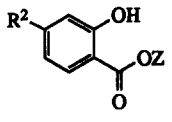
2

a; $R^2 = H$
b; $R^2 = OCH_2OCH_3$



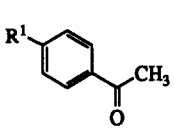
3

a; $R^1 = H, Z = Me$
b; $R^1 = OMe, Z = Me$
c; $R^1 = Z = Me$
d; $R^1 = Cl, Z = Me$
e; $R^1 = NO_2, Z = Me$
f; $R^1 = H, Z = Et$
g; $R^1 = H, Z = i\text{-}PrOH$



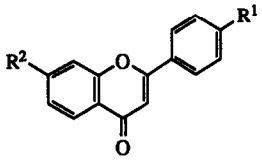
4

a; $R^2 = H, Z = Me$
b; $R^2 = OCH_2OCH_3, Z = Me$
c; $R^2 = H, Z = Et$
d; $R^2 = H, Z = i\text{-}Pr$



5

a; $R^1 = H$
b; $R^1 = OMe$
c; $R^1 = Me$
d; $R^1 = Cl$
e; $R^1 = NO_2$



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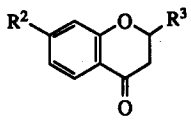
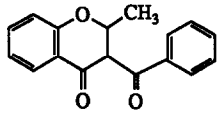


7

a; $R^2 = R^3 = H$
b; $R^2 = H, R^3 = Me$
c; $R^2 = OCH_2OCH_3, R^3 = H$



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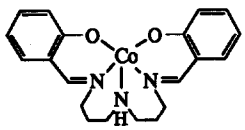
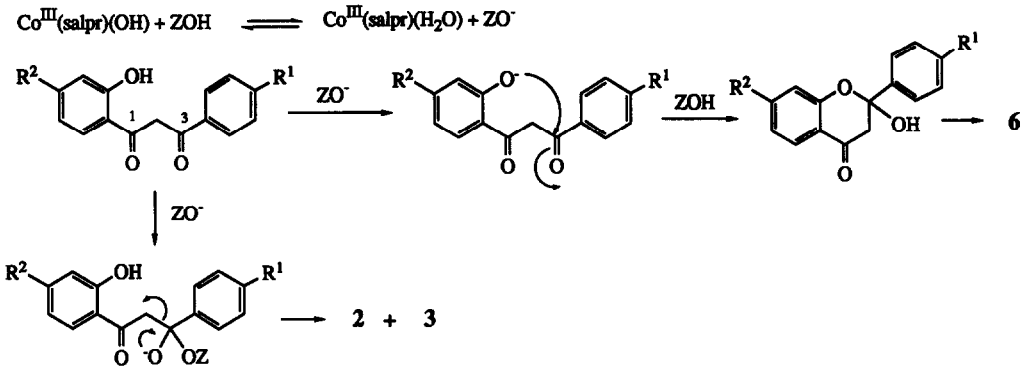


Co(salpr)

Table 1. The Co(salpr) Promoted Reaction of 1 in Alcohol under oxygen[a]

1	ZOH	Reaction time(h)	Conversion (%)	Product yield[b] 2	3	4	5	6	7	Other
1a	MeOH	2.5	100	20	23	6	4	42	5 (**7a**)	
1b	MeOH	5.5	100	15	28	8	8	37	4 (**7a**)	
1c	MeOH	3	100	19	20	6	6	44	5 (**7a**)	
1d	MeOH	2	100	26	35	7	6	24	4 (**7a**)	
1e	MeOH[c]	31	100	37	41	3	6	10	3 (**7a**)	
1f	MeOH	6.5	100	27	36	5	3	23	6 (**7c**)	
1a	EtOH	9	100	10	15(**3f**)	4(**4c**)	-[g]	38	6 (**7b**)	21[d]
1a	i-PrOH	4	100	-[g]	7(**3g**)	2(**4d**)	-[g]	18	-	24[d]
1a	EtOH[e]	120	67	11	16(**3f**)	3(**4c**)	-[g]	49	4 (**7b**)	17 (**8**)
1a	EtOH[f]	72	91	-	-	-	-	14	6 (**7b**)	80 (**8**)
1a	i-PrOH[f]	25	57	-	-	-	-	100	-	

[a] Reaction conditions: **1** (2 mmol), Co(salpr) (2 mmol), MeOH (50 ml) under 1 atm of oxygen at 60 °C. [b] Determined by ^{1}HNMR. [c] A mixture of MeOH (30ml) and CH_2ClCH_2Cl (30 ml) is used in order to dissolve **1e**. [d] Isolation yield. Co^{III}(salpr)(**1a**$^-$). [e] CH_2ClCH_2Cl (15 ml) containing EtOH (0.8 mol). [f] CH_2ClCH_2Cl (25 ml) containing ZOH (0.4 mol). [g] Not determined.

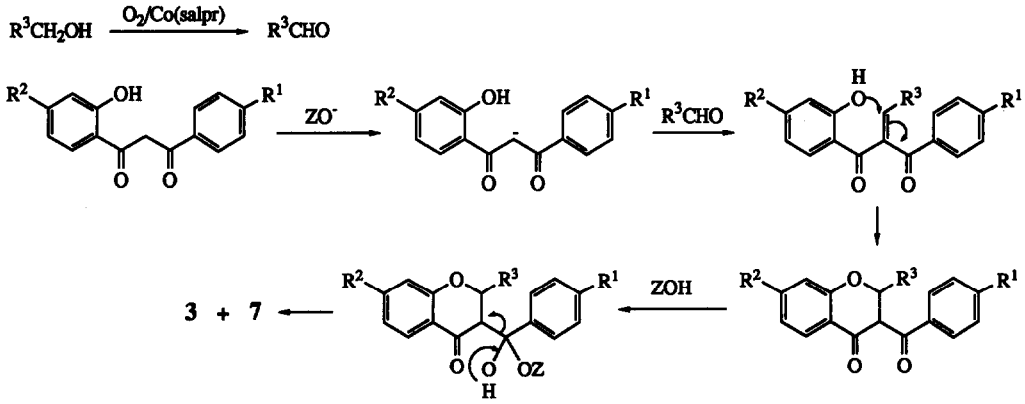


Scheme 1

the solvent used (Table 1), compounds **2** - **5** are the retro-Claisen reaction products of **1**. Flavones **6** result naturally from the intramolecular addition of phenoxide anion to the 3-carbonyl group in **1** followed by dehydration. These results suggest that Co^{III}(salpr)(OH) formed in the first place produces an alkoxide anion from the alcohol solvent by an acid-base reaction (Scheme 1). Actually, when Co^{III}(salpr)(OH)[11] was employed in methanol under nitrogen, the reactions of **1a** and **1f** were completed in 1.5 h and 4 h, respectively, giving rise to nearly the same product distributions as those shown in Table 1. The results indicate that in methanol the Co^{III}(salpr)(OH)/N_2 system is more effective than the Co^{II}(salpr)/O_2 system. On the other hand, when a solution of **1a** in methanol containing sodium methoxide was refluxed, the reaction was completed in 3 h to give similar product distribution, but not compound **7a**. Therefore, the formation of **7** is characteristic of the reaction promoted by Co^{III}(salpr)(OH). The higher yield of **2** and **3** compared to **4** and **5** is due to predominant attack by the alkoxide anion at the 3-carbonyl group. Thus, an electron-withdrawing group R^1 in **1** leads to increase in the yield of **2** and **3**. Interestingly, when 1,2-dichloroethane including a less amount of ethanol or 2-propanol was used as solvent, the reaction became slow and no esters were formed. Instead, compound **8**[12] was obtained in good yield with ethanol, whereas with 2-propanol flavone was the sole product. Compounds **7** should result from the condensation of **1** with the appropriate aldehyde: formaldehyde in methanol and acetaldehyde in ethanol, formed under the reaction conditions[4] (Scheme 2). In fact, heating an equimolar mixture of **1a**, Co^{III}(salpr)(OH), and formaldehyde in methanol gave **7a** (57%) and **3a** (61%).

Coordinately unsaturated Co^{III}(salen)(OH)[4] is catalytically inactive (no reaction within 50 h). However, upon the addition of twenty-fold concentration of pyridine to the solution of Co^{III}(salen)(OH), the reaction of **1a** was completed in 2 h to give the same products as those obtained in the reaction with Co^{III}(salpr)(OH). Furthermore, the use of Co^{III}(salpr)(OAc) in place of Co^{III}(salpr)(OH) slows down the reaction (55 h for completion with **1a**). The structurally dependent reactivity of the Co^{III} species indicates that

coordinately saturated structure of the hydroxocobalt(III) species enable to function as a good base is essential for the present reaction. Selection of the reaction conditions may develop a new convenient route to flavones and 3-acylchromanones, which is currently investigated.



Scheme 2

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12 Compound **7a** was synthesized according to the reported method:[14] ^{1}HNMR ($CDCl_3$), δ 2.77 (t, 2H, J = 6.4 Hz), 4.50 (t, 2H, J = 6.4 Hz), 6.8-8.0 (m, 4H). Compound **7c**: ^{1}HNMR($CDCl_3$), δ 2.77 (t, 2H, J = 6.2 Hz), 3.5 (s, 3H), 4.52 (t, 2H, J = 6.2 Hz), 5.2 (s, 2H), 6.5-7.9 (m, 3H). Compound **7b**: ^{1}HNMR ($CDCl_3$), δ 1.60 (d, 3H, J = 6.8 Hz), 2.74 (d, 2H, J = 6.8 Hz), 4.67 (sxt, 1H, J = 6.8 Hz), 6.9-8.2 (m, 4H). ^{13}CNMR($CDCl_3$), δ 20.92 (CH_3), 44.64 (3-C), 74.26 (2-C), 117.88 (8-C), 120.86 (4a-C), 121.16 (6-C), 126.94 (5-C), 135.88 (7-C), 161.69 (8a-C), 192.25 (4-C).
Compound **8**: mp, 77.0-78.5 °C; $\nu_{C=O}$ (KBr), 1688, 1678 cm^{-1}; ^{1}HNMR($CDCl_3$), δ 1.48 (d, 3H, J = 6 Hz), 4.64 (d, 1H, J = 12 Hz), 6.7-8.1 (m, 9H); ^{13}CNMR($CDCl_3$), δ 19.79 (CH_3), 59.81 (3-C), 76.24 (2-C), 117.90, 121.46, 127.22, 128.63, 128.73, 128.78, 136.40, 136.68, 137.74, 161.22, 189.98 (C=O), 196.57 (C=O). Anal. Calcd for $C_{17}H_{14}O_3$: C, 76.69; H, 5.26. Found: C, 76.34; H, 5.36.
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(Received in Japan 21 February 1990)