

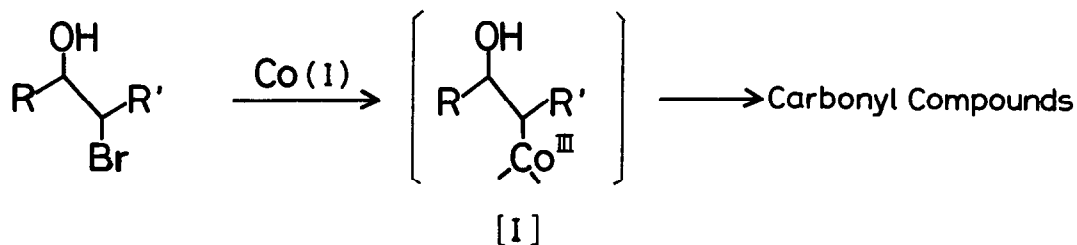
REACTION OF BROMOHYDRINS WITH CHLOROTRIS(TRIPHENYLPHOSPHINE)COBALT(I)

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Summary : Bromohydrins were converted into ketones in high yields by the reaction with chlorotris(triphenylphosphine)cobalt(I) in the presence of amine or olefin. A probable path-way for the formation of ketones from bromohydrins was also described.

Recently the conversion of bromohydrins to ketones catalyzed by $\text{Pd}(\text{OAc})_2$ was reported by Tsuji et al.¹ During the course of our investigation^{2,3} on the reaction of organic halides with a mono-valent cobalt compound $\text{CoCl}(\text{Ph}_3\text{P})_3$, we have found that bromohydrins are effectively converted into ketones by the reaction using the reagent. The present paper describes the reaction of the bromohydrins (1) and (5) with $\text{CoCl}(\text{Ph}_3\text{P})_3$ in the presence of amine or olefin giving the ketones (2) and (6), respectively, in high yields.

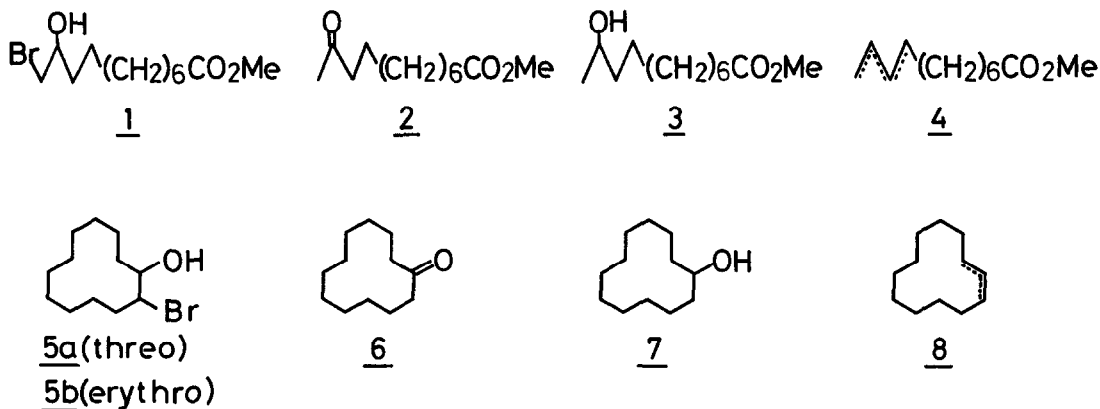


The present reaction is noted in view of the following biomimetic sense: the reaction might proceed through a β -hydroxyalkylcobalt intermediate [I], analogous to the intermediate encountered in the biological transformation of 1,2-diols into carbonyl compounds catalyzed by diol dehydrase and vitamin B₁₂.⁴

The reactions of the bromohydrins (1), (5a) and (5b) with $\text{CoCl}(\text{Ph}_3\text{P})_3$ in a dry solvent under an argon atmosphere employing different procedures were

carried out and the results are summarized in the Table.

Treatment of 1 with $\text{CoCl}(\text{Ph}_3\text{P})_3$ (1.3 equiv.) at room temperature for 6 h gave the ketone (2) (44% yield) accompanied with an alcohol (3) (42% yield) and an olefin (4) (10% yield). Similar reaction of both cyclododecene bromohydrins (5a) (threo) and (5b) (erythro) afforded 6, 7 and 8 in every case with nearly the same distribution as in 1.



A considerable increase of the formation of the ketones was shown in contrast to a decrease in the yield of the alcohols upon treating bromohydrins with $\text{CoCl}(\text{Ph}_3\text{P})_3$ in the presence of base or olefin. For example, the reaction of 5a with $\text{CoCl}(\text{Ph}_3\text{P})_3$ in the presence of triethylamine gave the ketone (6) (66% yield), the alcohol (7) (19% yield) and the olefin (8) (11% yield) (Entry 6). Use of cyclohexene as an additive⁵ resulted in the formation of 6 in a similar yield (Entry 8). Further improvement on the formation of the ketones was made when the solution of the reagent was added very slowly (over a period of 6-48 h) into a solution of the bromohydrin and triethylamine or cyclohexene. Applying this procedure⁶, exclusive conversion of 5a into 6 was effected as shown in Entry 7.

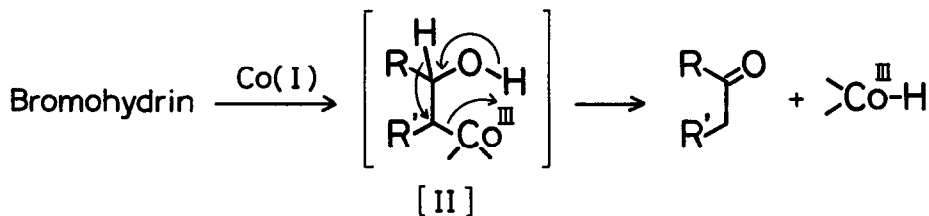
In contrast to the above-mentioned examples, the reaction of 3 β -acetoxy-5 α -bromocholestan-6 β -ol, whose hydroxyl group and bromine atom are fixed in a trans diaxial form, did not afford any ketone.⁷ It suggests that both bromine and hydroxyl group are necessary to locate in close proximity for the formation of ketones from bromohydrins. A plausible reaction pathway for the formation

Table. Product yields in the reaction of bromohydrins with $\text{CoCl}(\text{Ph}_3\text{P})_3$

Entry	Bromohydrin	Additive	Product yield (%) ^a		
			Ketone	Alcohol	Olefin
1	<u>1</u>	—	<u>2</u> (44)	<u>3</u> (42)	<u>4</u> ^b (10)
2	<u>5a</u>	—	<u>6</u> (40)	<u>7</u> (42)	<u>8</u> (10)
3	<u>5b</u>	—	<u>6</u> (40)	<u>7</u> (39)	<u>8</u> (10)
4	<u>1</u>	Et_3N	<u>2</u> (51)	<u>3</u> (35)	<u>4</u> ^b (7)
5 ^c	<u>1</u>	Et_3N	<u>2</u> (85)	<u>3</u> (9)	—
6	<u>5a</u>	Et_3N	<u>6</u> (66)	<u>7</u> (19)	<u>8</u> (11)
7 ^c	<u>5a</u>	Et_3N	<u>6</u> (90)	—	—
8	<u>5a</u>	Cyclohexene	<u>6</u> (64)	<u>7</u> (26)	<u>8</u> (5)
9 ^c	<u>5a</u>	Cyclohexene	<u>6</u> (82)	<u>7</u> (5)	—

a. Isolated yield. b. A mixture of methyl 8-undecenoate, methyl 9-undecenoate and methyl 10-undecenoate in a ratio of 5:3:2. c. Reaction performed by slow addition of $\text{CoCl}(\text{Ph}_3\text{P})_3$ in benzene into a mixture of the bromohydrin and the additive.

of ketones is illustrated in the Scheme. The β -hydroxyalkylcobalt intermediate [II] is initially formed by oxidative addition of the mono-valent cobalt to the carbon-halogen bond of the bromohydrin. Cleavage of the cobalt-carbon bond of [II] followed by 1,2-hydrogen shift through a cyclic transition state gives the ketone. The 1,2-hydrogen shift was proved by the experiment using the deuterated bromohydrin; the reaction of 1-D-2-bromocyclododecanol⁸ with $\text{CoCl}(\text{Ph}_3\text{P})_3$ in benzene afforded 2-D-cyclododecanone (75% D). The species of tri-valent cobalt hydride generated during the reaction undergoes a disproportion-



Scheme

tionation with the mono-valent cobalt yielding the di-valent cobalt hydride, which may cause the reduction of the bromohydrin to the alcohol. This reduction was prevented by addition of amine or olefin which can trap the acidic cobalt hydride species⁹, giving rise to the exclusive formation of the ketone. It is of interest that similar 1,2-hydrogen shift in a β -hydroxyalkylcobalt intermediate is also known in the biological transformation of diols into carbonyl compounds.⁴

The present reaction provides a useful synthetic method for the formation of ketones from bromohydrins.

References and Notes

1. J.Tsuji, H.Nagashima and K.Sato, *Tetrahedron Lett.*, 23, 3085 (1982).
2. Y.Yamada and D.Momose, *Chemistry Lett.*, 1277 (1981).
3. D.Momose, K.Iguchi, T.Sugiyama and Y.Yamada, *Tetrahedron Lett.*, 24, 921 (1983).
4. G.N.Schrauzer and J.W.Sibert, *J.Am.Chem.Soc.*, 92, 1022 (1970).
5. N,N-Diisopropylethylamine, pyridine, imidazole and 1-octene can also be used.
6. A typical experimental procedure : to a stirred solution of 184 mg of 5a (0.70 mmol) and 0.6 ml of triethylamine (4.30 mmol) in 14 ml of degassed benzene was added dropwise a solution of 1.23 g of $\text{CoCl}(\text{Ph}_3\text{P})_3$ (1.40 mmol) in 50 ml of benzene over a period of 6 h at 50 C under Ar and the mixture was stirred for 1 h. The reaction mixture was filtered and the filtrate was treated with methyl iodide.¹⁰ Precipitates were filtered off and the filtrate was concentrated under reduced pressure. Flash chromatography of the residue afforded 115 mg of cyclododecanone as colorless crystals.
7. Cholesteryl acetate, 3β -acetoxycholestan- 6β -ol and 3β -acetoxycholest-4-en- 6β -ol were obtained as the reaction products.
8. Satisfactory elemental analyses were obtained for all new compounds.
9. J.P.Collman and L.S.Hegedus, "Principles and Applications of Organotransition Metal Chemistry", University Science Books, Mill Valley California, p 67 (1980).
10. To remove triphenylphosphine liberated during the reaction as methyltriphenylphosphonium iodide.

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