Journal of Organometallic Chemistry, 101 (1975) C14—C16

Preliminary communication

THE HYDROLYSIS OF β-ACETAL COBALOXIMES

RICHARD B. SILVERMAN*

Department of Chemistry, Harvard University, Cambridge, Massachusetts 02138 (U.S.A.)

and D. DOLPHIN**

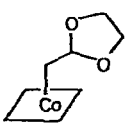
Department of Chemistry, The University of British Columbia, Vancouver V6T 1W5, B.C. (Canada)

(Received July 14th, 1975)

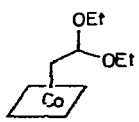
Summary

Cobaloxime acetals are hydrolyzed by two different routes, direct cobalt—carbon bond fission, and decomposition to the aldehyde followed by cobalt—carbon bond fission.

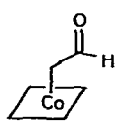
1,3-Dioxa-2-cyclopentylmethyl- and 2,2-diethoxyethyl-cobalamins (I and II) were shown [1] to decompose by two routes: hydrolysis of the acetal to fomylmethylcobalamin (III) followed by cobalt—carbon bond cleavage, and by direct cobalt—carbon bond fission.



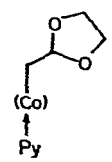
(I)



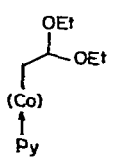
(II)



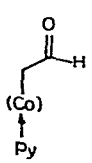
(III)



(IV)



(V)



(VI)

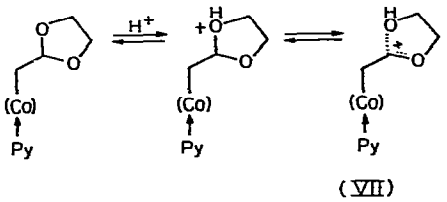
*NIH predoctoral trainee 1971-1974. Present address: Graduate Department of Biochemistry, Brandeis University, Waltham, Mass. 02154.

**Author to whom correspondence should be addressed.

The cobaloximes are widely used as models for the more complex cobalamins [2] and we wished to determine whether the corresponding cobaloxime acetals underwent analogous decompositions.

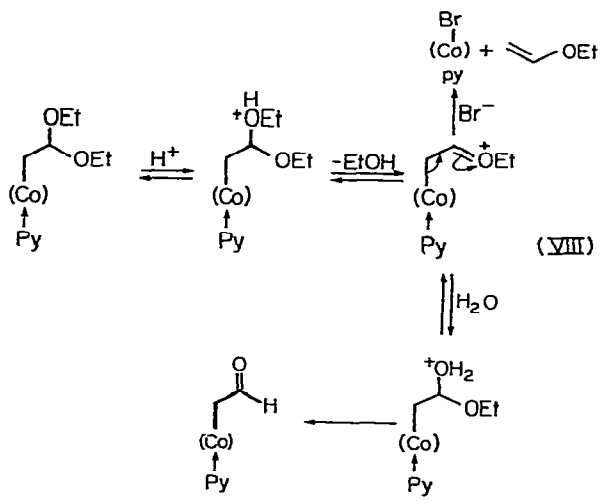
1,3-Dioxa-2-cyclopentylmethyl(pyridine)cobaloxime (IV) (62 mmol) remained unchanged after five days at room temperature in methylene dichloride containing triethylammonium hydrobromide (62 mmol) and triethylamine (31 mmol). However, under the same conditions, 2,2-diethoxyethyl-(pyridine)cobaloxime (V) decomposed to give a mixture of the starting material V (27%) formylmethylcobaloxime (VI) (18%) and unalkylated cobaloxime (55%)*. A control reaction, which contained no triethylammonium hydrobromide, produced no unalkylated cobaloxime and only 5% of the aldehyde. When formylmethyl(pyridine)cobaloxime (VI) was subjected to the same conditions only 9% underwent cobalt—carbon cleavage. Thus it can be concluded that nearly all of the 55% cobalt—carbon cleavage product from the diethyl acetal V occurred by direct cleavage, (this is supported by the identification (GLC) of ethyl vinyl ether from the reaction) with little of the product arising via decomposition of the aldehyde VI.

The stability of the cyclic acetal IV relative to the diethylacetal V under these mildly basic protic conditions may derive from the proximity of the



(VII)

SCHEME 1



SCHEME 2

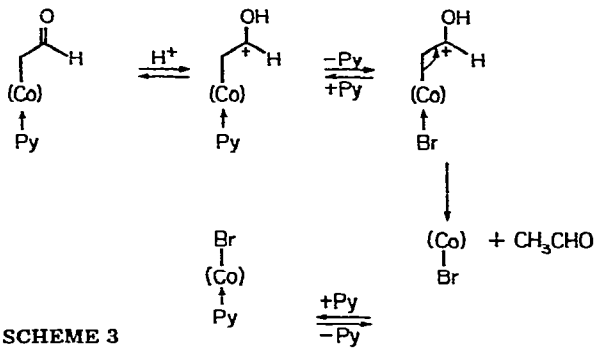
eliminated alcohol to the incipient carbonium ion center, forming a stabilized intermediate VII (Scheme 1). In the case of the diethyl acetal, however, once the alcohol is eliminated there is little probability for the reversal of this process. This then allows the common intermediate, carbonium ion VIII, to either undergo direct elimination of the organic ligand or to react with water to give the hemiacetal which then collapses to the aldehyde (Scheme 2).

---

*The percentages of products and starting material were estimated from relative NMR peak areas of dimethylglyoximato methyl protons. These absorbances occur at 2.10, 2.18, and 2.37 ppm (in CH_2Cl_2) for the acetal, the aldehyde, and the unalkylated material, respectively.

In 0.1 *M* aqueous methanolic acetic, sulfuric and hydrobromic acids the acetal V was immediately converted to the aldehyde VI. On standing for twelve hours in the acetic or sulfuric acid mixtures less than 2% cobalt—carbon bond cleavage of the aldehyde occurred. However, in the hydrobromic acid solution greater than 90% of cobalt—carbon bond fission occurred within 6 hours, suggesting that this process was assisted by the anion*.

Dissociation of the acidic bases of both cobalamins and cobaloximes is known to be a facile process when the *trans* ligand is an alkyl group [3]. In addition, the anion-assisted elimination of an alkyl group, bonded to cobalt, is exemplified by the reaction of cyanide ion with both 5′-deoxyadenosylcobalamin [4] and 5′-deoxyadenosyl(pyridine)cobaloxime [5]. This suggests that the decomposition of the aldehyde VI in the presence of hydrobromic acid can be envisaged as in Scheme 3:



SCHEME 3

While the cyclic acetal cobaloxime IV is stable in the presence of triethylammonium bromide it is readily hydrolysed by 0.1 *M* acetic acid to the aldehyde VI. This suggests that further protonation of the β-hydroxyl group of the intermediate VII eliminates the stabilizing interaction so that the carbonium ion can react with water to give the hemiacetal and then the aldehyde.

Thus the cobaloxime acetals, like the cobalamin acetals [1], can be hydrolyzed by two distinct routes. Direct cobalt—carbon bond fission, and hydrolysis to the formylmethylcobaloxime followed by cobalt—carbon bond fission. These observations further confirm the value of cobaloximes as model compounds for the naturally-occurring cobalamins.

Acknowledgments

This work was supported by the National Institutes of Health (Grant AM14343) and the National Research Council of Canada.

References

1 R.B. Silverman and D. Dolphin, J. Amer. Chem. Soc., 97 (1975) 2924.
2 G.N. Schrauzer, Accounts Chem. Res., 1 (1968) 97.
3 D. Dodd and M.D. Johnson, J. Organometal. Chem., 52 (1973) 1.
4 A.W. Johnson and N. Shaw, J. Chem. Soc., (1962) 4608.
5 G.N. Schrauzer and J.W. Sibert, J. Amer. Chem. Soc., 92 (1970) 1022.

*A similar decomposition occurred in 0.1 *M* hydrochloric acid.