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ACYL MIGRATION IN 2-SUBSTITUTED-2-ACYLPROPYL RADICALS. THE REACTION OF ORGANOCOBALOXIMES AS MIMICRIES OF COENZYME-B_{12}

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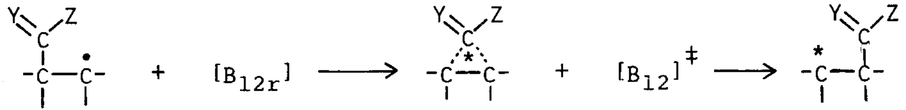
Radical cleavage of the carbon-cobalt bond of 2-acetyl-2-methoxycarbonylpropyl cobaloxime (1) and 2-benzoyl-2-phenylpropyl cobaloxime (5) gives the enones which are formed by the 1,2-migration of acyl-group.

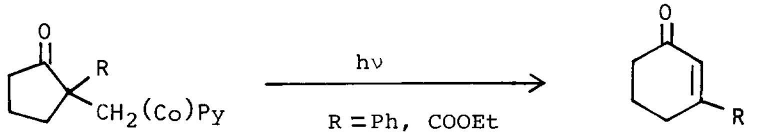
Methylmalonyl-CoA mutase, which promotes the 1,2-migration of the thioester group, requires coenzyme-B_{12}.1) Cation,2) radical,3) and anion4) mechanisms have been proposed for this kind of migration. Accumulating evidence shows that coenzyme-B_{12} splits into paramagnetic cobalamin [B_{12r}] and 5'-deoxyadenosyl radical which abstracts a hydrogen from a substrate to give the substrate radical.5) The initial formation of the radical does not mean radical nature of the migration since an electron transfer between the radical and [B_{12r}], which gives ion pair ($\star$ = + or -, ‡ = - or +), can be envisaged due to the electronic diversity of cobalamin6) (Eq. 1).



----(Eq. 1)

Organo-bisdimethylglyoximato(pyridine)cobalt(III), R-(Co)Py (organo-cobaloxime hereafter), is a good mimicry of organo-cobalamin1) and the photolysis of organocobaloxime cleaves the carbon-cobalt bond to generate organo-radical and paramagnetic cobaloxime7) which must be a good mimicry of a pair of substrate radical and paramagnetic cobalamin.

In the previous study8) we photolyzed 1-substituted-2-oxocyclopentylmethyl cobaloxime and observed acyl-migration in preference to alkyl, phenyl, and ethoxycarbonyl groups (Eq. 2). In these model systems, however, the driving force of the acyl-migration may arise from the ring enlargement. Here we report the radical rearrangement of 2-acylpropyl radicals, which are formed by the photolysis of the corresponding organo-cobaloximes.



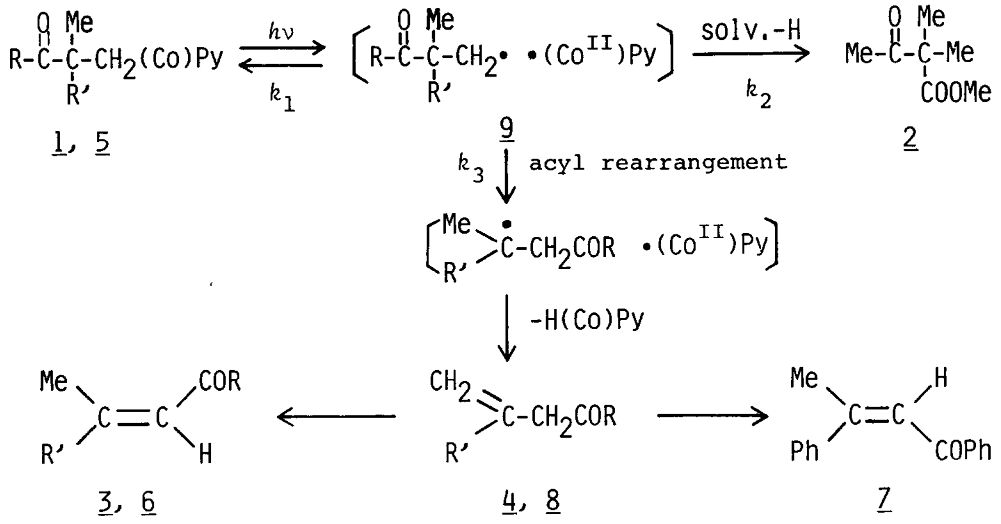
----(Eq. 2)

The photolysis of 2-acetyl-2-methoxycarbonylpropyl cobaloxime (1)9) gave methyl 2,2-dimethyl-3-oxobutanoate (2), methyl trans-2-methyl-4-oxo-2-pentenoate (3), and methyl 2-methylene-4-oxopentanoate (4). In the same procedure 2-benzoyl-2-phenylpropyl cobaloxime (5)9) gave (E)-1,3-diphenyl-2-buten-1-one (6), (z)-1,3-diphenyl-2-buten-1-one (7), and 1,3-diphenyl-3-buten-1-one (8). The results are summarized in the table. These results show that the acyl groups migrate in preference to alkyl, phenyl, and methoxycarbonyl groups. The formation of products 6, 7, and 8 from cobaloxime (5) is obviously faster than the formation of 2, 3, and 4 from cobaloxime (1) (see table). The formation of the rearranged products is competitive with the recombination of tha radical pair (9). The faster rate of the photolysis of 5 can be accounted for by the faster rearrangement of benzoyl group, since the recombination of the primary radical and cobaloxime radical ($(Co^{II})Py$), which is competitive with the rearrangement, must not be much different by the group R′ (COOMe or Ph). The photolysis of organo-cobaloxime (1) in chloroform is faster than in other solvents due to the existence of an additional quenching process, hydrogen abstraction, of the organo-radical to give the unrearranged product (2). Hydrogen abstraction of the organo-radical (9, R=Me, R′=COOMe) from solvent is competitive with the rearrangement, whereas the rearrangement is prefered in the organo-radical (9, R=R′=Ph) and no non-rearranged product was obtained. Thus the rate of photolysis and the product composition depend upon the relative value of rate constants k_1, k_2 (including the hydrogen donating ability of the solvents), and k_3.

A time-course analysis showed that main products were 4 and 8 at the early stage of the photolysis. This result indicates that the conjugated enones (3, 6, and 7) are, partly or wholly, formed by the isomerization of the primary products 4 and 8.

Radical nature of the acyl-migration mentioned above is further supported by the treatment of 2-benzoyl-2-phenylpropyl bromide (10, $2.5X10^{-2}$ mol/l) with tributyltin hydride. The reaction gave 2-benzoyl-2-phenylpropane (11) and 1,3-diphenyl-1-butanone (12); 11:12 = 15:85 (Bu_3SnH, 0.1 mol/l) and 56:44 (Bu_3SnH, 1.0 mol.l). The product composition depends on the concentration of tributyltin-hydride, and this result shows that the direct hydrogen capture of the intermediate radical (13) from tributyltin hydride is again competitive with the radical rearrangement of benzoyl group, which gives a saturated ketone (12) as the final product.

Our previous study has shown that both anion and cation mechanisms are not operative in the similar acyl migration (Eq. 2).8) The present experimental findings indicate that an acyl group rearranges to an adjacent radical center though the examples of acyl migration in radical mechanism are scarcely known.10)

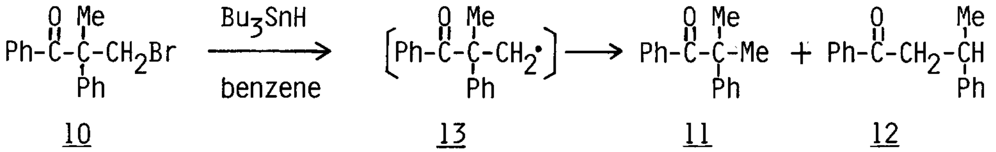


1, 3, 4: R=Me, R'=COOMe 5, 6, 8: R=R'=Ph

Table. The Photolysis of Organo-cobaloxime[a)]

Starting cobaloxime	Solvent	Irradiation time (hr)	Product (Yield, %)[b)] 2	3	4	Total yield (%)[c)]
1	$CHCl_3$	1	18	3	23	44
		3	28	4	29	61
1	CH_2Cl_2	3	2	2	15	19
		33	9	10	40	59
1	C_6H_6	3	-	4	10	14
		33	-	22	18	40
			6	7	8	
5	$CHCl_3$	1/3	14	1	18	33
		3	47	11	16	74
5	CH_3CN	1/3	11	2	17	30
		3	43	4	4	51
5	C_6H_6	1/3	9	1	8	18
		3	52	6	2	60

a) Organo-cobaloxime (1 or 5)(30 mg in 18 ml of solvent) was irradiated by a 40-w fluorescent lamp under anaerobic condition.
b) Based on the amount of the starting organo-cobaloxime.
c) Material balance was fairly kept by the residual starting cobaloxime.



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(6) Cobalamin exists in its Co(I), Co(II), Co(III) states and those are expressed by B_{12s}, B_{12r}, B_{12b}, respectively.

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(9) Organo-cobaloximes (1 and 5) were prepared from the corresponding bromides and cobaloxime(I), $[(Co^{I})Py]^{-}$ which was synthesized in methanol by reduction of cobaloxime(II), $(Co^{II})Py$, with $NaBH_4$ or Zn-powder. The cobaloximes (1 and 5) gave correct values in elemental analyses and spectral data.
1, mp 170-180°C(dec.); nmr($CDCl_3$)(δ)1.25(3H, s), 1.95(2H, s), 2.06(3H, s), 2.15(12H, s), 3.67(3H, s), 7.39(2H, t, J=8 Hz), 7.82(1H, t, J=8 Hz), and 8.62(2H, d, J=8 Hz); ir($CHCl_3$), 1733, 1702, 1560, 1450, 1200-1300(br), and 1085 cm^{-1}.
5, mp 140-145°C(dec.); nmr($CDCl_3$)(δ), 1.57(3H, s), 1.81(6H, s), 1.98(6H, s), 2.30(1H, d, J=10 Hz), 2.62(1H, d, J=10 Hz), 6.90-7.33(12H, m), 7.63(1H, t, J=8 Hz), and 8.48(2H, d, J=8 Hz);ir($CHCl_3$), 1675, 1560, 1453, 1200-1300(br.), and 1085 cm^{-1}.

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